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WEAVE SPRINT · PAPER II

Clinical Psychiatry

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WRITTEN BY

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First compiled 2026. Free to read, share and print for study.

The clinical content is written for doctors and doctors in training. It is a study and revision aid, not a substitute for current guidelines or clinical judgement. Verify doses and thresholds against the current references and your local protocols before any clinical use.

For every resident who has ever sat up the night before,
afraid it will not be enough.

ACKNOWLEDGEMENT

A word of thanks

I want to begin by thanking something I cannot quite name. Call it whatever you like. I have never been certain what to call it, and I have stopped needing to be. There is a part of this work that does not feel like mine. The line that arrives before I have thought of it, the connection I did not plan, the steadiness on a morning I had no reason to be steady. I only hold the pen. Something moves through the holding, and I have learned to thank it without asking it for a name.

Someone once asked me why I give all of this away. Why hand out the notes I sat up making, to the very people sitting the same exam beside me. It is a fair question. If I had kept them, I would probably have scored a few marks more than the next person, and I might have been thought of as the better student. I have turned that over honestly, and I have decided it is a small thing to want. What I get instead, by putting the work in your hands, is the chance to take a little of the fear out of a great many nights. That trade is not close. Easing that fear is not a detour on the way to becoming a good psychiatrist. It is the thing itself. I did not come here to be the best student in the room. I came here to be a good psychiatrist.

And to Niharika, who reads everything first and knows when to be honest and when to wait; and to the residents who study from these pages and write back with the corrections and the questions: thank you. The book is better for you, and so am I.

Dr. Wilfred D'souza

Foreword

This is the second paper of the written examination, gathered into one book. Where the first paper laid the ground the discipline stands on, this one is the discipline at work: the disorders themselves, from the psychoses and the mood disorders through substance use, anxiety and trauma to the disorders of personality, eating, sleep and the body, and the psychotherapies and the assessment that hold the clinical work together. This is the paper the ward and the clinic are made of.

The notes were written to be understood, not just revised. Each chapter is a full account of its subject, from the mechanism up to the point the exam tests, so that you can read to learn the first time and read to recall every time after. Where a fact is worth holding exactly, it is marked. Where a mistake is easy to make, it is named before you make it. The colour code on the next pages tells your eye what kind of fact it is looking at before your mind has to decide, and after a few pages it stops being a key you consult and becomes a sense you carry.

Read it in order if you are meeting the material, or open it anywhere if you are returning to it. The contents at the front and the index at the back both jump to the page you want. However you use it, the hope held in these pages is plain: that one ordered, trustworthy place to study from makes the work a little lighter, and that you walk into the hall steadier than you would have otherwise.

HOW TO USE THIS BOOK

The colour memory code

Every note in this volume speaks one visual language, so once you learn it in the first chapter you read the rest without thinking about it.

Concept and rule	The core idea and the principle that follows from it. When a line is petrol, it is the thing to understand, and the thing worth being able to state.
Key number	A figure to hold exactly: a dose, a threshold, a prevalence, a cut-off. Amber means memorise this number, not just the shape of it.
Trap	The mistake the exam is waiting for. When a line is coral, it is warning you off an error that looks right until it costs you the mark.

Hold this is the single line from a topic you must carry out of it. **Good to remember** gathers, for each named thing, what it is, when it matters, and the one number or formula worth keeping. Both help a tired brain find the centre of a dense page fast.

The contents at the front is clickable, and so is the index at the back: every entry jumps to its page. Read to learn once, and to recall as often as you need.

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PART I

Schizophrenia: Aetiology, Phenomenology, Classification and Course

What schizophrenia is, where it comes from, how it shows itself, and how it is classified and followed over time.

01 Aetiology and neurobiology

02 Clinical features and phenomenology

03 Classification, subtypes and nosological change

04 Course, prognosis and outcome

05 Apply and consolidate

PAPER II

Schizophrenia: aetiology, phenomenology, classification and course

Five sections · 23 topics · one complete notes document

This material gathers the first clinical chapter into one document, the illness that anchors the whole of psychotic disorders. The first band is **aetiology and neurobiology**: the epidemiology that sets the lifetime risk near one percent, the genetics with its high heritability, the dopamine hypothesis in its original, revised and aberrant-salience forms, the glutamate and other-transmitter models, the neurodevelopmental two-hit model with its environmental hits, and the structural neuroimaging and neuropathology. The second band is **clinical features and phenomenology**: the five symptom domains as the organising map, the positive symptoms and disorganisation, the negative symptoms and their deficit form, the cognitive impairment that carries the functional weight, the first-rank symptoms of Schneider and the fundamental symptoms of Bleuler read with their modern caveats, and the prodrome and first episode. The third band is **classification, subtypes and nosological change**: the current criteria of ICD-11 and DSM-5-TR set against the legacy ICD-10, the reason both systems dropped the historical subtypes, and the differential that separates schizophrenia from the disorders it resembles. The fourth band is **course, prognosis and outcome**: the phases and natural history, the good and poor prognostic factors, and the outcome including the mortality gap. The examinable skill is judgement across all four: to reason from mechanism to phenomenon, to apply the criteria, to tell schizophrenia from its mimics, and to weigh the outcome.

HOW TO USE THESE NOTES

Read the four bands as one argument that runs from cause to consequence. The **aetiology** band builds the mechanistic picture, each hypothesis ending with a **Good to remember** box giving what it claims, the evidence for it, and the one number or discriminator to hold. The **phenomenology** band maps the signs onto the five domains; the descriptive definitions of delusions, hallucinations, thought disorder and the first-rank symptoms are owned by the Psychometry, Assessment and Descriptive Psychopathology notes, so here they are applied to schizophrenia rather than redefined. The **classification** band runs ICD-11 forward, cross-maps DSM-5-TR, and keeps a legacy ICD-10 box showing what changed, and its payoff is the **differential**, the decision tree that separates schizophrenia from mood disorder with psychotic features, schizoaffective disorder, delusional disorder, the brief and schizophreniform pictures, and organic or substance-induced psychosis. The **course** band closes on prognosis and outcome. Figures declare one axis and code it in colour: **petrol** marks structure and the neutral case, **coral** marks the trap or the point of discrimination, and **marigold** highlights the number to hold. Four boundaries are worth stating up front: the dopamine and monoamine pathways and the imaging principles are developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the twin, family and adoption methods belong to the Psychiatric Genetics notes; antipsychotics, adverse effects and rehabilitation are taught in the Schizophrenia: management, antipsychotics and adverse effects notes; and the other psychotic disorders and catatonia as entities live in the Other psychotic disorders, delusional syndromes and catatonia notes. This is doctor-facing revision, so the full technical vocabulary is used.

Aetiology and neurobiology

1 · Orientation: what schizophrenia is and the criteria map

Schizophrenia is the anchor disorder of psychiatry and the most heavily examined single condition in the clinical papers, so every later topic in these notes reads back to the orientation set here. It is a **chronic psychotic disorder** of the young adult: onset clusters in late adolescence and early adulthood, the illness is multifactorial rather than the product of one lesion, its best-supported mechanism is dopaminergic but no single dopamine abnormality explains it, and it is defined by a **syndrome** recognised at the bedside rather than by any laboratory test (Kaplan & Sadock 2024). The examiner is never testing whether you can recite a definition in the abstract; they are testing whether you can place a psychotic presentation on the diagnostic criteria map and defend the placement against the mimics.

How to use this page. Fix three things before anything else. First, the illness at a glance, so the shape of the disorder is in your head before the detail arrives. Second, the **criteria map**, the diagnostic decision tree that every subsequent topic hangs from, run ICD-11 forward and cross-mapped to DSM-5-TR with ICD-10 flagged as legacy. Third, the master mnemonic that chains the four bands of the whole chapter, cause then phenomenon then criteria then course, so that one cue unpacks the entire note. The descriptive definitions of the individual signs, what a delusion, a hallucination, a first-rank symptom or formal thought disorder *is* as a phenomenon,

are not re-derived here; they belong to the Psychometry, Assessment and Descriptive Psychopathology notes, and this chapter applies them to schizophrenia.

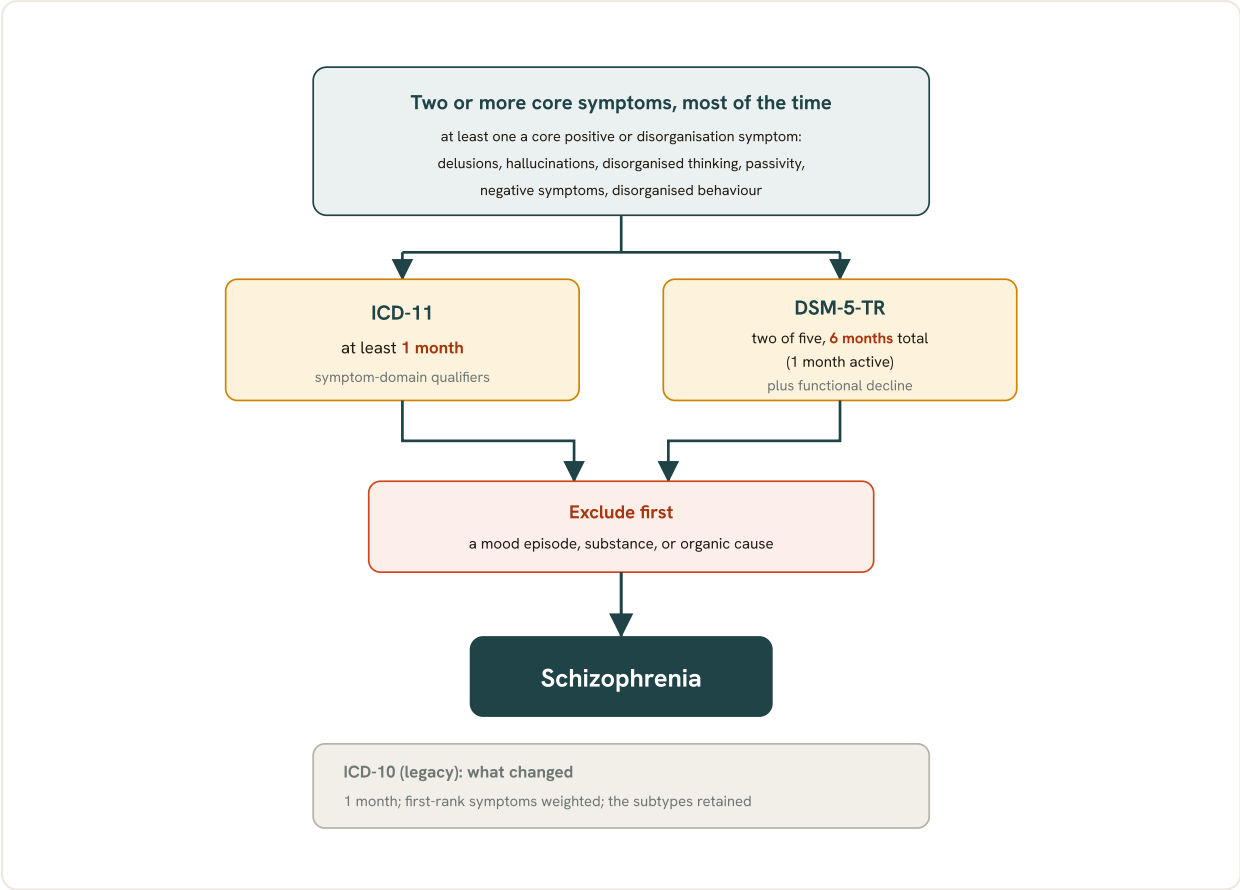


Fig 8.1 The diagnostic criteria as a decision map. Two or more core symptoms, at least one from the positive or disorganisation cluster, must persist for the required duration, ICD-11 asking one month and DSM-5-TR a six-month total with functional decline, and a mood, substance or organic cause must be excluded before the diagnosis is made. The legacy ICD-10 box records what the current systems changed.

1.1 The illness at a glance: one orientation before the detail

What kind of disorder this is. Schizophrenia is a severe, typically persistent disorder in which psychosis, a loss of contact with reality expressed as delusions, hallucinations and disorganisation, is coupled to a decline in functioning and, in most patients, an enduring deficit that outlasts the acute episodes. It presents in the second and third decades: the psychotic features usually emerge between the late teens and the mid-30s, with a peak in the early-to-mid 20s in men and the late 20s in women, and onset before adolescence is rare (Kaplan & Sadock 2024). The lifetime risk sits near **~1%** as the classic teaching figure, with rigorous population surveys giving a somewhat lower lifetime prevalence of about **0.3 to 0.7%** (DSM-5-TR 2022); the disorder is strongly familial, with a twin-study heritability of the order of **~80%** (Sullivan et al. 2003). The detailed epidemiology, the sex difference, the Indian figures and the WHO cross-cultural outcome finding are developed in the epidemiology topic and the genetic evidence in the genetics topic; twin, family and adoption study methods themselves belong to the Psychiatric Genetics notes.

~1%	~80%	late teens to mid-30s
LIFETIME RISK (CLASSIC FIGURE)	HERITABILITY (TWIN STUDIES)	TYPICAL ONSET WINDOW

The five-domain picture. The clinical phenomenon is not one thing but a spread across five symptom domains, and holding the domains from the start makes both the phenomenology band and the criteria map legible. A positive symptom is an addition to normal experience: delusions and hallucinations. A negative symptom is a subtraction from it: blunted affect, alogia, avolition, asociality and anhedonia. The cognitive domain is the impairment of attention, working memory, processing speed and executive function that carries much of the functional disability. The disorganisation domain is formal thought disorder and disorganised or bizarre behaviour. The affective domain is the mood disturbance, depression, dysphoria and, importantly, suicide risk, that runs through the course. These five recur as the spine of the whole chapter.

RULE **A syndrome, not a test.** Schizophrenia is diagnosed by recognising a constellation of signs and symptoms with functional decline over a required duration; there is no radiological, laboratory or psychometric test that confirms it, and no single symptom is pathognomonic.

TRAP **Diagnosing schizophrenia inside an untreated mood episode.** If delusions or hallucinations occur only during a depressive or manic episode, the diagnosis is a mood disorder with psychotic features, not schizophrenia; schizophrenia requires psychosis in the absence of a concurrent mood episode.

1.2 The criteria-map schema: the whole diagnosis on one decision tree

Why the criteria are the organising schema. Every clinical judgement in this chapter is a move on a single **criteria map**: does this presentation meet the symptom threshold, does it meet the duration threshold, and have the exclusions (mood, substance, medical) been cleared. Learn the map as a decision tree and the phenomenology, the classification and the differential all become branches of it rather than separate lists. The current **diagnostic criteria** come from two live systems that agree on the core and differ mainly on duration, with a third, ICD-10, now legacy.

ICD-11, run forward. Under ICD-11 (6A20), at least two of seven symptom groups must be present most of the time for a period of one month or more, and at least one of the two must be a core symptom, one of persistent delusions, persistent hallucinations, disorganised thinking (formal thought disorder), or experiences of influence, passivity or control (WHO ICD-11 CDDR 2024). The remaining three groups, negative symptoms, grossly disorganised behaviour and psychomotor (catatonic) disturbance, can supply the second symptom but cannot stand alone. The exclusion is that the picture is not due to another medical condition, a substance or a medication. Note the two features an examiner rewards: the qualifying-symptom rule (at least one core positive or disorganisation symptom) and the one-month duration.

DSM-5-TR, cross-mapped. Under DSM-5-TR (2022), Criterion A requires two of five symptoms, each present for a significant portion of a one-month period, and at least one must be delusions, hallucinations or disorganised speech; the other two options are grossly disorganised or catatonic behaviour and negative symptoms. The decisive difference is duration: DSM-5-TR adds Criterion B (functional decline) and Criterion C, a total illness duration of **at least 6 months** that must include that one month of active-phase symptoms, plus the mood (Criterion D), substance and medical (Criterion E) exclusions. So the two systems share the same symptom

core and the same one-month active-phase requirement; ICD-11 stops at one month, DSM-5-TR demands six months of total disturbance.

FEATURE	ICD-11 (6A20), CURRENT, PRIMARY	DSM-5-TR, CURRENT, CROSS-MAPPED
Symptoms required	At least two of seven groups, most of the time	**Criterion A: two of five symptoms**
Qualifying (core) symptom	At least one from delusions, hallucinations, disorganised thinking, or influence/passivity/control	**At least one from delusions, hallucinations, disorganised speech**
Active-phase duration	One month or more	**One month of Criterion A symptoms**
Total duration	Not separately required (one month suffices)	**At least 6 months of continuous signs (Criterion C)**
Functional decline	Impairment implied, not a separate criterion	**Criterion B, a required threshold**
Exclusions	Not substance/medication/medical condition	**Mood (D), substance and medical (E) ruled out**

The criteria map, ICD-11 run forward and DSM-5-TR cross-mapped; the single high-yield contrast is the duration threshold, one month versus six months, highlighted in the right column.

COMMON TRAP

Do not confuse the two duration figures. The one-month figure is the active-phase (florid) symptom requirement that both systems share; the six-month figure is DSM-5-TR's *total* illness duration including prodrome and residual. A florid picture of five weeks meets ICD-11 but a DSM-5-TR diagnosis at that point would be schizophreniform disorder, which converts to schizophrenia once the total disturbance reaches six months.

1.3 ICD-10 as legacy: what changed on the way to ICD-11

Why the older system still turns up. Many Indian examinations and case records still run on ICD-10, so it is flagged here as legacy rather than dropped. ICD-10 (F20) diagnosed schizophrenia on a list built around Schneiderian first-rank symptoms: one very clear first-rank or bizarre-delusion symptom, or two or more of a second group (other persistent hallucinations, thought disorder, catatonia, negative symptoms), present for most of the time during at least one month. ICD-11 made three examinable changes. It removed the privileged status of first-rank symptoms, so that thought insertion or a running commentary no longer carries diagnostic weight above other core positive symptoms. It replaced the historical subtypes (paranoid, hebephrenic, catatonic and the rest) with a dimensional set of symptom specifiers, on the grounds that the subtypes had poor reliability and predictive validity; that nosological change is developed in the classification band. The core one-month duration was retained. Where an exam paper is explicitly ICD-10, answer on ICD-10; where it is unmarked, lead with ICD-11 and note the DSM-5-TR six-month contrast.

TRAP **Calling first-rank symptoms pathognomonic.** First-rank symptoms are suggestive but not specific and not diagnostic; DSM-5 and ICD-11 both stripped them of special status, and they occur in mania and organic psychoses too. Their descriptive definitions are cross-referenced to the Psychometry, Assessment and Descriptive Psychopathology notes.

1.4 The master mnemonic: chaining the four bands of the chapter

The whole chapter on a single hook. This chapter runs in four bands, and one mnemonic chains them so that a single cue unpacks the entire note: *cause* (aetiology and neurobiology), *phenomenon* (clinical features and phenomenology), *criteria* (classification and the nosological change), and *course* (course, prognosis and outcome). Fix the four Cs in that order and every later topic slots onto its band; the criteria map you have just learned is the hinge in the middle, the schema the cause bands build toward and the course bands read forward from.

MNEMONIC

"CAUSE, PHENOMENON, CRITERIA, COURSE": the four bands, in reading order. Under phenomenon, the five domains are "P-N-C-D-A": Positive, Negative, Cognitive, Disorganisation, Affective.

Unpack it band by band. **Cause** is the aetiology climb: the dopamine and glutamate hypotheses, the neurodevelopmental and two-hit models, genetics and the imaging findings, no single lesion but a convergence. **Phenomenon** is the five-domain picture, held on **P-N-C-D-A**: a **P**ositive symptom (delusion, hallucination), a **N**egative symptom (the deficit), the **C**ognitive impairment, the **D**isorganisation (thought disorder, disorganised behaviour) and the **A**ffective disturbance. **Criteria** is the map itself, ICD-11 forward, DSM-5-TR cross-mapped, ICD-10 legacy, and the dropping of the subtypes. **Course** is the natural history: premorbid, prodrome, acute and residual phases, the good-versus-poor prognostic factors, and the outcome, suicide and the mortality gap. One seed, four bands, the whole chapter.

WORKED EXAMPLE

A 22-year-old man is brought in after six weeks of persecutory delusions and a running commentary of voices, with two months of prior social withdrawal and self-neglect. Walk the criteria map. Symptoms: two are present and one (delusions) is a core positive symptom, so the symptom threshold is met. Duration: the florid phase exceeds one month, so ICD-11 6A20 is met now. On DSM-5-TR, Criterion A and the one-month active phase are met, but total disturbance so far is roughly three-and-a-half months, short of the six-month Criterion C, so the DSM-5-TR label at this instant is schizophreniform disorder pending the six-month mark. Exclusions: confirm no concurrent mood episode and no substance or medical cause before the label is fixed. That single vignette exercises every branch of the map.

HOLD THIS

ICD-11 needs at least two symptoms, at least one a core positive or disorganisation symptom, for at least one month; DSM-5-TR needs the same one-month active phase but a six-month total duration, and both demand that psychosis occur outside a mood episode and outside a substance or medical cause.

GOOD TO REMEMBER

- **Schizophrenia:** chronic multifactorial psychotic disorder of the young adult, defined by a syndrome not a test; core criterion is psychosis plus functional decline over the required duration; the one discriminator is that no single symptom is pathognomonic, so it is a threshold-and-duration diagnosis.
- **ICD-11 (6A20):** at least two of seven symptom groups for one month or more, at least one a core symptom (delusions, hallucinations, disorganised thinking, or influence/passivity/control); discriminator is the one-month active-phase threshold with no separate total-duration rule.
- **DSM-5-TR:** Criterion A, two of five with at least one being delusions, hallucinations or disorganised speech; discriminator is Criterion C, a six-month total duration including one month of active-phase symptoms.
- **ICD-10 (legacy):** first-rank-weighted list, one clear first-rank symptom or two of a second group over one month; discriminator versus ICD-11 is that ICD-11 removed the special status of first-rank symptoms and dropped the subtypes.
- **Five symptom domains:** positive, negative, cognitive, disorganisation and affective; the map on which the whole phenomenology hangs; discriminator is that negative, cognitive and disorganisation symptoms, not the positive symptoms, carry most of the long-term disability.

Figure. The criteria map, the ICD-11-forward, DSM-5-TR-cross-mapped diagnostic decision tree with the ICD-10 legacy branch and the shared one-month versus DSM six-month duration gate, is drawn as Fig 8.1.

2 · Epidemiology: incidence, prevalence, onset and the mortality gap

The epidemiology of schizophrenia is a small set of numbers an examiner expects you to hold exactly, and to hold with their measure attached: a lifetime risk near one percent is meaningless unless you can say whether you mean point prevalence, lifetime prevalence, incidence or morbid risk, because each is a different denominator and each gives a different figure (Kaplan & Sadock 2024). This topic fixes the frequency measures, the age-and-sex pattern of onset, the Indian and cross-cultural picture, and the excess mortality that now defines the physical-health agenda for the disorder. The recurring exam trap is quoting a prevalence stripped of its year and source, so every figure below is tied to the study that produced it.

How to hold it. Anchor on three measures and their rough values, then let onset, the Indian data and the **mortality gap** attach to that spine. The descriptive definitions of the psychotic phenomena themselves belong to the Psychometry, Assessment and Descriptive Psychopathology notes; the twin, family and adoption evidence for familial risk belongs to the Psychiatric Genetics notes; and the WHO cross-cultural *outcome* finding and the cardiometabolic detail behind the mortality gap are developed in the course, prognosis and outcome topic, so this topic states them only as far as the epidemiology requires.

2.1 Three frequency measures, three different numbers

Why the measure decides the number. Prevalence is the proportion of a population that has the disorder at a point in time (point prevalence) or over a defined window (period or lifetime prevalence); incidence is the count of new, first-onset cases arising per unit population per year; and lifetime morbid risk is the probability that a person surviving through the entire age of risk

will develop the disorder. Because schizophrenia is chronic, prevalence pools accumulated surviving cases while incidence counts only new ones, so the two are not interchangeable, and morbid risk is higher than any cross-sectional prevalence because it projects across the whole lifespan. Confusing these is the single commonest epidemiology error in the disorder.

Prevalence, with its source. The most-cited systematic review of prevalence, drawing on studies from 46 countries published between 1965 and 2002, gave a median point prevalence of about **4.6 per 1,000** persons (roughly 0.46 percent), a period prevalence of 3.3 per 1,000, a lifetime prevalence of 4.0 per 1,000, and a lifetime morbid risk of about **7.2 per 1,000** (roughly 0.72 percent) (Saha et al. 2005). The Global Burden of Disease 2016 estimate, using a different Bayesian method across 195 countries, put the global age-standardised point prevalence at **0.28%**, and found it did not vary widely between countries (Kaplan & Sadock 2024). The classic teaching figure of a lifetime risk near **~1%** therefore sits at the upper edge of the rigorous survey estimates; the American Psychiatric Association guideline quotes a lifetime prevalence of approximately **0.7%** (McGrath et al. 2008, in APA 2020), which is the number to reach for when an examiner presses on the difference between the round teaching figure and the survey data.

RULE **State the measure before the number.** Lifetime risk near one percent, point prevalence near half a percent, and incidence near 15 per 100,000 per year are three different statements about three different denominators, not three versions of one figure.

TRAP **Quoting a prevalence without its year and source.** A bare "prevalence of schizophrenia is 1%" invites the follow-up you cannot then answer; tie the figure to Saha et al. 2005 or GBD 2016 (point prevalence about 0.3 to 0.5 percent) or to McGrath et al. 2008 (lifetime about 0.7 percent).

2.2 Incidence and the McGrath finding of real geographic variation

The incidence figure. First-onset incidence is the more informative measure for causal epidemiology because, unlike prevalence, it is not distorted by illness duration or differential mortality. A systematic review of studies published between 2002 and 2017 gave a median incidence of about 0.22 per 1,000 persons per year, and the Global Burden of Disease 2017 update gave an age-standardised incidence rate of roughly **15 per 100,000** per year (14.98 per 100,000 in 1990 and 14.39 per 100,000 in 2017), so the working figure to carry is an incidence of the order of **~15 per 100,000** per year (Kaplan & Sadock 2024). That is the number an examiner wants when they ask for incidence rather than prevalence.

Variation is real, not artefact. The older orthodoxy that schizophrenia occurs at a uniform rate everywhere was overturned by a systematic review that found genuine, several-fold variation in incidence, prevalence and mortality between sites and populations, argued to reflect real environmental and demographic differences rather than only differences in method (McGrath 2006; McGrath et al. 2008). The parsed reviews record incidence rising with urbanicity and a markedly raised rate in migrant and some ethnic-minority groups: pooled incidence rate ratios of about 2.3 for first-generation and 2.1 for second-generation migrants, and a near-ninefold excess in the African-Caribbean population of the United Kingdom (Kaplan & Sadock 2024). Hold the

headline as McGrath's: the incidence of schizophrenia has "surprisingly rich contours," and geographic variation is a substantive finding.

~1%	~0.7%	~0.3%	~15/100k/yr
LIFETIME RISK (CLASSIC FIGURE)	LIFETIME PREVALENCE (MCGRATH ET AL. 2008)	POINT PREVALENCE (GBD 2016, 0.28%)	INCIDENCE (GBD AGE-STANDARDISED)

2.3 Age of onset and the sex difference

The onset window. Schizophrenia is a disorder of the young adult: onset clusters in the late teens through the mid-30s, with a peak in early adulthood, and onset before adolescence or after the mid-40s is uncommon (Kaplan & Sadock 2024). This early-adulthood peak is one of the features that recurs across cultures and supports the view that the same disorder is being counted in different populations.

The sex difference. The age of onset shows a robust sex difference: onset is earlier in men, typically in the early-to-mid twenties, than in women, typically in the late twenties, and women show a characteristic second, smaller peak of onset in the peri-menopausal years that men do not (Hafner et al. 1998; Kaplan & Sadock 2024). Alongside the earlier male onset, men carry a modestly higher incidence than women (a male-to-female incidence rate ratio of the order of 1.3 to 1.4 in pooled data), and the female illness tends to run a somewhat more benign course, a pattern the parsed textbooks attribute in part to a putative protective effect of oestrogen (McGrath et al. 2008). The classic bedside summary is that onset is earlier and outcome poorer in men.

RULE **Earlier onset, poorer outcome in men.** Men present in the early-to-mid twenties with a modestly higher incidence and a worse average course; women present in the late twenties, carry a second peri-menopausal peak, and run a relatively more benign course.

2.4 The Indian picture and the cross-cultural frame

What the Indian survey shows. The National Mental Health Survey 2015-16, the reference community-epidemiology study for India, reported a lifetime prevalence of any mental disorder of 13.7 percent and a current prevalence of 10.6 percent, with a large treatment gap for severe mental disorders (Gururaj et al. 2016; Kaplan & Sadock 2024). The survey did publish a disorder-specific figure for schizophrenia and other non-affective psychoses, but the exact percentage is not confirmed in the parsed reference set, so it is flagged rather than quoted here to avoid reporting an unverified number.

INDIA

The National Mental Health Survey 2015-16 (Gururaj et al., NIMHANS) gives the national frame you should cite for any Indian prevalence claim: any mental disorder, lifetime 13.7 percent and current 10.6 percent, across 12 states, with a treatment gap for severe mental disorders reported in the region of 75 to 92 percent. The specific psychosis and schizophrenia prevalence from this survey is commonly quoted in Indian teaching but is not verifiable in the parsed sources here, so quote it only from the NMHS report itself, with the survey year attached.

The cross-cultural frame. No human community studied has been found to be free of schizophrenia, and the core clinical picture and the age-and-sex distribution of onset are broadly similar across cultures, which is the strongest argument that a single disorder is being diagnosed worldwide (Jablensky 2000; Kaplan & Sadock 2024). Against this backdrop of similar frequency and presentation, the WHO cross-cultural programme reported the counterintuitive finding that the *course and outcome* were, on average, better in patients from developing than from developed countries; that outcome finding, and the debate about it, is developed in the course, prognosis and outcome topic and is only cross-referenced here.

2.5 The mortality gap

The size of the gap. Schizophrenia carries a large excess mortality that is now treated as a core epidemiological fact rather than a footnote. People with the disorder die, on average, some **15 to 20 years** earlier than the general population, a reduction in life expectancy documented across care systems (Kaplan & Sadock 2024). Expressed as a standardised mortality ratio, all-cause mortality is roughly two-fold to four-fold that of the general population (APA 2020; Saha, Chant & McGrath 2007), and the differential mortality gap has, if anything, widened rather than closed over recent decades despite improving general-population life expectancy (Saha, Chant & McGrath 2007).

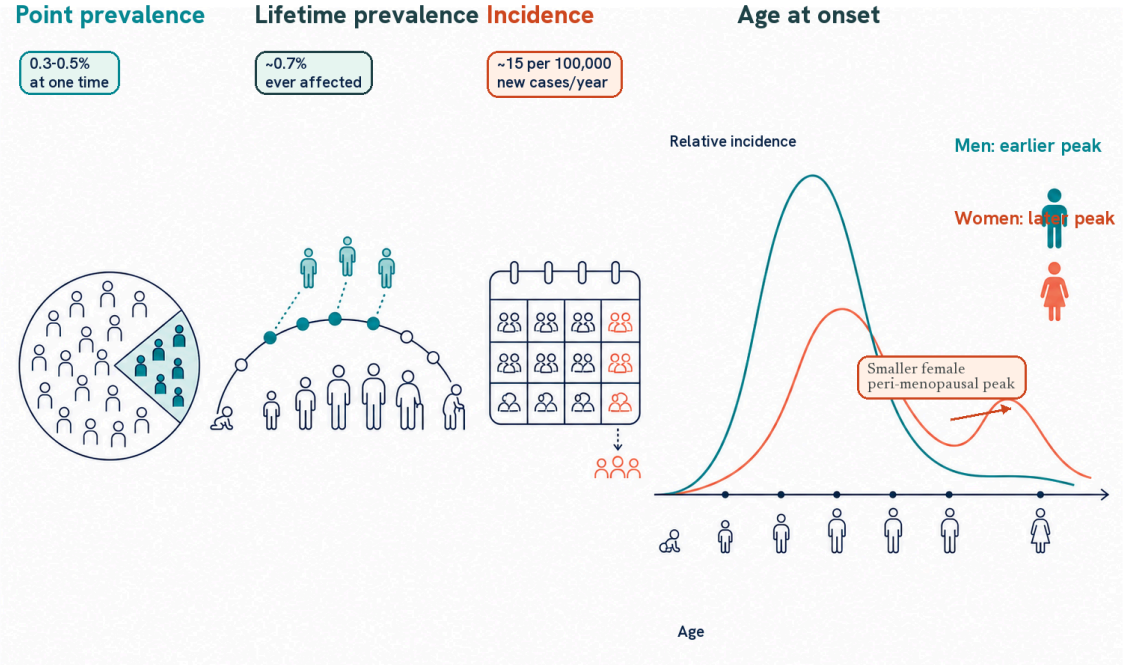


Fig 8.2 Schizophrenia epidemiology on one page. Point prevalence is about 0.3 to 0.5 per cent, lifetime prevalence about 0.7 per cent and incidence about 15 per 100,000 per year; onset peaks earlier in men, later in women, with a smaller female peri-menopausal second peak.

What drives it. Suicide accounts for a substantial share of the early excess deaths, particularly in the early years of illness, but the larger and growing part of the mortality gap is natural-cause death, dominated by cardiometabolic disease: cardiovascular disease, driven by smoking, obesity, dyslipidaemia and the metabolic effects of antipsychotic treatment, together with under-recognition and under-treatment of physical illness (Kaplan & Sadock 2024; APA 2020). The

cardiometabolic detail, and the management response to it, belong to the Schizophrenia: management, antipsychotics and adverse effects notes and are developed in the course, prognosis and outcome topic; the epidemiological headline to hold is the 15-to-20-year figure and its mostly cardiometabolic cause.

TRAP **Attributing the whole gap to suicide.** Suicide raises mortality most in the first years, but across the lifespan most of the excess death is natural-cause and cardiometabolic; the correct one-line cause of the mortality gap is cardiovascular disease, not suicide alone.

HOLD THIS

Lifetime risk near one percent, point prevalence near 0.3 to 0.5 percent, incidence near 15 per 100,000 per year with real geographic variation (McGrath); onset earlier in men (early-to-mid twenties) than women (late twenties, plus a peri-menopausal peak); and a mortality gap of 15 to 20 years that is mostly cardiometabolic.

GOOD TO REMEMBER

- **Point prevalence:** proportion of the population with schizophrenia at one time; central estimate about 0.3 to 0.5 percent (GBD 2016 point prevalence 0.28%; Saha et al. 2005 median 4.6 per 1,000); discriminator is that it pools all surviving chronic cases, so it exceeds incidence but is not the lifetime figure.
- **Lifetime prevalence and lifetime risk:** proportion ever affected / probability of developing the disorder across the lifespan; classic teaching figure about one percent, rigorous surveys about 0.7 percent (McGrath et al. 2008); discriminator is that the round 1 percent figure is the memorised anchor while 0.7 percent is the survey-derived value.
- **Incidence:** new first-onset cases per population per year; about 15 per 100,000 per year age-standardised (GBD); discriminator is that it varies genuinely by place and group (McGrath), higher with urbanicity and in migrants, so it is not uniform worldwide.
- **Age of onset and sex difference:** peak in early adulthood; earlier in men (early-to-mid twenties) than women (late twenties), women with a second peri-menopausal peak; discriminator is the modestly higher male incidence and the earlier, poorer-outcome male illness.
- **Mortality gap:** excess early death in schizophrenia; life expectancy reduced by 15 to 20 years, standardised mortality ratio about two-fold to four-fold; discriminator is that most of the gap is cardiometabolic natural-cause death, not suicide, and the gap has widened over time (Saha, Chant & McGrath 2007).

PEARL

The four numbers that carry every epidemiology viva on schizophrenia are: lifetime risk **~1%**, incidence **~15 per 100,000** per year, onset in the twenties (earlier in men), and a mortality gap of **15 to 20 years**. Attach a source to each and you have answered before the follow-up arrives.

Figure. The three frequency measures side by side, point prevalence against lifetime prevalence against incidence with their verified values and sources, plus the onset curve showing the earlier male peak, the later female peak and the female peri-menopausal second peak, is drawn as Fig 8.x.

3 · Genetics: heritability, twin and adoption data, CNVs and polygenic risk

Schizophrenia is among the most heritable of all common disorders, yet it obeys no Mendelian law. The examinable story is a layered one: a very high heritability established by family, twin and adoption designs, then a genetic architecture that is overwhelmingly **polygenic**, common and of small effect, studded with a handful of rare high-penetrance variants. **High heritability, but no single gene.** The commonest trap in vivas is to hunt for the schizophrenia gene when the correct answer is a distributed liability across thousands of loci plus a few large-effect exceptions (Sullivan et al. 2003, Owen et al. 2016).

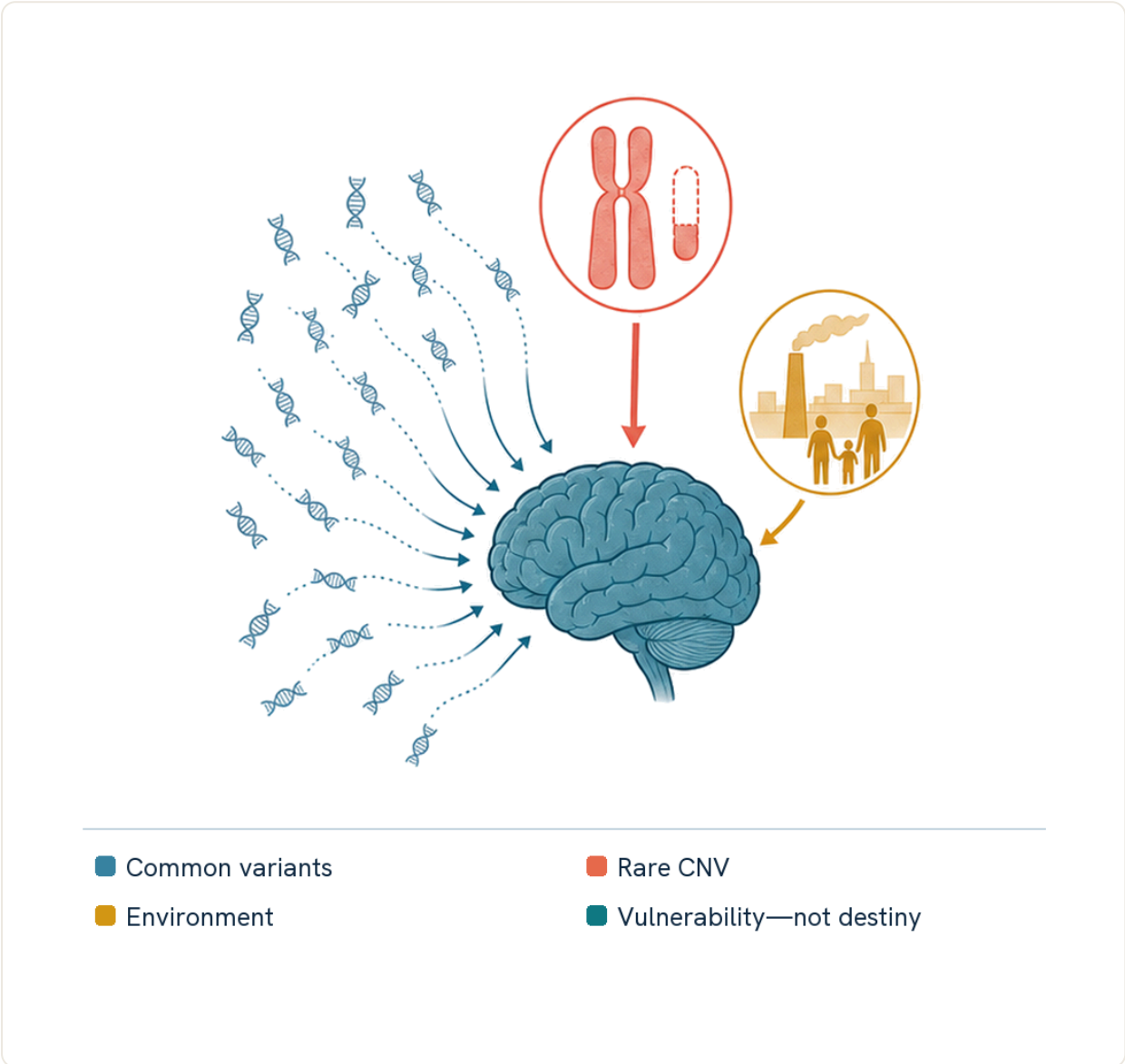


Fig 8.3 Polygenic liability in schizophrenia. Many common variants of small effect, occasional higher-impact copy-number variants and environmental exposures converge on neurodevelopmental vulnerability; none is individually deterministic.

The raw study designs, how family, twin and adoption methods actually separate genes from environment, are taught in the Psychiatric Genetics notes; here we apply them to schizophrenia and hold the numbers a resident must recite. The descriptive signs those relatives share (delusion, hallucination, first-rank symptom) are defined in the Psychometry, Assessment and Descriptive Psychopathology notes.

~80%	~40-50%	~10-15%	>100
HERITABILITY	MZ CONCORDANCE	DZ CONCORDANCE	GWAS RISK LOCI

3.1 Heritability: the strongest single risk factor is an affected relative

The headline figure. The heritability of schizophrenia is high, of the order of **~80%**; the Sullivan meta-analysis of twelve twin studies gave a point estimate of 0.81 for liability to schizophrenia (Sullivan et al. 2003). Heritability names the proportion of the variance in liability to the phenotype accounted for by additive genetic effects in that population, not the proportion of an individual's illness that is genetic. **What predicts risk.** Against a general-population lifetime risk of **~1%**, the single strongest risk factor a resident can name is having an affected **first-degree relative**: controlled family studies converge on an average relative risk near 9 to first-degree relatives (Tasman 2015). Population-register estimates run lower than twin estimates (about 64 percent in Lichtenstein et al. 2009), a discrepancy worth flagging but not fatal to the ~80 percent teaching figure.

RULE **Risk tracks genetic loading.** The more genes shared with an affected proband, the higher the risk: lowest in the general population, highest in the monozygotic co-twin and in the 22q11.2 deletion carrier.

3.2 Twin data: MZ versus DZ concordance

The pivotal comparison. Twin studies separate genes from environment by contrasting concordance in monozygotic (MZ) and dizygotic (DZ) pairs. For schizophrenia, MZ concordance is roughly **~40-50%** against DZ concordance of about **~10-15%** (Sullivan et al. 2003). A rough heritability estimate is twice the difference in concordance, which recovers the high figure above. **The two lessons in one datum.** MZ concordance well above DZ proves a large genetic contribution; MZ concordance well below 100 percent proves that genes are necessary but not sufficient, leaving room for environmental and stochastic (non-shared) influences. The twin method's assumptions (equal-environment, representativeness) are the province of the Psychiatric Genetics notes.

3.3 Adoption studies: separating genes from rearing

Why they matter. Twin and family studies cannot fully disentangle shared genes from shared rearing; adoption studies can, by studying children reared apart from their biological relatives. **Heston (1966).** The first adoption study of schizophrenia found significantly higher rates of schizophrenia in adults adopted away at birth from mothers with schizophrenia than in adoptees of unaffected parents, implying the excess risk is carried independently of the rearing environment (Heston 1966). **The Danish adoption studies.** Rosenthal, Wender and Kety extended this in a large Copenhagen and nationwide Danish sample, using adoptees' biological and adoptive relatives (and half-sibling designs to control the prenatal environment) to show that schizophrenia aggregated in the biological, not the adoptive, relatives (Kety et al. 1976, Rosenthal et al. 1971). Together they established, as close to unequivocally as this field allows, a substantial genetic component. The twin, family and adoption study methods themselves are taught in the Psychiatric Genetics notes.

WORKED EXAMPLE

A resident is asked why Heston's 1966 result cannot, by itself, prove the transmission is genetic rather than intrauterine. The answer: adopted-away offspring still shared the biological mother's prenatal environment. The half-sibling arm of the Danish adoption studies was designed precisely to control for that, and it still showed genetic aggregation.

3.4 Polygenic architecture: GWAS, small-effect common variants

The modern picture. After early linkage and single-**candidate gene** studies largely failed to replicate, well-powered genome-wide association studies (GWAS) reshaped the field. Large consortium GWAS have identified more than one hundred common genome-wide-significant risk loci (108 in the 2014 Psychiatric Genomics Consortium analysis, rising with sample size), each of individually tiny effect (Schizophrenia Working Group of the PGC 2014). **Common disease, common variant.** This is the polygenic model: susceptibility is spread across many common alleles of small effect that sum toward a threshold of liability. Common variants collectively explain a large share of heritability but no single one is diagnostic or necessary.

3.5 Polygenic risk score and the C4 / MHC signal

Aggregating the signal. The polygenic risk score (PRS) sums an individual's burden of risk alleles weighted by GWAS effect sizes. It shifts risk at the group level and is a powerful research tool, but its predictive value in any one patient is currently far too weak for clinical or diagnostic use. **The strongest single locus.** The most robust and largest common-variant signal sits in the major histocompatibility complex (MHC) region on chromosome 6. This was mechanistically resolved to structurally diverse alleles of the complement component 4 gene (C4): higher-expressing C4 alleles raise schizophrenia risk, plausibly through excessive complement-mediated synaptic pruning in adolescence (Sekar et al. 2016). This is the one common variant with a candidate mechanism worth naming in an exam.

TRAP **Never call any single gene causal.** C4, DISC1, NRG1 and the rest are risk contributors, not deterministic causes; treating one candidate gene as the cause of schizophrenia is a classic error.

3.6 Rare high-penetrance copy number variants and 22q11.2

The other end of the architecture. Alongside common small-effect variants sit rare copy number variants (**CNVs**): submicroscopic deletions or duplications, individually rare but of much larger effect and often arising de novo (Marshall et al. 2017). De novo cnv burden is enriched in schizophrenia, especially in sporadic cases, and several recurrent CNVs carry substantial risk. **The one to know: 22q11.2.** The recurrent microdeletion at 22q11.2, the basis of **velocardiofacial syndrome** (DiGeorge / 22q11.2 deletion syndrome), was the first de novo CNV described in schizophrenia (Karayiorgou et al. 1995). Up to about a third (around 25 to 30 percent) of deletion carriers develop a schizophrenia-spectrum psychosis by early adulthood, one of the highest known single-locus risks; conversely the deletion is found in roughly 1 to 2 percent of unselected schizophrenia cases (Murphy et al. 1999, Bassett & Chow 2008). Other high-risk CNVs include deletions at 1q21.1, 15q13.3 and NRXN1.

INDIA

22q11.2 deletion syndrome is under-recognised in Indian psychiatric practice; a young patient with psychosis plus congenital cardiac disease, cleft or velopharyngeal problems, hypocalcaemia, a nasal voice or learning difficulty warrants a low threshold for referral for genetic testing (FISH or microarray), where available.

3.7 Candidate genes and the shift to polygenic and CNV models

The historical layer. Before GWAS, the field pursued individual **candidate gene** hypotheses. The three most examined historical **risk gene** candidates were DISC1 (Disrupted-in-Schizophrenia 1), NRG1 (neuregulin 1) and DTNBP1 (dysbindin) (Owen et al. 2016). **Why they faded.** Most single candidate-gene associations failed robust replication in large samples; the field moved decisively to the two-tier model, common polygenic variation plus rare high-penetrance CNVs. Residents should present these three as historical candidates, not confirmed causal genes.

3.8 Gene-environment interaction

Genes are not destiny. Because MZ concordance is well under 100 percent, genetic liability interacts with environmental exposures rather than acting alone. Established environmental contributors (obstetric complications, cannabis use, urbanicity, migration) plausibly act on a genetically susceptible substrate, so that genetic loading raises the impact of a given exposure and vice versa. The dopamine and monoamine pathways through which these converge are covered in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes. The practical corollary: a positive family history sharpens vigilance for prodromal features but never fixes an individual's outcome.

HOLD THIS

Schizophrenia is ~80 percent heritable, MZ concordance ~40-50 percent versus DZ ~10-15 percent, driven by >100 common small-effect loci (polygenic, strongest signal C4/MHC) plus rare high-penetrance CNVs, above all the 22q11.2 deletion, in which about one third of carriers develop psychosis.

GOOD TO REMEMBER

- **Heritability ~80%:** proportion of population liability variance from additive genes (Sullivan 0.81); discriminator is that the single strongest risk factor is an affected first-degree relative (relative risk ~9), not any one gene.
- **Twin concordance:** MZ ~40-50% versus DZ ~10-15%; discriminator is that MZ well above DZ proves genes matter, while MZ well below 100% proves genes are necessary but not sufficient.
- **Heston (1966):** first schizophrenia adoption study, higher rates in adopted-away offspring of affected mothers; discriminator is that it separated genes from rearing but not from the prenatal environment.
- **Danish adoption studies (Kety, Rosenthal, Wender):** aggregation in biological not adoptive relatives; discriminator is the half-sibling design controlling the prenatal environment.
- **Polygenic / GWAS:** >100 common risk loci of small effect summed as a polygenic risk score; discriminator is that PRS shifts group risk but does not diagnose an individual.
- **C4 / MHC:** strongest single common-variant signal (chromosome 6); discriminator is the candidate mechanism of excess complement-mediated synaptic pruning (Sekar 2016).
- **22q11.2 deletion (velocardiofacial):** first de novo CNV in schizophrenia, high-penetrance; discriminator is that ~1/3 of carriers develop psychosis and it is found in ~1-2% of schizophrenia cases.
- **Candidate genes DISC1, NRG1, DTNBP1:** historical single-gene hypotheses; discriminator is that most failed robust replication, prompting the shift to polygenic + CNV models.

4 · The dopamine hypothesis and aberrant salience

No idea in schizophrenia is examined more often than the dopamine hypothesis, and none has been revised more radically. The examinable story is generational: an **original** hypothesis of global dopamine excess, argued backwards from drugs; a **pathway** refinement that localised the excess and explained why one drug helps positive but not negative symptoms; a **regional** hypothesis of striatal excess with prefrontal deficit; and finally aberrant salience, which converts a neurochemical fact into a phenomenological account of what a delusion actually is (Howes & Kapur 2009, Kapur 2003). **One molecule, four hypotheses, and a bridge to phenomenology.** The commonest viva error is to recite the original excess model as though it were current, when the field long ago moved to a regional, salience-based reading.

This topic applies the neurochemistry to schizophrenia and its symptoms; the mechanics of how the dopamine tracts run and how antipsychotics act on them are developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes, and the descriptive definitions of the delusion and the hallucination it explains are set out in the Psychometry, Assessment and Descriptive Psychopathology notes. Treatment itself, antipsychotics and their adverse effects, points forward to the Schizophrenia: management, antipsychotics and adverse effects notes.

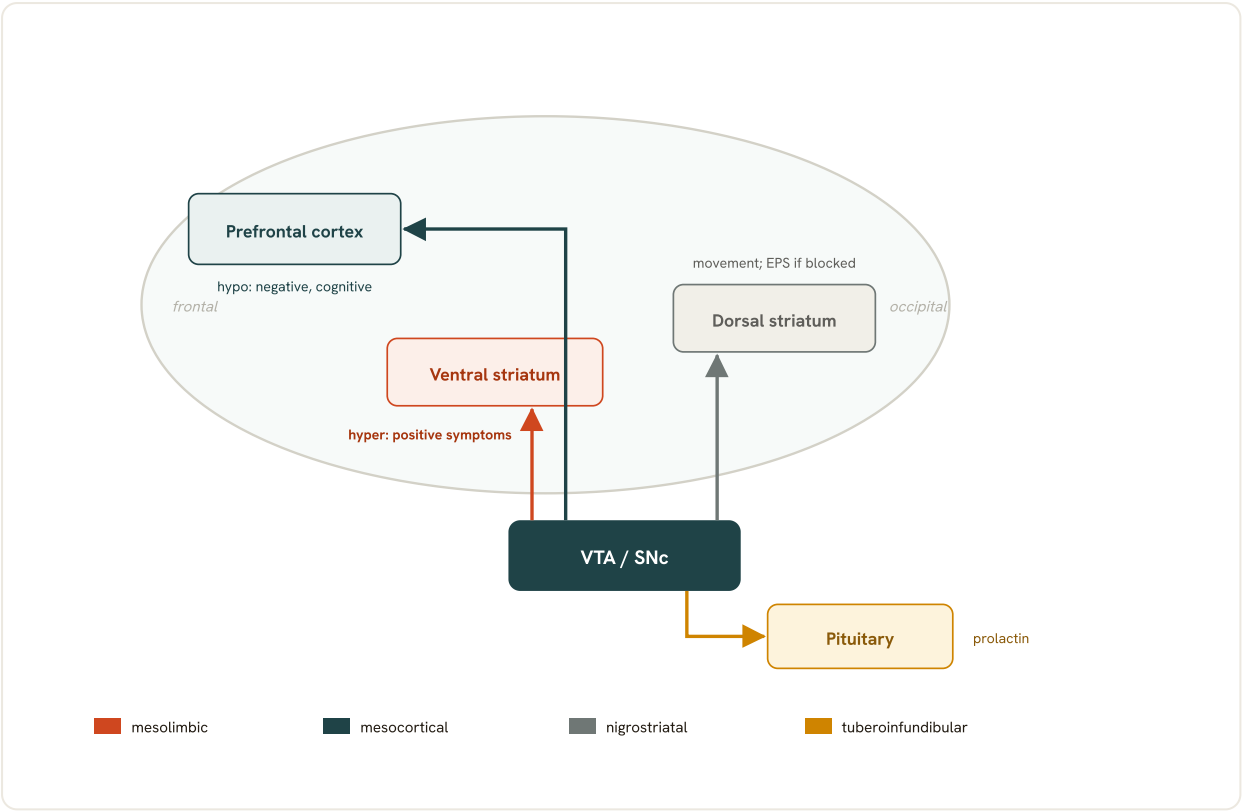


Fig 8.4 The four dopamine pathways on a schematic sagittal brain, colour-coded in the legend. The revised hypothesis is regional: the mesolimbic tract to the ventral striatum is overactive and drives the positive symptoms, while the mesocortical tract to the prefrontal cortex is underactive and underlies the negative and cognitive symptoms. The nigrostriatal and tuberoinfundibular tracts explain the movement and prolactin effects seen once dopamine is blocked.

4.1 The original hypothesis: dopamine excess and D2 overactivity

The claim. The original dopamine hypothesis held that psychosis arises from excess dopaminergic transmission, specifically overactivity at the dopamine D2 receptor (Kaplan & Sadock 2024). **The two pillars of evidence.** First, drugs that raise synaptic dopamine, above all amphetamine, can produce a paranoid psychosis in healthy people (**amphetamine psychosis**) and worsen established schizophrenia. Second, and more decisively, the clinical antipsychotic potency of the classical drugs correlates closely with their affinity for and blockade of the **D2 receptor**: the tighter a drug binds D2, the lower its effective dose (Seeman et al. 1976, Creese et al. 1976). **Why it was necessary but not sufficient.** The model explained why D2 blockade treats hallucinations and delusions, but never accounted for the negative and cognitive symptoms, and post-mortem D2 upregulation was confounded by prior antipsychotic exposure.

RULE **Potency tracks D2 affinity.** Antipsychotic clinical potency correlates with D2 receptor blockade, and dopamine-releasing drugs like amphetamine are psychotogenic, the twin observations that founded the hypothesis.

4.2 The four dopamine pathways

Localising the molecule. A global excess model could not stand once the anatomy was mapped: dopamine runs in four distinct dopamine pathways, and only some are dysregulated in schizophrenia while others explain the side effects of blocking dopamine indiscriminately (Stahl 2021). The four are the mesolimbic, the mesocortical, the nigrostriatal and the

tuberoinfundibular pathways. The projection anatomy and receptor pharmacology of each are drawn out in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; here we hold what each does and what its dysregulation produces.

PATHWAY	ROUTE	NORMAL FUNCTION	DYSREGULATION
Mesolimbic	VTA to ventral striatum / nucleus accumbens	Reward, salience, motivation	**Hyperactivity drives positive symptoms**
Mesocortical	VTA to prefrontal cortex	Cognition, executive function, affect	**Hypoactivity drives negative and cognitive symptoms**
Nigrostriatal	Substantia nigra to dorsal striatum	Motor control	D2 blockade here causes EPS and tardive dyskinesia
Tuberoinfundibular	Hypothalamus to anterior pituitary	Tonic inhibition of prolactin	D2 blockade here causes hyperprolactinaemia

The four dopamine pathways: only two carry the disease signal in schizophrenia; the other two explain the motor and endocrine costs of blocking dopamine non-selectively.

4.3 Mesolimbic hyperdopaminergia and the positive symptoms

The positive-symptom pathway. The core symptom correlation is that mesolimbic hyperdopaminergia, excess dopamine transmission in the mesolimbic projection to the ventral striatum, drives the positive symptoms of psychosis: delusions, hallucinations and thought disorder (Stahl 2021). Stahl frames this as the classic dopamine hypothesis of the positive symptoms of psychosis. **Why D2 blockade works.** Antipsychotics reduce positive symptoms precisely because they block D2 receptors in this overactive mesolimbic pathway, which is also why in-vivo PET and SPECT work shows elevated striatal dopamine synthesis and release in drug-naive patients and after amphetamine challenge (Kaplan & Sadock 2024). The raw descriptive definitions of these positive-symptom signs belong to the Psychometry, Assessment and Descriptive Psychopathology notes.

4.4 Mesocortical hypodopaminergia and the negative and cognitive symptoms

The corollary pathway. The mesocortical projection to the prefrontal cortex shows the opposite deficit: mesocortical hypodopaminergia, a deficient dopamine tone in the prefrontal cortex, underlies the negative symptoms (blunting, avolition, asociality) and the cognitive symptoms (Stahl 2021). Stahl frames this as the corollary to the classic hypothesis, mesocortical hypodopaminergia driving the cognitive, negative and affective symptoms. **The clinical sting.** Because these symptoms reflect too little dopamine in the cortex, D2 blockade cannot correct them and, by further reducing an already low mesocortical tone, may worsen them (the neuroleptic-induced deficit syndrome). This asymmetry, one pathway too high, the other too low, is the single most examinable feature of the pathway model.

TRAP **D2 blockade is not a cure-all.** Blocking D2 treats the positive symptoms but does not treat the negative or cognitive symptoms, which stem from mesocortical hypofunction, not mesolimbic excess.

4.5 The revised regional hypothesis: striatal excess, prefrontal deficit

The third generation. The revised regional hypothesis fused the pathway data into a single spatial statement: schizophrenia is characterised by **striatal hyperdopaminergia** together with **prefrontal hypodopaminergia**, rather than a uniform whole-brain excess (Davis et al. 1991, Howes & Kapur 2009). Davis, Kahn and colleagues first proposed this regional reformulation; Howes and Kapur then set it out as the definitive version, locating the abnormality at the level of presynaptic dopamine dysregulation in the striatum. **Why it matters.** The regional model reconciles the paradox of the pathway account: it explains simultaneously why raising dopamine (amphetamine) worsens positive symptoms, why blocking striatal D2 treats them, and why a prefrontal deficit leaves negative and cognitive symptoms untouched by D2 antagonism.

4.6 Aberrant salience: dopamine, meaning and the making of a delusion

Kapur's reframe. The fourth generation, aberrant salience, is the conceptual leap that links neurobiology to phenomenology (Kapur 2003). Kapur observed that mesolimbic dopamine normally assigns **salience**, converting a neutral mental representation into one that grabs the attention of the individual. **The mechanism.** In psychosis, dysregulated striatal dopamine fires independently of context and assigns undue salience to neutral, insignificant stimuli, thoughts and percepts: an unremarkable car, a passing glance or a stray idea becomes charged with unearned significance (the prodromal delusional mood). **Delusions as explanation.** Kapur's crucial move is that delusions and hallucinations are not the primary lesion but the patient's cognitive effort to explain that aberrant salience, a top-down narrative built to make sense of experiences that feel urgently meaningful (Kapur 2003, Kaplan & Sadock 2024). **Why it unifies the field.** This reframes psychosis as a disorder of salience: it recasts delusion formation as prediction error and salience misattribution, and it explains why antipsychotics dampen the conviction and preoccupation (they blunt the salience) without instantly erasing the belief itself.

PEARL

The aberrant salience model reframes the antipsychotic response phenomenologically: patients often report not that the delusion vanished but that it stopped mattering, that it receded and lost its grip. That is D2 blockade turning down the dopaminergic salience signal, exactly what the model predicts.

HOLD THIS

Mesolimbic (striatal) hyperdopaminergia drives the positive symptoms and is treated by D2 blockade; mesocortical (prefrontal) hypodopaminergia drives the negative and cognitive symptoms and is not; and aberrant salience (Kapur) explains delusions and hallucinations as the mind's effort to account for undue salience assigned by dysregulated striatal dopamine.

GOOD TO REMEMBER

- **Original dopamine hypothesis:** psychosis reflects dopamine excess / D2 overactivity; central claim rests on amphetamine psychosis plus the correlation of antipsychotic potency with D2 blockade; discriminator is that it never explained the negative or cognitive symptoms.
- **Mesolimbic pathway:** VTA to ventral striatum, subserves salience and reward; central claim is that mesolimbic hyperdopaminergia drives the positive symptoms; discriminator is that it is the pathway D2 blockade acts on to treat them.
- **Mesocortical pathway:** VTA to prefrontal cortex, subserves cognition and affect; central claim is that mesocortical hypodopaminergia drives the negative and cognitive symptoms; discriminator is that D2 blockade cannot treat and may worsen them.
- **Nigrostriatal pathway:** substantia nigra to dorsal striatum, subserves motor control; not primarily diseased in schizophrenia; discriminator is that blocking D2 here causes EPS and tardive dyskinesia.
- **Tuberoinfundibular pathway:** hypothalamus to pituitary, tonically inhibits prolactin; not primarily diseased in schizophrenia; discriminator is that blocking D2 here causes hyperprolactinaemia.
- **Revised regional hypothesis (Davis, Howes & Kapur):** striatal hyperdopaminergia with prefrontal hypodopaminergia, not a global excess; discriminator is the localisation to presynaptic striatal dopamine dysregulation.
- **Aberrant salience (Kapur 2003):** dysregulated striatal dopamine assigns undue salience to neutral stimuli; central claim is that delusions and hallucinations are the cognitive effort to explain that salience; discriminator is that it reframes psychosis as a disorder of salience and links neurobiology to phenomenology.

5 · Glutamate, GABA and the other transmitter systems

The dopamine hypothesis is the historical spine of schizophrenia neurochemistry, but on its own it fails a decisive test: amphetamine, which drives dopamine, reproduces only the positive symptoms, and antipsychotics that block **D2 receptors** barely touch the negative and cognitive burden that carries most of the long-term disability. This topic is the set of transmitter systems that step in where dopamine stops, and the examinable heart of it is the **glutamate hypothesis**. The dopamine and monoamine pathways themselves, and the neuroimaging methods behind these findings, belong to the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; here the systems are applied specifically to schizophrenia.

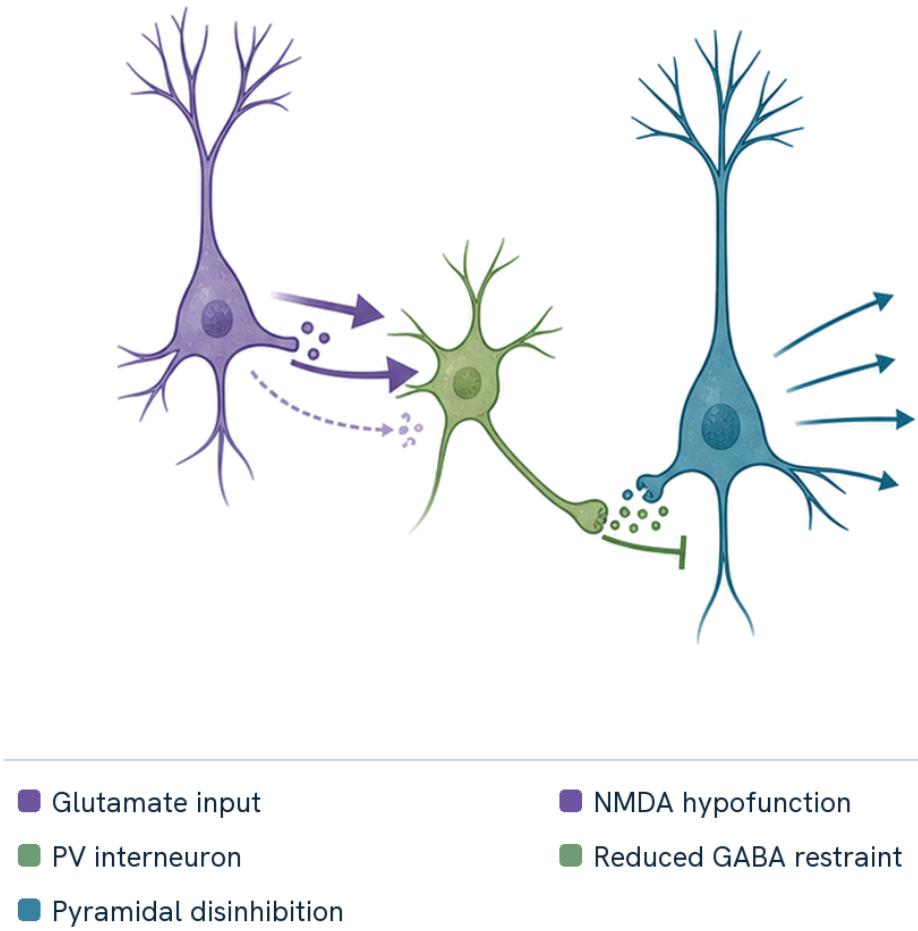


Fig 8.5 A simplified NMDA-GABA cortical microcircuit. Reduced NMDA drive to a parvalbumin interneuron weakens inhibitory restraint and leaves pyramidal output relatively disinhibited.

How to hold this. Anchor everything to one causal chain: an **NMDA receptor** that is underactive on inhibitory interneurons disinhibits downstream circuits, and from that single lesion the positive, negative and cognitive symptoms all follow, together with the GABA and dopamine changes seen in imaging. Then hang the other four systems (GABA, serotonin, acetylcholine, neuroinflammation) off that spine. The examiner's favourite move is to ask why the glutamate model beats a pure dopamine account, and the answer is always the same: the drug models. What antipsychotics reach forward into treatment, and the receptor-binding basis of the atypicals, is developed in the Schizophrenia: management, antipsychotics and adverse effects notes.

5.1 The glutamate hypothesis: NMDA receptor hypofunction as the core lesion

The central claim. The glutamate hypothesis holds that schizophrenia arises from underactivity of glutamatergic signalling at the NMDA receptor, the calcium-permeable ionotropic glutamate receptor gated jointly by glutamate and glycine and by voltage. The specific proposition is NMDA receptor hypofunction: the receptor is not fully blocked but functionally underactive, and critically the deficit is located on inhibitory neurons, not on the excitatory pyramidal cells

(Tasman 2015). Because glutamate is the brain's principal excitatory transmitter, a hypofunctioning NMDA receptor on an inhibitory interneuron removes a brake, and the net effect downstream is disinhibition and dysregulated cortical and subcortical firing rather than a simple loss of excitation.

Why hypofunction on interneurons, not pyramidal cells. The NMDA receptors that matter sit preferentially on GABAergic interneurons, in particular the fast-spiking parvalbumin cells (developed in 5.3). When their NMDA drive falls, they release less GABA, the pyramidal neurons they normally restrain fire excessively, and glutamate is released in an uncontrolled, noisy fashion in terminal regions. This reframes the illness as one of disinhibition and lost signal-to-noise, and it explains why a hypofunction hypothesis can paradoxically produce cortical hyperexcitability. Downstream, this same interneuron lesion dysregulates the mesolimbic and mesocortical dopamine systems, so the dopamine abnormalities are recast as a consequence of glutamatergic pathology rather than its cause (Tasman 2015).

HOLD THIS

The glutamate hypothesis is NMDA receptor hypofunction on GABAergic (parvalbumin) interneurons; the resulting disinhibition drives the positive, negative and cognitive symptoms and dysregulates dopamine downstream, which is why it explains what a pure dopamine account cannot.

5.2 The ketamine and PCP model: the strongest challenge to a pure dopamine account

The drug argument. The evidence that lifts NMDA hypofunction from hypothesis to leading model is pharmacological. The dissociative anaesthetics ketamine and phencyclidine are non-competitive NMDA-receptor antagonists that block the open channel, and in healthy volunteers a single subanaesthetic dose reproduces a strikingly complete schizophrenia-like state (Krystal et al. 1994). The point that wins exam marks is the breadth of what it reproduces. Phencyclidine (PCP, "angel dust") and ketamine produce positive symptoms (delusion-like ideas, hallucinations), negative symptoms (blunting, withdrawal) and cognitive impairment (deficits in working memory and executive function), and they even reproduce the electrophysiological endophenotypes of the illness, blunting mismatch negativity and P50 auditory gating after a single administration (Umbricht et al. 2000).

The contrast with amphetamine. Set the NMDA-antagonist psychosis against the classic dopamine-agonist psychosis. Amphetamine, which floods the synapse with dopamine, reproduces the positive symptoms and can precipitate a paranoid psychosis, but it does not reproduce the negative or cognitive syndrome. The dissociative anaesthetics do all three domains. That single dissociation is the strongest challenge to a purely dopaminergic account of schizophrenia: if dopamine excess were the whole story, a dopamine agonist should model the whole illness, and it does not (Kaplan & Sadock 2024). A further supporting strand is genetic: several risk genes converge on the NMDA receptor or glutamatergic transmission, and the metabotropic glutamate receptor gene GRM3 regulates glial glutamate transporters (Tasman 2015).

DRUG MODEL	ACTS ON	POSITIVE SYMPTOMS	NEGATIVE SYMPTOMS	COGNITIVE SYMPTOMS
Amphetamine	Dopamine release (agonist)	Yes	No	**No**
Ketamine / PCP (phencyclidine)	NMDA receptor block (antagonist)	Yes	Yes	**Yes, plus MMN and P50 gating deficits**
LSD / psilocybin	5-HT2A agonist	Mainly (visual) hallucinations	No	**No**

The three pharmacological psychosis models; the discriminator is that only the NMDA antagonists reproduce the negative and cognitive symptoms, which is why the ketamine model is the strongest evidence against a pure dopamine account.

RULE **The ketamine model does what dopamine cannot.** NMDA antagonists reproduce positive AND negative AND cognitive symptoms in healthy volunteers; amphetamine reproduces only positive symptoms, which is the single strongest argument that schizophrenia is more than a dopamine disorder.

TRAP **Treating glutamate and dopamine as rival hypotheses.** They are complementary, not competing: NMDA hypofunction on interneurons is upstream and dysregulates dopamine downstream, so the modern account is one integrated glutamate-dopamine circuit, not a contest between two theories.

5.3 GABA: the parvalbumin fast-spiking interneuron deficit

The GABAergic lesion. The inhibitory arm of the glutamate story is a specific and highly consistent GABA abnormality. Postmortem dorsolateral prefrontal cortex shows reduced expression of GAD67, the 67 kDa isoform of glutamic acid decarboxylase and the rate-limiting enzyme for GABA synthesis, and the deficit falls selectively on the parvalbumin interneuron, the fast-spiking cell that provides feedforward inhibition onto pyramidal neurons (Lewis et al. 2005; Lewis et al. 2012). Because NMDA antagonists reproduce exactly this parvalbumin-selective GABA change in animals, the field reads the GABA deficit as a downstream consequence of NMDA hypofunction rather than an independent lesion (Lewis & Gonzalez-Burgos 2006).

Why it matters for cognition: gamma oscillations. Parvalbumin fast-spiking cells are the pacemakers of gamma oscillations, the roughly 30 to 80 Hz synchrony that binds distributed cortical activity and underpins working memory and attention. Lose parvalbumin inhibition and gamma synchrony degrades, which maps neatly onto the cognitive impairment of schizophrenia and gives the negative-and-cognitive domain a concrete circuit mechanism. This is the mechanistic bridge from a molecular deficit to the functional disability, and it is why the GABA-parvalbumin story is asked alongside cognition.

5.4 Serotonin: the 5-HT2A receptor and the psychedelic model

The historical argument. A role for serotonin (5-hydroxytryptamine) was first proposed on the structural resemblance between serotonin and the hallucinogen LSD (Gaddum 1954). LSD, mescaline and psilocybin were later shown to be serotonin agonists, and their psychotomimetic effect is driven predominantly by agonism at the 5-HT2A receptor (Gresch et al. 2002). The

model is imperfect: psychedelics produce mainly visual hallucinations, whereas schizophrenic hallucinations are characteristically auditory, so this is a model of a fragment of the illness, not the whole.

Why it survives: the atypical antipsychotics. The serotonin hypothesis earns its keep through treatment. Excitatory 5-HT2A and inhibitory 5-HT1A receptors sit on cortical glutamatergic pyramidal cells and on GABAergic interneurons, so serotonin modulates the very glutamate circuits at the centre of the illness. Clozapine and the other second-generation ("atypical") agents combine potent 5-HT2A antagonism with relatively lower-potency D2 blockade, and it is this serotonin-dopamine profile, rather than D2 blockade alone, that is thought to underlie their broader effect and lower extrapyramidal burden. The receptor-binding pharmacology of the atypicals is developed in the Schizophrenia: management, antipsychotics and adverse effects notes.

5.5 Acetylcholine: nicotinic, muscarinic, and the smoking question

Two receptor families. Acetylcholine is implicated through both of its receptor classes: the ionotropic nicotinic receptor (nAChR) and the metabotropic muscarinic receptor (mAChR). Patients show abnormal expression of central nicotinic receptors, with the alpha-7 and alpha-4-beta-2 subtypes most implicated; the alpha-7 receptor is tied specifically to the P50 auditory sensory-gating deficit seen in patients and their first-degree relatives, which makes it an endophenotype marker as much as a treatment target (Tasman 2015). The muscarinic system is separately implicated, with reduced muscarinic receptor density reported in postmortem tissue.

Smoking as possible self-medication. People with schizophrenia smoke at a strikingly high rate, far above the general population, and one reading is **self-medication**: nicotine transiently normalises the alpha-7-dependent P50 sensory-gating deficit and may briefly sharpen attention, so heavy smoking may be an attempt to correct a cholinergic abnormality. This sets up the cholinergic and muscarinic treatment targets, an approach developed further in the cognition topic and in the Schizophrenia: management, antipsychotics and adverse effects notes; the recent arrival of muscarinic-agonist antipsychotics has made this system newly examinable.

> **PEARL**
>
> The alpha-7 nicotinic receptor is the thread that ties three exam facts together: the P50 auditory-gating deficit (an endophenotype found in unaffected relatives), the high smoking rate read as self-medication, and the cholinergic treatment target. One receptor, three questions.

5.6 Neuroinflammation: microglial activation and the kynurenine pathway

The immune strand. A newer body of work frames schizophrenia partly as a disorder of neuroinflammation. PET studies using TSPO ligands and postmortem work show microglial activation in the same regions that show grey-matter loss, and maternal immune activation in pregnancy is an established environmental risk factor, linking the immune hypothesis back to the neurodevelopmental account (Kaplan & Sadock 2024). Activated microglia are the resident

immune cells of the brain, and their over-activation is proposed to prune synapses excessively and to shift neurochemistry through inflammatory signalling.

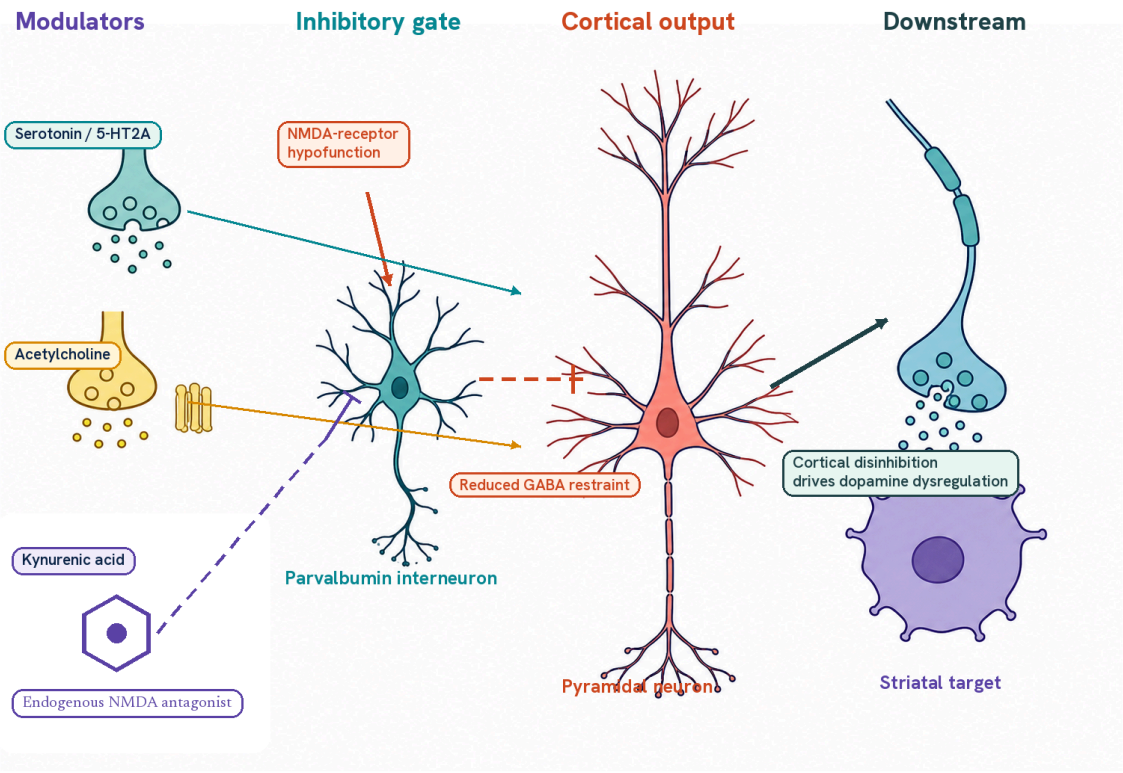


Fig 8.6 An integrated cortical circuit for schizophrenia. NMDA-receptor hypofunction on a parvalbumin interneuron reduces GABA restraint on a pyramidal neuron, producing cortical disinhibition and downstream dopamine dysregulation; serotonin, acetylcholine and kynurenic acid modulate the circuit.

The kynurenine link back to glutamate. The mechanistic bridge that makes neuroinflammation examinable alongside the glutamate hypothesis is the kynurenine pathway. Pro-inflammatory cytokines induce indoleamine 2,3-dioxygenase (IDO), which diverts tryptophan down the kynurenine pathway (Kaplan & Sadock 2024). One kynurenine metabolite, kynurenic acid, is an endogenous NMDA-receptor antagonist: raised brain kynurenic acid is reported in schizophrenia and would itself produce NMDA hypofunction. So the inflammatory strand does not sit apart from the glutamate hypothesis; through kynurenic acid it feeds directly into it, giving one plausible route by which an immune insult becomes an NMDA-hypofunction state.

COMMON TRAP

Do not present neuroinflammation as a fifth independent theory competing with dopamine and glutamate. Its examinable value is precisely that it converges on the glutamate hypothesis: cytokines to IDO to kynurenic acid to NMDA-receptor antagonism. State the convergence, not a list of rivals.

MNEMONIC

"GABA-SAN", the beyond-dopamine systems: Glutamate (NMDA), GABA, Serotonin, Acetylcholine, Neuroinflammation.

Glutamate: NMDA hypofunction on interneurons, argued from ketamine and PCP. **GABA**: parvalbumin fast-spiking cell deficit (low GAD67), degrades gamma oscillations and cognition. **S**erotonin: 5-HT2A and the LSD model, the basis of the atypicals. **A**cetylcholine: alpha-7 nicotinic (P50 gating, smoking self-medication) and muscarinic targets. **N**euroinflammation: microglial activation and kynurenic acid feeding back into NMDA hypofunction.

GOOD TO REMEMBER

- **Glutamate hypothesis:** schizophrenia as NMDA receptor hypofunction on inhibitory interneurons, causing disinhibition; central claim is that glutamate pathology is upstream of and dysregulates dopamine; the discriminator is that it explains negative and cognitive symptoms that dopamine alone cannot.
- **Ketamine / PCP (phencyclidine) model:** non-competitive NMDA antagonists reproduce a full schizophrenia-like state in healthy volunteers; core claim is that they reproduce positive, negative AND cognitive symptoms plus MMN/P50 deficits; the discriminator versus amphetamine is that amphetamine reproduces only positive symptoms.
- **GABA / parvalbumin deficit:** reduced GAD67 in DLPFC, selective to parvalbumin fast-spiking interneurons; central link is to gamma oscillations and cognition; the discriminator is that it is read as downstream of NMDA hypofunction, not an independent lesion.
- **Serotonin / 5-HT2A:** proposed from the LSD-serotonin structural similarity, psychedelic effect is 5-HT2A agonism; central relevance is that atypical antipsychotics are potent 5-HT2A antagonists; the discriminator is that psychedelics give mainly visual (not the auditory) hallucinations, so it models only a fragment.
- **Acetylcholine:** nicotinic (alpha-7, alpha-4-beta-2) and muscarinic abnormalities; central facts are the alpha-7 link to P50 gating and the high smoking rate read as self-medication; the discriminator is that alpha-7 ties the endophenotype, the smoking and the cholinergic treatment target together.
- **Neuroinflammation:** microglial activation (TSPO PET, maternal immune activation) and the kynurenine pathway; central claim is that inflammation raises kynurenic acid, an endogenous NMDA antagonist; the discriminator is that it converges on, rather than competes with, the glutamate hypothesis.

Figure. The integrated circuit, NMDA hypofunction on a parvalbumin interneuron disinhibiting a pyramidal cell, with dopamine dysregulation downstream and serotonin, acetylcholine and kynurenic acid as modulators feeding in, is drawn as Fig 8.x.

6 · The neurodevelopmental model and environmental risk

Schizophrenia is now framed as a disorder of **brain development** whose seed is sown long before the first psychotic symptom appears. The high heritability established by twin and adoption work (see "the Psychiatric Genetics notes") does not by itself explain onset: genes set a liability, but a cascade of early and later environmental hits determines who crosses the threshold and when. This topic organises that cascade into two explanatory frameworks, the **neurodevelopmental hypothesis** and the **two-hit** model, and then walks through the

individual risk exposures, early (obstetric, infective, seasonal) and late (cannabis, urban, migratory, familial), that examiners test one by one.

Why it matters. This is the single most heavily examined aetiology block in the schizophrenia paper. The favourite traps are causal ones: mistaking an association (low social class, urban residence) for a cause, and forgetting that most exposures act only on a genetically primed brain. Hold the odds ratios, the eponymous cohorts, and the two-hit logic, and you can answer almost any stem.

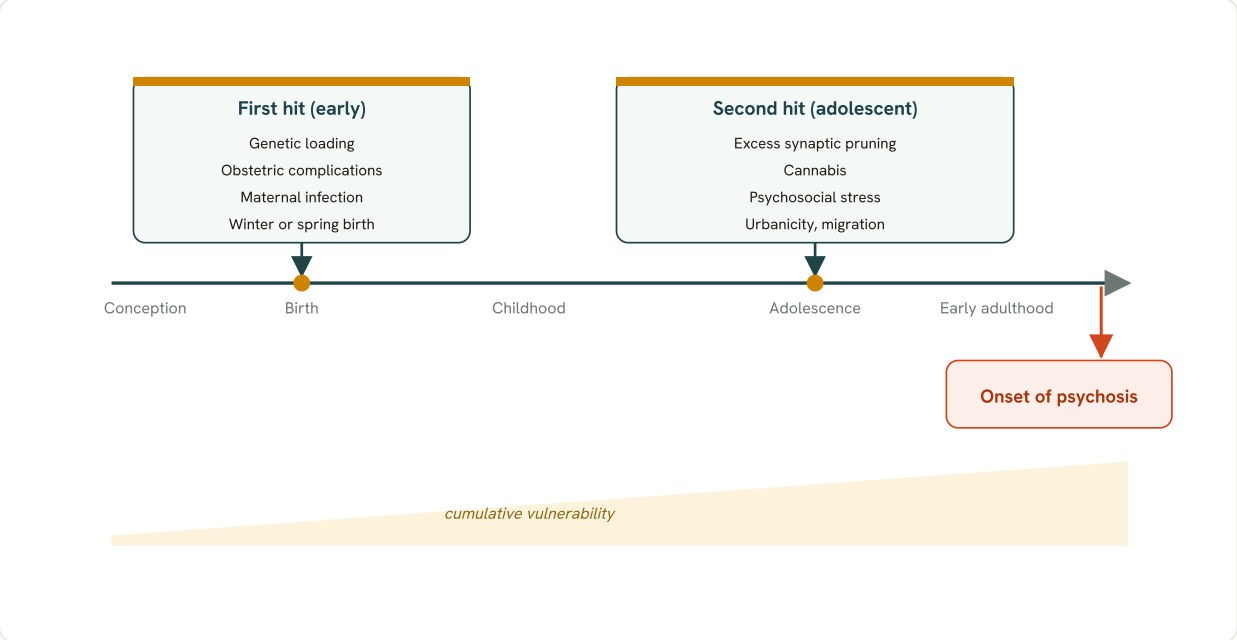


Fig 8.7 The neurodevelopmental two-hit model across the lifespan. An early first hit, genetic and prenatal, primes the vulnerability, which then accumulates until an adolescent second hit, synaptic and psychosocial, precipitates the onset of psychosis as the affected circuits mature. Neither hit alone is usually sufficient; the illness emerges from their convergence on a developing brain.

6.1 The neurodevelopmental hypothesis: an early static lesion

Core claim. The neurodevelopmental hypothesis (Weinberger 1987; Murray & Lewis 1987), also called the developmental hypothesis, proposes that schizophrenia originates in a fixed, early lesion of brain development (a disturbance of neuronal migration, connectivity and pruning arising in utero or early life) that lies clinically silent for years. The affected fronto-temporal and limbic circuits are not yet functionally loaded in childhood; only when they normally come online in late adolescence and early adulthood does the latent abnormality express itself as psychosis. This is why onset clusters in the late teens to twenties despite a lesion laid down before birth.

The gliosis argument. The strongest structural support is a negative finding: the modest brain changes of schizophrenia (ventricular enlargement, reduced cortical and hippocampal volume) occur *without* reactive gliosis, the astrocytic scarring that marks any acquired or degenerative lesion after roughly the second trimester. Absent gliosis points to an early developmental (organisational) origin rather than a neurodegenerative one, and it distinguishes schizophrenia from a dementing process. The neuroimaging and gliosis evidence is developed in "the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes".

RULE **Static, not progressive.** An early fixed lesion expressed at circuit maturation, and the absence of gliosis is the histological signature that it is developmental, not degenerative.

6.2 The two-hit model: first hit plus second hit

Central logic. The two-hit model (a "two hit" or two hit account) reconciles the early lesion with adolescent onset. The **first hit** is the early priming: genetic liability plus an early neurodevelopmental insult (obstetric, infective, nutritional) that leaves a vulnerable but compensated brain. The **second hit** arrives in adolescence, when physiological synaptic pruning strips cortical connections and psychosocial or substance stressors are superimposed; on an already-primed substrate this tips the system past threshold into frank psychosis.

Pruning as the trigger. Normal adolescent synaptic pruning, if excessive on a primed brain, is the mechanistic candidate for the second hit; complement C4 (implicated in microglial synaptic pruning) gives this a molecular anchor (Sekar et al 2016). The model explains both the premorbid trait markers of childhood and the sharp adolescent inflection.

HOLD THIS
Two-hit: hit one is genes plus early neurodevelopmental insult (a primed brain); hit two is adolescent synaptic pruning plus psychosocial or substance stress; onset is where the two meet.

6.3 Early risk: obstetric complications

What they are. An obstetric complication is any antenatal, perinatal or neonatal adverse event (antepartum haemorrhage, pre-eclampsia, gestational diabetes, hypoxia or asphyxia, low birth weight, Rhesus incompatibility, emergency section). Meta-analysis puts the pooled effect sizes generally below 2 (Cannon et al 2002), and the effect is amplified in those already carrying genetic liability (Nicodemus et al 2008), a clean gene-environment interaction. Fetal hypoxia is the leading proposed mechanism.

TRAP **Association, not necessarily cause.** An obstetric complication may be directly causal (hypoxia), or merely mark a pre-existing fetal abnormality, or reflect maternal characteristics, so do not report the odds ratio as proof of causation.

6.4 Early risk: maternal infection and malnutrition

Maternal infection. Second-trimester maternal infection is a candidate exposure, historically anchored to the 1957 influenza A2 pandemic, with later associations for toxoplasmosis, herpes simplex virus 2 and rubella. The evidence is inconsistent (a meta-analysis of the 1957 pandemic was negative, Selten et al 2010), and the modern reading is that maternal immune activation and inflammation, rather than a specific pathogen, prime the fetal brain (Cannon et al 2014).

Maternal malnutrition. Prenatal famine roughly doubles risk (odds ratio about 2), first shown in the Dutch Hunger Winter of 1944 and replicated in two Chinese famine cohorts; the proposed mechanism is epigenetic, with altered DNA methylation in exposed offspring (Kirkbride et al 2012).

6.5 Early risk: season of birth

The finding. A robust, replicated excess of winter and spring births exists among people who later develop schizophrenia, the season of birth effect. The excess is small (of the order of 5 to 10 per cent) but consistent across Northern Hemisphere studies, with the mirror pattern in the Southern Hemisphere. It is usually read as an indirect fingerprint of a seasonal early exposure, most plausibly second-trimester maternal viral infection or a nutritional or vitamin D factor, converging with 6.4.

> **PEARL**
> Season of birth is not itself a cause; it is a proxy that points to a seasonally varying prenatal exposure. Winter and spring births carry the excess in the Northern Hemisphere.

6.6 Later risk: cannabis as a component cause

The evidence. Prospective data make cannabis the best-established modifiable later exposure. The landmark Swedish conscript cohort found a relative risk of about 2.5 for schizophrenia in cannabis users, rising roughly sixfold in the heaviest users (Andreasson et al 1987); subsequent longitudinal studies give a pooled odds ratio of about 2, and cannabis use brings forward the age of onset (Large et al 2011). The risk is dose-dependent, greater with adolescent-onset use, and steepest with high-potency preparations (high delta-9-THC, low cannabidiol).

How to phrase it. Cannabis is neither necessary nor sufficient; it is a *component cause* that raises risk in the vulnerable, interacting with genotype (for example COMT, Caspi et al 2005). Cannabidiol content and route of onset matter, which is why high-potency and early-adolescent use dominate the risk.

RULE **Cannabis is a dose- and age-dependent component cause of psychosis.** Highest risk with heavy, adolescent-onset, high-potency use; it advances onset and interacts with genetic liability.

6.7 Later risk: urbanicity, migration and minority status

Urbanicity. Urbanicity shows a dose-response gradient: psychosis risk rises linearly with degree of urban birth and upbringing (odds ratio about 1.57; van Os et al 2003), independent of age, sex, education and family psychiatric history, and the urban effect is greater in those with a family history, again a gene-environment interaction.

Migration and minority status. Migration and ethnic-minority status carry a marked excess; in the UK AESOP first-onset study the relative risk for all psychoses was 6.7 in the Afro-Caribbean and 1.5 in the Asian population versus the white population (Fearon et al 2006), and the excess is often greatest in the second generation, arguing for social rather than purely biological mechanisms. Low ethnic density (being a small minority locally) more than doubles risk, pointing to social defeat, chronic discrimination and exclusion rather than selective migration alone.

INDIA

Indian teaching describes the "hemp insanity" or cannabis psychosis (Dhunjibhoy 1930) in heavy cannabis-using populations, where florid psychotic symptoms followed unusually heavy use and remitted with abstinence. Useful as an early Indian description of the cannabis-psychosis link, distinct from primary schizophrenia.

6.8 Later risk: childhood adversity and expressed emotion

Childhood adversity. Childhood trauma, abuse and neglect are dose-dependently associated with adult psychosis and form part of the **psychosocial risk** load that acts as a second hit on a primed brain.

Expressed emotion. Expressed emotion is a relapse (course) factor rather than an aetiological (onset) one. High-EE households (marked by critical comments, hostility and emotional over-involvement) strongly predict relapse after recovery from an acute episode (Brown et al 1972; Vaughn & Leff 1976; Leff & Vaughn 1985). This is the empirical basis for family intervention and psychoeducation to lower EE, covered in "the Schizophrenia: management, antipsychotics and adverse effects notes".

TRAP **Expressed emotion drives relapse, not onset.** High-EE families predict recurrence in an established illness; do not cite EE as a cause of the first episode.

6.9 Low socioeconomic status: social drift versus social causation

The observation. Schizophrenia is over-represented in the lowest socioeconomic groups and in deprived inner-city areas (Hollingshead & Redlich 1958; Faris & Dunham 1939). Two competing readings exist.

HYPOTHESIS	DIRECTION OF CAUSATION	KEY EVIDENCE
Social drift (drift hypothesis)	Illness leads to low SES	**Patients fall below their fathers' social status after onset (Goldberg & Morrison 1963); genetic liability itself contributes to the downward drift (Sariaslan et al 2016)**
Social causation	Low SES leads to illness	Patients more likely born into socially deprived households (Castle et al 1993); place of birth and early upbringing predict risk and cannot be explained purely as a consequence of illness

The low-SES association is best explained by social drift, though a residual social-causation (early-environment) contribution is supported by birth-cohort data.

The resolution. The social drift account (the drift hypothesis) carries most of the association: the prodrome and illness erode occupational and social standing, so patients drift down the social scale. Social causation retains a foothold because place of birth and early deprivation predict risk

independently of later drift. SES is therefore largely a consequence, with a smaller upstream contribution, not a primary cause.

TRAP **Low SES is mostly downstream.** Social drift explains the low-SES association without socioeconomic status itself causing the illness; reserve social causation for the birth and early-upbringing findings.

6.10 Synthesis: a lifespan risk architecture

Putting it together. The frameworks nest cleanly. Genes and early insults (the first hit) build a developmentally abnormal brain that is clinically silent (neurodevelopmental hypothesis, no gliosis); adolescent pruning plus psychosocial and substance stressors (the second hit) express it as psychosis (two-hit model). Each named exposure carries a modest odds ratio (around 2 for most) and repeatedly interacts with genetic liability, which is the through-line examiners want you to state explicitly.

<2 OR, OBSTETRIC COMPLICATIONS (CANNON 2002)	**2.5** RR, CANNABIS; ~6X HEAVY (ANDREASSON 1987)	**1.57** OR, URBANICITY (VAN OS 2003)	**6.7** RR, AFRO-CARIBBEAN PSYCHOSIS (AESOP 2006)

MNEMONIC

CoMMANDER SUC

Early hits: **Co**mplications (obstetric), **M**alnutrition, **M**aternal infection, **A**utumn/winter birth (season). Late hits: **N**o family (drift), **D**eprivation/urbanicity, **E**xpressed emotion, **R**acial-minority migration; plus **S**ubstance (cannabis), **U**rban, **C**hildhood adversity.

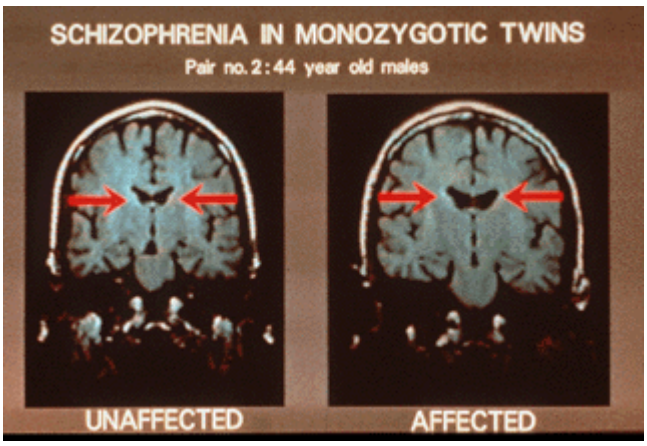
GOOD TO REMEMBER

- **Neurodevelopmental hypothesis (Weinberger; Murray & Lewis):** an early fixed lesion of brain development expressed at adolescent circuit maturation; discriminator is the absence of gliosis (developmental, not degenerative).
- **Two-hit model:** first hit = genes plus early neurodevelopmental insult; second hit = adolescent synaptic pruning plus psychosocial or substance stress; discriminator is that both are needed for onset.
- **Obstetric complications:** antenatal/perinatal adverse events (hypoxia the key mechanism); discriminator is pooled OR about 2, magnified by genetic liability.
- **Maternal malnutrition:** prenatal famine roughly doubles risk (Dutch Hunger Winter); discriminator is the proposed epigenetic (DNA-methylation) mechanism.
- **Season of birth:** winter and spring birth excess; discriminator is that it is a proxy for a seasonal prenatal exposure, not a cause in itself.
- **Cannabis:** dose- and age-dependent component cause (RR about 2.5, ~6x in heavy users, Andreasson 1987); discriminator is high-potency, adolescent-onset use and earlier age of psychosis onset.
- **Urbanicity:** linear dose-response with urban birth/upbringing (OR about 1.57); discriminator is the gene-environment interaction (stronger with family history).
- **Migration and minority status:** marked excess, greatest in second generation and at low ethnic density (AESOP RR 6.7 Afro-Caribbean); discriminator is social defeat, not selective migration.
- **Expressed emotion:** high-EE families (criticism, hostility, over-involvement) predict relapse; discriminator is that it is a course (relapse) factor, not an onset cause.
- **Social drift vs social causation:** low-SES association is mostly drift (illness lowers status, Goldberg & Morrison 1963; genetic liability contributes, Sariaslan 2016); discriminator is that residual social causation is supported only by place-of-birth and early-upbringing data.

7 · Structural neuroimaging and neuropathology

For a century schizophrenia was called a **functional** disorder precisely because Alzheimer and others could find no lesion, and the modern story of its neuroimaging and neuropathology is the story of that null hypothesis being overturned. The examinable spine is short and must be held cold: at the group level the brain in schizophrenia shows enlarged ventricles and a modest global and regional loss of tissue, present already at the first episode; the cellular substrate is reduced neuropil and dendritic spines with an altered cytoarchitecture; and, decisively, there is no gliosis and no neurodegeneration, which is the single fact that pushes the whole field toward a neurodevelopmental rather than a degenerative reading (Harrison 1999, Weinberger & Radulescu 2016). **Real changes, group-level only, and no scar.**

This topic applies the imaging and post-mortem findings to schizophrenia; the physics and technique of how a CT, the MRI sequences and PET actually work are developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes, and the descriptive definitions of the symptoms these changes are correlated with belong to the Psychometry, Assessment and Descriptive Psychopathology notes. The neurodevelopmental model that this evidence feeds, and the environmental hits behind it, sit in the aetiology material; here we hold the anatomy and the histology themselves.



Dr Daniel Weinberger, NIMH Clinical Brain Disorders Branch. Public domain (US Government).

Fig 8.8 Lateral ventricular enlargement in schizophrenia, shown in monozygotic twins discordant for the illness. The unaffected twin is on the left and the affected twin on the right, with the arrows marking the enlarged lateral ventricles. Because the twins are genetically identical, the difference cannot be genetic alone, which is why this image is the classic demonstration that structural change in schizophrenia is real and not wholly inherited.

7.1 Johnstone 1976: the landmark that reopened the question

The study that started it. In a landmark study, Johnstone and colleagues used the then-novel technique of computerized tomography and found significantly larger ventricles and more cortical atrophy in patients with schizophrenia than in controls (Johnstone et al. 1976). **Not the first, but the decisive one.** Lateral ventricular enlargement had actually been reported decades earlier using pneumoencephalography, but it was the Johnstone CT study that stimulated the renewed interest which the whole subsequent MRI literature grew out of (Kaplan & Sadock 2024). This is the exam-safe eponym for the birth of structural imaging in schizophrenia.

7.2 Ventricular enlargement: the most replicated structural finding

The single most robust result. Lateral (and third) **ventricular enlargement** is the most consistently replicated structural finding in schizophrenia, confirmed across hundreds of studies and, crucially, present in antipsychotic-naive patients, which argues it is not merely a drug effect (Haijma et al. 2013). **The number to hold.** A meta-analysis of brain volumes in over 18,000 subjects found that ventricular volume is increased by roughly a quarter to a third in schizophrenia relative to controls (Haijma et al. 2013). **The paired reductions.** The same meta-analysis found whole-brain volume decreased by about **2.6%** and intracranial volume reduced by about **2%**; that last figure is telling, because intracranial volume is fixed early in life, so a reduction in it points to a process that acted in childhood, before the illness declared itself.

~30%	~2.6%	~2%
VENTRICULAR VOLUME INCREASE	WHOLE-BRAIN VOLUME DECREASE	INTRACRANIAL VOLUME REDUCTION

RULE **Ventricular enlargement is the flagship.** Lateral ventricular enlargement is the most replicated structural finding in schizophrenia, seen even in antipsychotic-naive patients, so it is a disease signal and not just a consequence of treatment.

7.3 Grey matter loss: global, and regionally weighted to medial temporal and prefrontal cortex

The tissue that goes. Alongside the ventricles, there is a reduction in grey matter, both a modest global loss and a regionally weighted one: cortical grey matter is thinner overall, and the effect is greatest in the medial temporal structures and the prefrontal cortex (Haijma et al. 2013). The reduction is greater for grey matter than for white matter. Reporting conventions differ, so the term also appears as **gray matter** in the American literature; it is the same tissue and the same finding. **Where it bites hardest.** In that 18,000-subject meta-analysis the largest effect sizes were in the hippocampus and the thalamus, with the whole picture broadly similar in antipsychotic-naive and in medicated patients, again separating disease from drug.

7.4 Hippocampal and thalamic reduction: the strongest regional signal

The regions that carry the signal. Of all the structures examined, the hippocampal and thalamic volume reductions are the largest and most reproducible regional findings in schizophrenia, and they are present at the first episode (Haijma et al. 2013, Weinberger & Radulescu 2016). Smaller hippocampus and smaller thalamus sit at the top of the standard summary list of structural changes. **Why the hippocampus matters clinically.** Its involvement dovetails with the memory and declarative-learning deficits of the illness and with the aberrant-salience account of psychosis, giving a structural anchor for symptoms that are otherwise defined purely descriptively (cross-referenced to the Psychometry, Assessment and Descriptive Psychopathology notes).

7.5 Present at first episode, modestly progressive: the time course

Neither purely fixed nor frankly degenerative. Longitudinal work shows the time course is genuinely complex: some of the volume reductions are present before the onset of symptoms and track the genetic predisposition, others emerge at the first episode, and thereafter there is some further, modest loss of grey and white matter whose timing, magnitude and cause remain unclear (Weinberger & Radulescu 2016). **The confounder that muddies progression.** The extent to which any progressive reduction is the disease itself, versus antipsychotic exposure, smoking and other confounders, is unresolved (Fusar-Poli et al. 2013). The examinable phrase is that the changes are present at first episode and only modestly progressive, and that whatever progression exists is not neurotoxic or degenerative in the classic sense (Zipursky et al. 2013).

> **PEARL**
>
> The reduction in intracranial volume is the quiet giant of this evidence. Because the skull vault stops growing early in childhood, a shrunken intracranial volume cannot be explained by an adult-onset degeneration or by years of medication: it fingerprints a process that acted long before the first psychotic symptom, and it is one of the cleanest single arguments for a neurodevelopmental origin.

7.6 Functional imaging: hypofrontality on executive tasks

The functional counterpart. The first functional study (Ingvar & Franzen 1974) found decreased perfusion of the frontal cortex relative to posterior regions in chronic patients, a pattern christened hypofrontality: reduced frontal activation, classically elicited on executive and

word-generation tasks such as the Wisconsin Card Sorting Test and verbal fluency. **Confirmed, but conditional.** Many individual studies were negative, but hypofrontality was confirmed in meta-analysis (Hill et al. 2004), and the relationship is stronger when the phase of illness and symptom profile are taken into account, above all its link with psychomotor poverty and negative symptoms (Shorter Oxford, Semple & Smyth 2019). The technical basis of how cerebral blood flow, PET and BOLD fMRI actually measure this is set out in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

7.7 Functional imaging: reduced efficiency and aberrant connectivity

Not simply less, but less efficient. fMRI during working-memory tasks refines the crude hypofrontality picture: when patients are matched to controls for task performance, they require greater prefrontal activation to achieve the same output, indicating reduced cortical efficiency rather than a simple flat deficit (Callicott et al. 2003, Minzenberg et al. 2009). **The dysconnectivity turn.** The dominant contemporary functional framing is dysconnectivity: aberrant coordination between brain circuits and networks rather than a single hot or cold region (Stephan et al. 2009). This revives Bleuler's original idea of a failure of integration of mental functions, now recast as disturbed connectivity and abnormal neural oscillations, and it aligns with the white-matter and structural findings above.

7.8 Neuropathology: reduced neuropil, dendritic spines and altered cytoarchitecture

What the microscope adds. Post-mortem neuropathology was sought to explain the imaging at a cellular level, and the positive findings are consistent (Harrison 1999, Dorph-Petersen & Lewis 2011). Brain weight is decreased by about 2 to 3%. The core finding is reduced neuropil: reductions in markers of synapses and dendrites, with smaller neurons packed more densely, so that neuronal loss is minimal but the felt-work of connections between neurons is thinned. **The specific cells.** There are reductions in dendritic spine density, and in specific populations, notably the parvalbumin subclass of GABAergic interneurons and layer III pyramidal neurons (Lewis et al. 2005). **Altered cytoarchitecture.** An abnormal position or clustering of neurons, a disturbed cytoarchitecture, has been reported particularly in the entorhinal cortex and subcortical white matter, the kind of misplacement expected from disordered neuronal migration in fetal life rather than from any adult insult.

7.9 The absence of gliosis: the argument for neurodevelopment, not neurodegeneration

The negative finding that decides the question. The most examinable single fact of the whole topic is a negative one: there is an absence of gliosis and no evidence of any neurodegenerative process in the schizophrenic brain (Roberts et al. 1986, Harrison 1999). **Gliosis**, the reactive proliferation of astrocytes, is the brain's universal scar and appears whenever mature tissue is injured or degenerates. Its absence means the structural and cellular abnormalities did not arise from an insult to a formed adult brain. **Why this points to neurodevelopment.** Injuries occurring before roughly the end of the second trimester, while glia are still immature, heal without a glial scar; a lesion laid down that early therefore leaves reduced neuropil, malpositioned neurons and smaller structures but no gliosis. The finding thus argues that schizophrenia is a disorder of early brain development, and that whatever mild progression is

seen on serial MRI is not neurotoxic or degenerative (Weinberger 1987, Murray & Lewis 1987, Zipursky et al. 2013).

TRAP **Do not scan to diagnose.** Ventricular enlargement and grey matter loss are group-level statistical findings with wide overlap between patients and controls; they are not a diagnostic test, and a normal or an abnormal scan neither confirms nor excludes schizophrenia in an individual.

7.10 Excess adolescent synaptic pruning: linking the histology to onset

Why an early lesion declares itself in late adolescence. If the pathology is developmental, why does psychosis emerge only in the late teens and twenties? The influential answer is the excessive synaptic pruning hypothesis (Feinberg 1982): normal adolescence involves a large, programmed elimination of cortical synapses, and if that pruning is excessive or mistimed it could push an already vulnerable, synapse-poor cortex past a threshold, producing symptoms at exactly the age pruning peaks. **The modern genetic support.** This once-speculative idea gained hard support when the strongest common-variant genetic signal, at the MHC locus, was traced largely to the complement component 4 (C4) gene: risk alleles drive higher C4 expression and, at least in mice, more synaptic pruning (Sekar et al. 2016), converging with the post-mortem finding of reduced neuropil and giving a mechanism for the loss of synapses over adolescence.

WORKED EXAMPLE

A registrar presents a drug-naive man at his first episode whose MRI shows mildly enlarged lateral ventricles and reduced hippocampal volume, and is asked what this proves. The disciplined answer: it is consistent with schizophrenia at the group level and, being present at first episode and before treatment, argues the changes are neither purely a drug effect nor a late degeneration. It does not, on its own, diagnose him, because these are statistical findings with large patient-control overlap. The clinching conceptual point the examiner wants is that the underlying neuropathology shows an absence of gliosis, marking this as a neurodevelopmental and not a neurodegenerative disorder.

HOLD THIS

The brain in schizophrenia shows enlarged ventricles (the most replicated finding, ventricular volume up by roughly a quarter to a third) with reduced grey matter, hippocampus and thalamus, present at first episode and only modestly progressive; the histology is reduced neuropil, dendritic spines and altered cytoarchitecture with, crucially, an absence of gliosis, which marks the process as neurodevelopmental, not neurodegenerative.

GOOD TO REMEMBER

- **Ventricular enlargement:** enlargement of the lateral and third ventricles; the most consistently replicated structural finding, seen even in antipsychotic-naive patients; discriminator is the meta-analytic finding of ventricular enlargement of roughly a quarter to a third (Haijma et al. 2013).
- **Grey matter (gray matter) reduction:** global and regional cortical thinning, greater for grey than white matter; central claim is that loss is regionally weighted to medial temporal and prefrontal cortex; discriminator is that whole-brain volume falls about 2.6% and the effect is broadly equal in naive and medicated patients.
- **Hippocampal and thalamic reduction:** smaller hippocampus and thalamus; the largest and most reproducible regional volume losses; discriminator is that they carry the biggest effect sizes and are already present at the first episode.
- **Johnstone et al. 1976:** the landmark CT study showing larger ventricles and cortical atrophy; central claim is that it reopened schizophrenia as a brain disorder; discriminator is that it used computerized tomography and revived a finding first hinted at by pneumoencephalography.
- **Hypofrontality (Ingvar & Franzen 1974):** reduced frontal cerebral blood flow and activation on executive tasks; central claim is a functional prefrontal deficit; discriminator is that it is confirmed on meta-analysis (Hill et al. 2004) and is tied to psychomotor poverty and negative symptoms, and that it reflects reduced cortical efficiency, not simple inactivity.
- **Reduced neuropil and dendritic spines:** thinned synaptic and dendritic markers with smaller, densely packed neurons and loss of parvalbumin interneurons and layer III pyramidal cells; central claim is that connections, not neurons, are lost; discriminator is that neuronal loss is minimal and gliosis is absent.
- **Altered cytoarchitecture:** abnormal neuronal position and clustering, notably in entorhinal cortex and subcortical white matter; central claim is disordered neuronal migration; discriminator is that malposition without gliosis implicates a fetal, second-trimester developmental error.
- **Absence of gliosis:** no reactive astrocytic scarring and no neurodegenerative change; the pivotal negative finding; discriminator is that its absence excludes an adult degenerative process and is the core argument that schizophrenia is neurodevelopmental (Roberts et al. 1986, Weinberger 1987).
- **Excess synaptic pruning (Feinberg 1982):** excessive programmed elimination of cortical synapses in adolescence; central claim is that it explains the late-adolescent onset of an early lesion; discriminator is the modern C4 complement genetic support (Sekar et al. 2016) converging with the reduced-neuropil finding.

Clinical features and phenomenology

8 · The symptom domains and the dimensional models

The phenomenology of schizophrenia does not resolve into a single presentation, and the examiner rewards the resident who can organise it. The organising map is a set of semi-independent **symptom domains**: a patient is described by a **profile** across them, not by one label. This topic sets out the modern five domain map and then the historical dimensional and phenotype models, Crow's type I and type II and Liddle's three-syndrome scheme, that fed into it. The raw descriptive definitions of the individual signs, what a delusion, a hallucination, a first-rank symptom or formal thought disorder *is* as a phenomenon, are not re-derived here; they belong to the Psychometry, Assessment and Descriptive Psychopathology notes, and this chapter applies them to schizophrenia.

Why this is the payoff. The domains are the spine that the criteria map, the classification band and the differential all hang from, and the same domain vocabulary drives the reason both ICD-11 and DSM-5 dropped the classical subtypes in favour of a dimensional specifier approach. Fix the five domains and their representative signs first; the two eponymous models then read as historical attempts to compress the same variation into two or three biologically motivated syndromes (Kaplan & Sadock 2024).

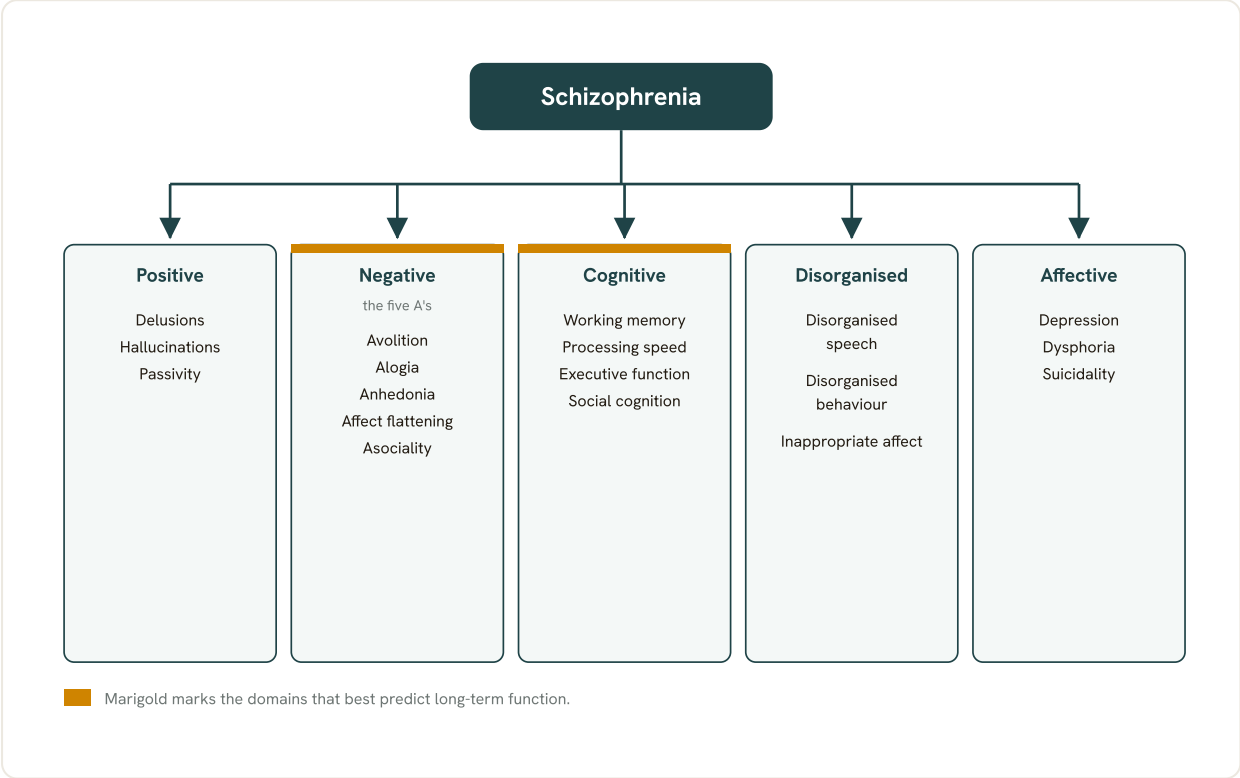


Fig 8.9 The five symptom domains of schizophrenia as one map. A patient is described by a profile across these semi-independent dimensions rather than by a single subtype. The negative and cognitive domains, marked in marigold, carry the greatest weight for long-term functional outcome even though the positive symptoms are the most visible.

8.1 The five-symptom-domain map: a profile, not a subtype

The map. Contemporary phenomenology describes schizophrenia across five semi-independent symptom domains, and a given patient carries a **profile** of varying weight across all five rather than belonging to one discrete category (Kaplan & Sadock 2024). Holding the five domain map converts a sprawling symptom list into a compact grid, and it is the grid the classification band builds on when it replaces subtypes with dimensional specifiers. The five are positive, negative, cognitive, disorganised, and affective (mood).

Positive. A positive symptom is an addition to normal experience: delusions and hallucinations are the representative signs, the florid features that most often bring the patient to attention and drive admission. They are the domain most responsive to dopamine-blocking treatment and the one the classic type I picture is built from.

Negative. A negative symptom is a subtraction from normal experience, the loss or diminution of a normal function. The representative signs cluster as blunted (flat) affect, alogia (poverty of speech), avolition, asociality and anhedonia, conventionally chained on the mnemonic below.

This domain carries much of the long-term disability and responds least well to antipsychotics. The distinction between primary (enduring, deficit) and secondary negative symptoms, and the deficit syndrome, is developed in the next topic.

Cognitive. The cognitive domain is the impairment of attention, processing speed, working memory, verbal learning and executive function. Deficits average about one standard deviation below expected performance, are present at the first episode, and are the strongest single predictor of functional outcome; executive function and attention may be the core deficits (Kaplan & Sadock 2024). Kraepelin's original *dementia praecox* foregrounded exactly this, then it was neglected for decades before contemporary studies restored it to the map.

Disorganised. The disorganisation domain is formal thought disorder (derailment, tangentiality, loosening of associations, incoherence) together with disorganised or bizarre behaviour and inappropriate affect. Factor-analytic work repeatedly pulls disorganisation out as its own factor distinct from the positive symptoms it was once bundled with, and it maps onto reduced dorsolateral prefrontal activity (Tasman 2024).

Affective (mood). The affective domain is the mood disturbance woven through the illness: depression, dysphoria, hopelessness and, decisively, suicide risk, plus the anxiety and demoralisation that accompany insight. It is not an epiphenomenon; it carries a large part of the mortality of the disorder and is easily missed when attention fixes on positive symptoms.

RULE **Describe the profile, not the subtype.** The five domains are semi-independent dimensions that vary in weight within and between patients; the correct clinical description is a profile across all five, and any one patient can score high on several at once.

TRAP **Reading a domain as a diagnosis.** A prominent negative-symptom picture is a point on the profile, not a "type II patient" filed away in a box; the domains coexist, and the affective and cognitive domains are the two most often forgotten because they are quieter than florid positive symptoms.

MNEMONIC

Domains "P-N-C-D-A"; negative symptoms "the 5 As"

The five domains read **P**ositive, **N**egative, **C**ognitive, **D**isorganised, **A**ffective. Within the negative domain, the representative signs are the **5 As**: **A**ffective blunting, **A**logia, **A**volition, **A**sociality, **A**nhedonia (with attentional impairment sometimes added as a sixth A, though attention properly belongs to the cognitive domain).

8.2 The domains as a table: representative signs and significance

The grid. The value of the map is that each domain has a short list of representative signs and a one-line clinical significance, which is what an examiner wants back when they ask you to "describe the symptom domains of schizophrenia."

DOMAIN	REPRESENTATIVE SIGNS	ONE-LINE SIGNIFICANCE
Positive	Delusions, hallucinations	**Florid, dopamine-responsive; drives admission; the type I core**
Negative	Blunted affect, alogia, avolition, asociality, anhedonia	**Enduring disability; poor drug response; the type II core**
Cognitive	Attention, working memory, processing speed, executive function	**Strongest predictor of functional outcome; present at first episode**
Disorganised	Formal thought disorder, disorganised behaviour, inappropriate affect	**Separates from positive on factor analysis; frontal-linked**
Affective (mood)	Depression, dysphoria, hopelessness, suicidality, anxiety	**Carries much of the mortality; the most-missed domain**

The five semi-independent symptom domains, each with its representative signs and the single fact to attach; the significance column is the discriminator an examiner rewards.

8.3 Crow's type I and type II: the two-syndrome phenotype model

The model. Crow (1985) proposed two syndromes of schizophrenia built from a combination of clinical and neurobiological features (Crow 1980, 1985). Type I is the positive-symptom syndrome: acute onset, delusions and hallucinations to the fore, preserved social functioning during remissions, a good response to antipsychotics, an underlying dopamine overactivity, potentially reversible, and no structural brain change. Type II is the negative-symptom syndrome: insidious onset, blunting and poverty to the fore, cognitive impairment, poor outcome and poor antipsychotic response, no clear dopamine overactivity but structural brain change, classically ventricular enlargement, and thought to be less reversible. The model was influential as an early re-focusing on the neurobiology of the disorder, but subsequent research did not strongly support the predicted biological subtypes and their correlations (Shorter Oxford Textbook of Psychiatry).

FEATURE	TYPE I	TYPE II
Dominant symptoms	Positive (delusions, hallucinations)	**Negative (blunting, poverty)**
Onset and course	Acute; potentially reversible	**Insidious; chronic, less reversible**
Cognition	Relatively preserved	**Cognitive impairment**
Antipsychotic response	Good	**Poor**
Proposed mechanism	Dopamine overactivity	**Structural change (ventricular enlargement)**
Structural brain change	Absent	**Present**

Crow's type I versus type II; the discriminating axis is positive-and-reversible-and-dopaminergic against negative-and-structural-and-treatment-resistant.

TRAP **Treating type I and type II as mutually exclusive boxes.** Crow himself allowed that a patient could show both, and most patients do; the two syndromes are poles of a dimension, not two disjoint categories, and a single patient commonly has positive and negative features together.

COMMON TRAP

Do not attach the dopamine hypothesis to schizophrenia as a whole through the Crow model. Crow tied dopamine overactivity specifically to the type I, positive-symptom, treatment-responsive picture and left the type II, negative-and-structural picture outside it. The dopamine and monoamine pathways themselves are cross-referenced to the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

8.4 Liddle's three-syndrome model: the factor-analytic dimensions

The model. Liddle (1987) studied patients with chronic schizophrenia and, from the clustering of symptoms, described three overlapping clinical syndromes, a three-syndrome model that he linked to distinct neuropsychological deficits and to patterns of regional cerebral blood flow (Liddle 1987; Liddle et al. 1992). The three are reality distortion, the disorganisation syndrome, and psychomotor poverty, and they map cleanly onto the positive, disorganised and negative groupings of the modern domain map.

Reality distortion

Delusions and hallucinations; the positive-symptom cluster.

Disorganisation syndrome

Formal thought disorder, inappropriate affect and bizarre behaviour; the disorganised cluster.

Psychomotor poverty

Flat affect, poverty of speech and decreased spontaneous movement; the negative cluster.

The neurobiological linkage. The single most reproducible finding from the model is the link between psychomotor poverty, impaired performance on frontal-lobe tasks, and decreased frontal blood flow ("hypofrontality"); disorganisation was associated with abnormal activity in the anterior cingulate and prefrontal cortex, and reality distortion with medial temporal and cingulate activity (Liddle et al. 1992). The three-factor structure, positive, negative and disorganisation, is the finding factor-analytic studies most consistently recover and is the historical bridge to the modern domains (Tasman 2024). The neuroimaging principles themselves belong to the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

RULE **Liddle's three collapse into the domain map.** Reality distortion is the positive domain, the disorganisation syndrome is the disorganised domain, and psychomotor poverty is the negative domain; the modern five-domain map simply adds the cognitive and affective dimensions.

8.5 From dimensions to nosology: why the models matter for classification

The through-line. The dimensional models are not museum pieces. The observation that positive, negative and disorganisation vary semi-independently, and that classical categories (paranoid, hebephrenic, catatonic) had poor reliability, temporal instability and low predictive

validity, is precisely the argument that led both ICD-11 and DSM-5 to drop the schizophrenia subtypes and replace them with a set of dimensional symptom specifiers rated on severity (Tandon et al. 2013; Kaplan & Sadock 2024). That nosological-change point is developed in the classification band; here the point is that Crow and Liddle are the intellectual ancestors of the specifier approach, and the five-domain profile is what the specifiers operationalise. The subtypes were dropped because dimensions describe the same patients better than categories do.

What this leaves for exams. Where a paper is explicitly ICD-10, the subtypes still exist and may be asked; where it is unmarked, describe the domains and note the dimensional turn. The management implications, that positive symptoms respond to antipsychotics and negative and cognitive symptoms respond poorly, point forward to the Schizophrenia: management, antipsychotics and adverse effects notes.

HOLD THIS

Schizophrenia is a profile across five semi-independent domains (positive, negative, cognitive, disorganised, affective), not a subtype; Crow compressed this into positive-reversible-dopaminergic type I versus negative-structural-treatment-resistant type II, and Liddle into reality distortion, disorganisation syndrome and psychomotor poverty, and the same dimensional logic is why both ICD-11 and DSM-5 dropped the classical subtypes.

GOOD TO REMEMBER

- **Five symptom domains:** positive, negative, cognitive, disorganised, affective; each a semi-independent dimension; the discriminator is that a patient carries a profile across all five, not a single subtype.
- **Positive domain:** delusions and hallucinations; an addition to normal experience; discriminator is dopamine-responsiveness and its central place in the type I picture.
- **Negative domain:** the 5 As (affective blunting, alogia, avolition, asociality, anhedonia); a subtraction from normal experience; discriminator is that it carries long-term disability and responds least to antipsychotics.
- **Cognitive domain:** attention, working memory, processing speed, executive function; discriminator is that it is the strongest predictor of functional outcome and is present at first episode.
- **Disorganised domain:** formal thought disorder, disorganised behaviour, inappropriate affect; discriminator is that factor analysis separates it from the positive domain.
- **Affective domain:** depression, dysphoria, suicidality; discriminator is that it carries much of the mortality and is the most-missed domain.
- **Crow type I:** positive symptoms, acute, good antipsychotic response, reversible, dopamine overactivity, no structural change; discriminator against type II is reversibility with treatment.
- **Crow type II:** negative symptoms, insidious and chronic, cognitive impairment, poor response, structural change (ventricular enlargement); discriminator is that it is not mutually exclusive from type I, they coexist.
- **Liddle three-syndrome:** reality distortion (positive), disorganisation syndrome (disorganised), psychomotor poverty (negative); discriminator is the reproducible link of psychomotor poverty to hypofrontality and impaired frontal-lobe task performance.

9 · Positive symptoms: delusions, hallucinations and thought disorder

Why this matters. The **positive symptom** cluster is what most residents call to mind when they think of schizophrenia, and it is where examiners test whether you can distinguish a phenomenon from a diagnosis. A **positive symptom** is an added, distorted experience: a belief, a percept or a disorder of the flow of thought that is present in the illness but absent in health. The raw descriptive definitions of these phenomena, what a delusion, a hallucination or a formal thought disorder actually is, are owned by the Psychometry, Assessment and Descriptive Psychopathology notes; here we do not re-define them from scratch but apply them to schizophrenia and ask which forms are characteristic.

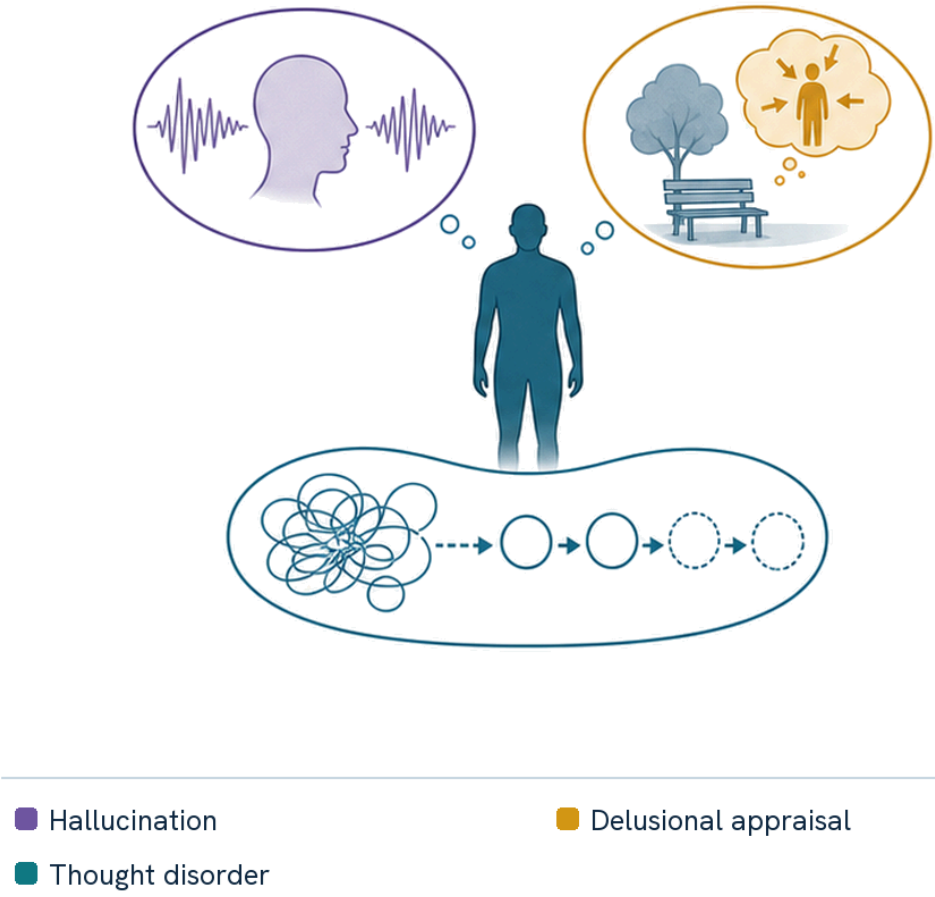


Fig 8.10 Three positive-symptom forms: perception without an external stimulus, fixed delusional interpretation of an event, and disruption of the form and sequence of thought or speech.

The governing principle for the whole topic is one line: no single positive symptom is specific to schizophrenia. Every delusion, every hallucination, every thread of disorganised speech can appear in mood disorder, in an organic state or in substance-induced psychosis. What matters in

the exam is the *form* that is characteristic, the company it keeps, and the differentials it should raise (Kaplan & Sadock 2024, Gelder et al. 2013).

9.1 Positive symptoms within the symptom domains

Both current classifications describe schizophrenia through symptom domains rather than a pathognomonic sign, and the positive domain sits alongside negative, cognitive, affective and psychomotor domains. The positive symptoms proper are **delusions, hallucinations, formal thought disorder** (inferred from disorganised speech) and grossly disorganised behaviour. ICD-11 requires at least two symptoms present most of the time for one month, with at least one drawn from its "core" list, and its items a) to d) are exactly the positive-symptom phenomena: persistent delusions, persistent hallucinations, disorganised thinking, and experiences of influence, passivity or control (ICD-11 CDDR 2024). DSM-5-TR cross-maps to the same phenomena but frames them under Criterion A and adds a six-month total duration.

RULE **No single positive symptom is specific to schizophrenia.** Diagnose on form, persistence and context, never on the presence of one delusion or one voice.

9.2 Delusions characteristic of schizophrenia: the themes

A delusion applied to schizophrenia keeps the descriptive definition from the Psychometry, Assessment and Descriptive Psychopathology notes, a fixed false belief held on inadequate grounds, unshakeable by reason and out of keeping with the person's background, and adds a characteristic set of themes. Persecutory content and delusions of reference are the most frequent, but themes alone carry little diagnostic weight; the attitude to them can help. In a depressive psychosis the patient accepts persecution as deserved punishment, whereas in schizophrenia he resents it as unwarranted (Gelder et al. 2013).

Persecutory delusion

Belief that people or organisations intend harm, are conspiring or spying; common but low specificity across psychoses.

Delusions of reference

Neutral events, remarks, articles or gestures are read as carrying a personal message about the patient; the referential form.

Grandiose delusion

Exaggerated belief in one's own importance, powers or identity; more typical of mania but occurs in schizophrenia.

Control and passivity delusion

Actions, impulses, sensations or thoughts are experienced as made or controlled by an outside agency; strongly suggestive of schizophrenia.

Bizarre delusion

Content that is culturally impossible and cannot derive from ordinary life (thoughts removed by radio waves); high weight in classification.

9.3 Control and passivity: the phenomena that point to schizophrenia

Among delusional themes, the passivity phenomena (delusions of control) carry the most diagnostic weight. Here the patient firmly believes that his movements, impulses, feelings or thoughts are brought about by an external agency rather than willed by himself (Gelder et al. 2013). The thought-possession delusions belong here: thought insertion (thoughts placed into the mind by others), thought withdrawal (thoughts removed, often with thought blocking) and thought broadcasting (unspoken thoughts known to others). These map directly to ICD-11 item d), experiences of influence, passivity or control, and to the classic Schneiderian first-rank symptoms whose descriptive definition is developed in the Psychometry, Assessment and Descriptive Psychopathology notes. Distinguish thought insertion from the obsessional patient, who is distressed by alien thoughts but never doubts they are his own.

9.4 Delusional mood and delusional perception: the onset phenomena

Two primary (autochthonous) experiences mark the onset of a delusional illness and are worth eliciting because they carry weight in the diagnosis of schizophrenia. Delusional mood (Wahnstimmung) is a strange, uncanny sense of foreboding that something sinister is about to happen; the world feels changed and charged with unspecified significance before any belief has crystallised. Delusional perception is a fully formed delusion arising directly from a normal, correctly perceived percept: the perception itself is normal, and it is the abnormal significance attached to it that is delusional (for example, a letter left on the desk is instantly known to mean that the patient must die). Note that delusional perception is a disorder of thought, not of perception (Gelder et al. 2013).

WORKED EXAMPLE

A young man says that over two weeks the streets began to feel "loaded", as if everyone knew something was coming; he could not say what (delusional mood). Then, seeing a red car turn the corner, he knew with total certainty and no reasoning that he had been chosen to save the city (delusional perception). The percept, a red car, was accurate; the sudden unquestionable meaning is the delusion. Both are primary phenomena and, taken with persistence over a month, weigh toward schizophrenia rather than a mood disorder.

9.5 Hallucinations: auditory hallucinations are the most characteristic

A hallucination applied to schizophrenia again takes its descriptive definition from the Psychometry, Assessment and Descriptive Psychopathology notes, a percept without an external stimulus, experienced as real and located in external space, and asks which modality and which content are characteristic. The answer is the auditory modality: the auditory hallucination, specifically voices, is the most characteristic hallucination of schizophrenia, and ICD-11 item b) notes hallucinations are "most commonly auditory" (ICD-11 CDDR 2024). Second-person voices that address the patient directly do not point to any one diagnosis; it is particular forms of the auditory hallucination that carry weight (Gelder et al. 2013).

Third-person voices

Voices referring to the patient as "he" or "she", discussing or arguing about him among themselves; characteristic of schizophrenia.

Running commentary

A voice giving a continuous commentary on the patient's actions as they happen; a Schneiderian first-rank form.

Thought echo

Hearing one's own thoughts spoken aloud, either as they are thought (Gedankenlautwerden) or repeated just after (echo de la pensee); characteristic.

TRAP **Treating any auditory hallucination as diagnostic.** A second-person voice, a derogatory voice or a single voice is not diagnostic; only the characteristic forms (third-person, running commentary, thought echo) carry weight, and even they are not pathognomonic.

9.6 Other modalities and the organic search

Hallucinations in modalities other than hearing are less common in schizophrenia and should lower your threshold for an organic workup. Visual hallucinations should always suggest the possibility of an organic disorder (delirium, temporal lobe epilepsy, drug intoxication or withdrawal, a space-occupying lesion), although they do occur in severe affective disorder and in schizophrenia; the content of a visual hallucination is of little diagnostic value (Gelder et al. 2013). Olfactory and gustatory hallucinations are infrequent and, when present, raise temporal lobe epilepsy and tumours of the olfactory pathway. Investigate the physical substrate before you settle on a primary psychotic disorder; the neuroimaging principles are set out in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

TRAP **Prominent visual hallucinations should prompt an organic workup.** Vivid or predominant visual, olfactory or tactile hallucinations point away from uncomplicated schizophrenia and toward a delirium, epilepsy, intoxication or a lesion until proven otherwise.

9.7 Formal thought disorder: the positive form in schizophrenia

Formal thought disorder, sometimes shortened to thought disorder, is a disturbance not of the content of individual thoughts but of the form and linkage between them, and it is inferred from disorganised speech because thought itself cannot be observed. Its descriptive definition sits in the Psychometry, Assessment and Descriptive Psychopathology notes; here we apply the positive form to schizophrenia. The positive form is a loosening of the normal connections between ideas so that speech drifts, jumps or fragments. ICD-11 lists it as item c), disorganised thinking, giving tangentiality, loose associations, irrelevant speech and neologisms, with "word salad" as its severe end (ICD-11 CDDR 2024). The clinical assessment and grading of disorganised speech is developed in the disorganisation topic; here hold only that the positive form of formal thought disorder is a positive symptom.

Loosening of associations

Ideas slide from one to another without logical connection; the core positive formal thought disorder in schizophrenia.

Tangentiality

Replies veer off the point and never return to it; the answer is oblique to the question.

Neologism

A newly coined word or a familiar word used in a private idiosyncratic sense.

MNEMONIC

PDF for the positive triad

Perceptions gone wrong (hallucinations, auditory above all), **D**elusions (persecutory, referential, grandiose, control and passivity, bizarre), **F**ormal thought disorder (loosening, tangentiality, neologism). Three phenomena, one positive-symptom domain.

9.8 First-rank symptoms: a useful map, not a diagnostic test

Many of the characteristic positive phenomena above, thought echo, running commentary and third-person voices, thought insertion, withdrawal and broadcasting, passivity and delusional perception, are the Schneiderian first-rank symptoms (Schneider 1959). ICD-10 placed considerable weight on them; the phenomena themselves are defined in the Psychometry, Assessment and Descriptive Psychopathology notes. The examiner's point is that first-rank symptoms are neither necessary nor sufficient: they occur in roughly 10 to 20 percent of manic patients and in organic psychoses, and are absent in many people with schizophrenia. Treat them as a memory scaffold for the characteristic forms, not as a diagnostic test.

TRAP **Calling first-rank symptoms pathognomonic.** They are characteristic, not specific; present in mania and organic states, absent in many with schizophrenia. ICD-11 and DSM-5 no longer give them privileged diagnostic status.

9.9 Where the positive symptoms sit in the criteria and the differential

ICD-11 runs the positive symptoms forward as items a) to d) and needs at least one core symptom over one month; DSM-5-TR cross-maps the same phenomena under Criterion A and asks for six months total. A legacy ICD-10 box below shows what changed. In the differential, the same positive symptoms in a full mood episode point to a mood disorder with psychotic features, in a short-lived acute picture to an acute and transient psychotic disorder, and in an encapsulated non-bizarre belief to delusional disorder; those entities are developed in the Other psychotic disorders, delusional syndromes and catatonia notes. Management of the positive symptoms, antipsychotics and their adverse effects, belongs to the Schizophrenia: management, antipsychotics and adverse effects notes.

POSITIVE PHENOMENON	CHARACTERISTIC FORM IN SCHIZOPHRENIA	DISCRIMINATOR TO HOLD
Delusion	Persecutory, referential, control and passivity, bizarre	**Passivity and bizarre content weigh most; themes alone are low-specificity**
Auditory hallucination	Third-person, running commentary, thought echo	**Second-person or derogatory voices are not diagnostic**
Non-auditory hallucination	Uncommon; visual, olfactory, tactile	**Prominent visual hallucinations should prompt an organic workup**
Formal thought disorder	Loosening of associations, tangentiality, neologism	**Positive form; inferred from disorganised speech, graded in the disorganisation topic**

The positive-symptom phenomena, their characteristic schizophrenia form, and the single discriminator to carry into a viva.

INDIA

Where the exit examination and many Indian question banks still test ICD-10, the positive symptoms are examined through Schneider's first-rank symptoms and the ICD-10 group (a) to (d). Know both: run ICD-11 forward, but be able to reproduce the ICD-10 first-rank framing when the paper asks for it.

COMMON TRAP

Diagnosing schizophrenia on a florid positive picture that is unfolding inside an untreated manic or depressive episode. Mood-congruent grandiose or nihilistic delusions and even brief first-rank symptoms occur in mania; the positive symptoms must be assessed against the mood state and its timeline before the label is applied.

GOOD TO REMEMBER

- **Delusion in schizophrenia:** a fixed false belief out of keeping with background; characteristic themes are persecutory, referential, grandiose, control and passivity, and bizarre; the discriminator is that passivity and bizarre content weigh most while theme alone is low-specificity.
- **Delusional mood (Wahnstimmung):** an uncanny foreboding that something significant is about to happen, before any belief forms; a primary onset phenomenon weighing toward schizophrenia.
- **Delusional perception:** a full delusion arising from a normally perceived percept; the discriminator is that the perception is normal and only the attached meaning is delusional, and it is classed as a disorder of thought.
- **Passivity phenomena (delusions of control):** actions, impulses, feelings or thoughts felt as made by an outside agency, including thought insertion, withdrawal and broadcasting; the discriminator is the loss of the sense of ownership or agency, strongly suggestive of schizophrenia.
- **Auditory hallucination:** the most characteristic hallucination of schizophrenia; the discriminator forms are third-person voices commenting or arguing, running commentary and thought echo, whereas second-person voices are non-specific.
- **Formal thought disorder (positive form):** a disturbance of the linkage of thoughts inferred from disorganised speech; core forms are loosening of associations, tangentiality and neologism, with word salad at the severe end.
- **Schneiderian first-rank symptoms:** a map of characteristic positive phenomena (Schneider 1959); the discriminator is that they are neither necessary nor sufficient, occurring in 10 to 20 percent of manic patients and dropped from privileged status in ICD-11 and DSM-5.

GOOD TO REMEMBER

- **ICD-10 (legacy) positive-symptom framing:** weighted the first-rank symptoms heavily, grouping thought echo/insertion/withdrawal/broadcasting (a), passivity and delusional perception (b), third-person and running-commentary voices (c) and bizarre persistent delusions (d); one such symptom for one month sufficed.
- **What changed in ICD-11 and DSM-5:** first-rank symptoms lose their special diagnostic weight, no positive symptom is privileged as pathognomonic, and the emphasis shifts to at least two symptoms (one core) over the duration threshold with a dimensional symptom-domain description.

HOLD THIS

No positive symptom is specific to schizophrenia; the characteristic forms are third-person auditory hallucinations, thought echo and passivity phenomena, and prominent visual hallucinations should send you looking for an organic cause.

10 · Negative symptoms and the deficit syndrome

The negative symptoms are the quiet half of schizophrenia and the half that decides the patient's life. They are a subtraction from normal experience, and the examiner tests whether the resident can list the domains, separate **primary** from **secondary** forms, and recognise the validated deficit-syndrome subgroup. This topic applies the descriptive signs to schizophrenia; the raw phenomenological definitions of flat affect, poverty of speech and the rest belong to the Psychometry, Assessment and Descriptive Psychopathology notes and are not re-derived here.

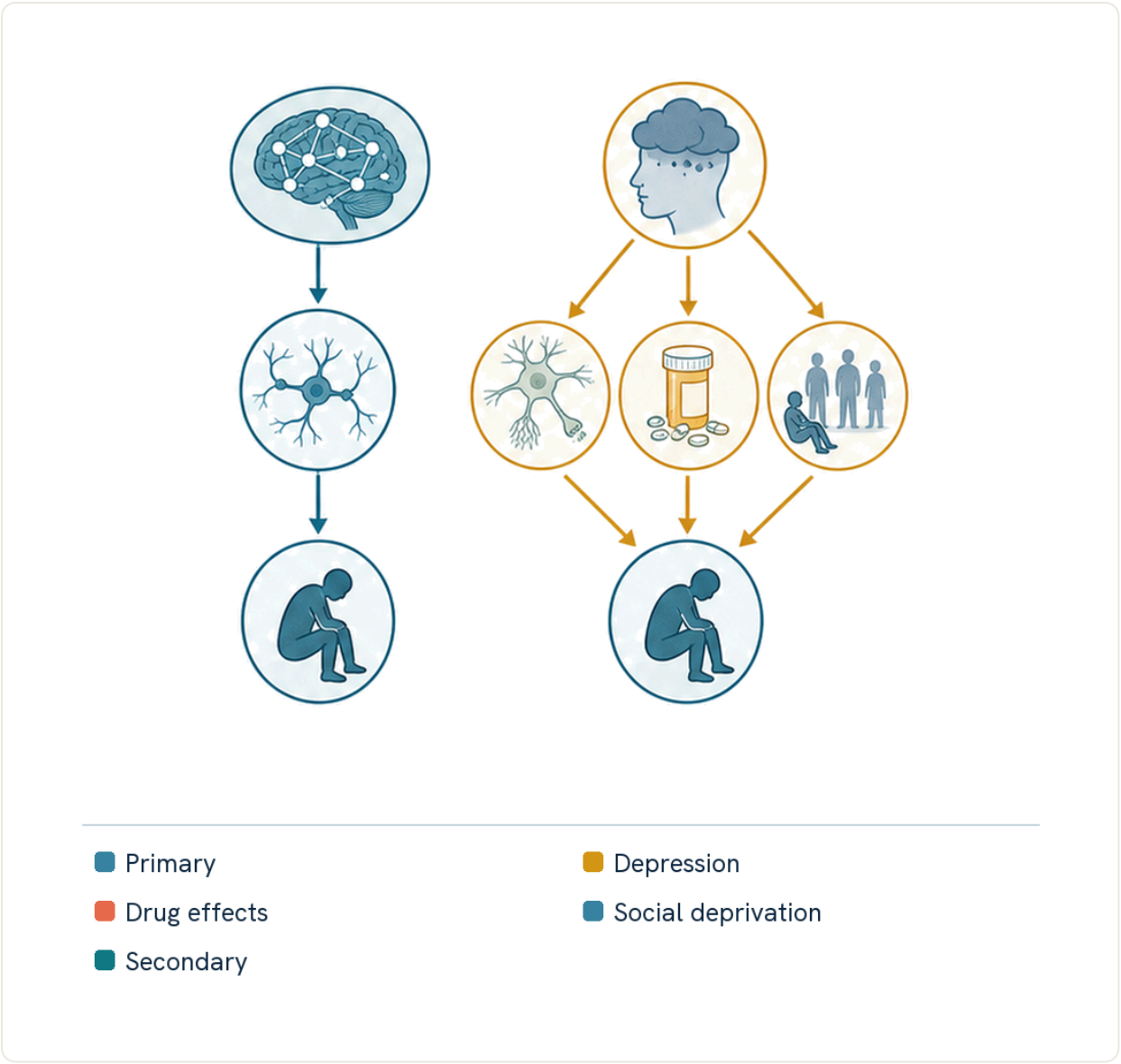


Fig 8.11 Primary and secondary negative symptoms. A direct illness-domain pathway must be distinguished from reduced motivation or expression secondary to depression, extrapyramidal effects, sedation or environmental deprivation.

Why this is the payoff. Negative symptoms predict short-term and long-term disability, social function and quality of life better than positive or disorganisation symptoms, they are more stable across time, and they respond least well to antipsychotics (Kaplan & Sadock 2024). The single most examinable move is to always split a negative-symptom picture into what the disease is doing and what a drug, a delusion or a depression is doing, because the treatable causes differ. Get that split right and the deficit syndrome, the assessment scales and the management pointers all follow.

10.1 What a negative symptom is

Definition. A negative symptom represents a loss or diminution of a normal mental function, and stands in contrast to a positive symptom, where a perception, cognition or behaviour is added to normal mental life (Kaplan & Sadock 2024). The concept is old: Kraepelin foregrounded emotional dullness and loss of the "mainsprings" of volition, and for Bleuler emotional deterioration stood at the forefront of the picture. Negative symptoms are not specific to

schizophrenia, mild forms appear in a minority of the general population, but the pattern of multiple enduring negative symptoms not due to medication or social effects is most characteristic of schizophrenia.

RULE **Negative symptoms drive disability.** The severity of negative symptoms predicts social function and long-term outcome better than positive or disorganisation symptoms, and they are the more stable dimension across time.

10.2 The five domains: the five A's

The five. The NIMH-MATRICS consensus conference (2005) fixed five negative-symptom domains: affective flattening (blunted affect), alogia, avolition, anhedonia and asociality (social withdrawal), memorised as the five A's (Kaplan & Sadock 2024). Each is a loss of a distinct function, and a patient carries a profile of varying weight across the five.

Affective flattening

A reduction in the intensity of emotional expression: deficits in facial expression, prosody, gesture and vocal production; near-absence is flat affect. More common in men, early onset and poor premorbid function.

Alogia

A decrease in the production of speech, the "negative thought disorder": increased response latency, short replies, long pauses and paucity of spontaneous speech. It is one of the commoner negative symptoms. Poverty of content with normal volume is a disorganisation sign, not alogia.

Avolition

A loss of will or drive, an inability to initiate and persist in goal-directed activity (neurological *abulia*). Impairs grooming, self-care, work and study, and is the single largest driver of negative-symptom disability. Closely related to apathy.

Anhedonia

A loss of the capacity to derive pleasure or interest from experiences, activities or relationships; likely the most persistent negative symptom. When part of a negative syndrome it is not a manifestation of depression.

Asociality

Passive or apathetic social withdrawal: indifference to relationships, reduced drive to socialise, decreased sexual and intimate interest; linked to theory-of-mind deficits.

MNEMONIC

The 5 A's

Affective flattening, **A**logia, **A**volition, **A**nhedonia, **A**sociality. Attentional impairment is sometimes offered as a sixth A, but attention belongs to the cognitive domain and is not a negative symptom proper.

10.3 The modern two-factor grouping

Two factors, not five islands. Repeated factor-analytic studies collapse the five domains into two correlated groups: an avolition-apathy (motivation-and-pleasure) factor made of avolition,

anhedonia and asociality, and a diminished expression factor made of affective flattening and alogia (Kaplan & Sadock 2024). The clinical logic is elegant: the avolition-apathy factor is elicited by interview (what the patient does and wants), whereas diminished expression is observed by the clinician (how the patient looks and speaks). This two-factor structure is exactly why DSM-5-TR names "diminished emotional expression or avolition" as the representative negative symptoms in its Criterion A.

FACTOR	COMPONENT DOMAINS	HOW IT IS CAPTURED
Avolition-apathy (motivation and pleasure)	Avolition, anhedonia, asociality	**Elicited by interview (internal drive and pleasure)**
Diminished expression	Affective flattening, alogia	**Observed by the clinician (behaviour and speech)**

The two-factor grouping of the five negative-symptom domains; the discriminator is interview-elicited motivation versus clinician-observed expression, and it underlies the DSM-5-TR pairing of avolition with diminished emotional expression.

10.4 Primary versus secondary negative symptoms

The split that changes management. A secondary negative symptom is a negative symptom produced by another, potentially removable cause: untreated positive symptoms (a suspicious, hallucinating patient withdraws), depression, extrapyramidal side effects of antipsychotics, or understimulation of an institutionalised or socially isolated patient (Tasman 2024). Secondary negative symptoms are potentially reversible when the driver is treated. A primary negative symptom is intrinsic to the disease process, is the least variable of the symptoms of schizophrenia, tends to persist throughout the illness course, and predicts future disability (Kaplan & Sadock 2024). The clinical task is to strip out every treatable secondary cause before concluding that what remains is primary and enduring.

SOURCE OF THE NEGATIVE SYMPTOM	MECHANISM	TREATABLE? / ACTION
Positive symptoms	Withdrawal driven by paranoia, hallucinations, preoccupation	**Yes; optimise antipsychotic for positive symptoms**
Depression	Depressive anhedonia, amotivation, psychomotor slowing	**Yes; treat the depressive episode**
Extrapyramidal side effects	Drug-induced parkinsonism mimicking blunting and avolition	**Yes; reduce dose, switch agent, or add anticholinergic (neuroleptic-induced deficit syndrome)**
Understimulation	Institutionalism, social isolation, poverty of environment	**Yes; enrich environment, rehabilitation**
Primary (intrinsic)	Core disease process, enduring	**Poor drug response; the residue after secondary causes are excluded**

The four treatable sources of secondary negative symptoms against the intrinsic primary form; the discriminator is reversibility, and each secondary cause has a different remedy, which is why they must be separated.

RULE **Always separate primary from secondary.** Exclude positive symptoms, depression, extrapyramidal side effects and understimulation first; only the residue is primary. The treatable causes differ, so the split dictates the treatment.

TRAP **Calling drug-induced parkinsonism or a depressive episode "primary negative symptoms."** Masked facies, bradykinesia and amotivation from an antipsychotic, or depressive anhedonia, are reversible mimics; labelling them primary abandons a treatable patient.

COMMON TRAP

The neuroleptic-induced deficit syndrome is the classic mimic: high-dose D2 blockade blunts affect and drive so closely that it looks like the disease's own negative symptoms (Stahl). A parkinsonian patient on a high antipsychotic dose who is flat and avolitional needs the dose questioned, not a "poor prognosis" label. Antipsychotics, their adverse effects and dosing are developed in the Schizophrenia: management, antipsychotics and adverse effects notes.

10.5 The deficit syndrome (Carpenter)

The validated subgroup. The deficit syndrome, defined by Carpenter and colleagues, is the presence of enduring **primary** negative symptoms that persist between episodes and during periods of clinical stability, not attributable to positive symptoms, depression, medication or understimulation (Carpenter et al. 1988; Kaplan & Sadock 2024). It is operationalised by the Schedule for the Deficit Syndrome, which requires at least two negative symptoms present in the preceding year, from restricted affect, diminished emotional range, poverty of speech, curbing of interests, diminished sense of purpose and diminished social drive. It is now generally accepted as a separate disease process within schizophrenia, not merely severe illness.

The distinct picture. Deficit-syndrome patients have a poorer prognosis for functional recovery, more insidious onset with progressive negative symptoms, worse premorbid function, lower quality of life and a poor response of the negative symptoms to medication or social-skills training. Notably they have no more delusions or hallucinations than non-deficit patients, less prominent dysphoria, and fewer suicidal ideas and attempts, a discriminating profile the examiner rewards. Where a formal deficit assessment is impractical, Buchanan's persistent negative symptoms criterion offers a pragmatic proxy: schizophrenia plus at least two negative symptoms for at least 12 months during clinical stability, not due to comorbidity or medication.

~15%	25 to 30%	≥2
DEFICIT SYNDROME, FIRST-EPISODE	DEFICIT SYNDROME, CHRONIC	NEGATIVE SYMPTOMS IN PAST YEAR (SDS)

A meta-analysis of 23 studies put the overall rate near 30 percent, with rates lower early in the illness and rising over the first five years (Kaplan & Sadock 2024). Roughly **~15%** of first-episode and **25 to 30%** of chronic patients meet deficit-syndrome criteria (Tasman 2024).

TRAP **Equating "deficit syndrome" with "severe schizophrenia."** It is a distinct, validated subgroup with its own course and a paradoxically *lower* suicide and dysphoria burden, not simply the worst end of a severity spectrum.

10.6 Assessment: the scales

The instruments. The first purpose-built scale was Andreasen's sans (Scale for the Assessment of Negative Symptoms), paired with the SAPS for positive symptoms; it covers affective flattening, alogia, avolition-apathy, anhedonia-asociality and attentional impairment (Andreasen 1982). In practice the negative subscale of the panss (Positive and Negative Syndrome Scale) became the research and trial standard, though its original three-subscale split (30 items: 7 positive, 7 negative, 16 general psychopathology) does not map cleanly onto the true five-factor structure (Kay et al. 1987). The newer second-generation scales, built directly on the MATRICS five-domain consensus, are the BNSS (Brief Negative Symptom Scale, Kirkpatrick 2011) and the CAINS (Clinical Assessment Interview for Negative Symptoms, Kring & Blanchard 2013); both separate the motivation-and-pleasure factor from diminished expression, and the BNSS was designed for both research and busy clinical settings.

SCALE	WHAT IT IS	ONE THING TO KNOW
SANS	Andreasen's dedicated negative-symptom scale (with SAPS)	**First purpose-built; five sub-scales including attention**
PANSS negative subscale	Negative arm of the 30-item PANSS	**Trial standard; original split predates the five-factor model**
BNSS	Brief Negative Symptom Scale (Kirkpatrick)	**MATRICS-based; separates the two factors; clinic-usable**
CAINS	Clinical Assessment Interview for Negative Symptoms	**MATRICS-based; motivation-and-pleasure vs expression**

The four assessment instruments; the discriminator is generation, SANS and the PANSS negative subscale are first-generation, while the BNSS and CAINS are second-generation, built on the two-factor MATRICS consensus.

HOLD THIS

Deficit syndrome = enduring PRIMARY negative symptoms (Carpenter), persisting between episodes and NOT due to positive symptoms, depression, extrapyramidal side effects or understimulation; that persistence between episodes is the whole discriminator.

GOOD TO REMEMBER

- **Negative symptom:** a loss or diminution of normal function (contrast the positive symptom, an addition); best single predictor of long-term social disability.
- **The five A's:** affective flattening, alogia, avolition, anhedonia, asociality; the MATRICS (2005) five negative-symptom domains.
- **Two-factor grouping:** avolition-apathy (avolition, anhedonia, asociality, interview-elicited) versus diminished expression (affective flattening, alogia, clinician-observed); the basis for DSM-5-TR "diminished emotional expression or avolition."
- **Secondary negative symptoms:** caused by positive symptoms, depression, extrapyramidal side effects or understimulation; potentially reversible; treat the driver.
- **Primary negative symptoms:** intrinsic, enduring, the least variable symptoms; poor drug response; the residue after secondary causes are excluded.
- **Deficit syndrome (Carpenter):** enduring primary negative symptoms persisting between episodes; a validated distinct subgroup, roughly 15 percent first-episode and 25 to 30 percent chronic; discriminator is persistence outside episodes and outside depression/extrapyramidal effects.
- **Scales:** SANS (Andreasen) and PANSS negative subscale (first-generation); BNSS and CAINS (second-generation, MATRICS-based, two-factor).

11 · Disorganisation: disorganised speech and behaviour

The **disorganisation** (disorganization) domain is the third arm of the phenomenology of schizophrenia, distinct from the positive and negative domains and repeatedly pulled out as its own factor on factor-analytic work. It has two observable faces: **disorganised speech** (disorganized speech), which is the clinically visible surface of formal thought disorder, and **disorganised behaviour** (disorganized behavior), the disturbance of goal-directed action together with inappropriate affect. Both are inferences drawn from what the examiner can watch and hear, which is exactly why they carry weight in an assessment.

Why this matters. The raw descriptive definitions of the signs, what formal thought disorder, a neologism or inappropriate affect *is* as a phenomenon, are not re-derived here; they belong to the Psychometry, Assessment and Descriptive Psychopathology notes, and this topic applies them to schizophrenia. The examiner rewards the resident who understands that we never observe thought directly: we observe speech and behaviour and infer a disorder of thought form from them. In ICD-11 this domain is written explicitly as "formal thought disorder (typically manifested as disorganized speech) and disorganized behaviour" (ICD-11 CDDR 2024), so the vocabulary of this topic is the vocabulary the criteria themselves use.

11.1 Disorganised speech is the observable face of formal thought disorder

The core principle. Formal thought disorder refers to an abnormality in the coherence and logical structure of thought, the "how" or mechanics of thinking rather than its content, which makes conversation difficult to follow or at times incomprehensible (Companion to Psychiatric Studies). We cannot inspect the form of thought directly, so disorganised speech (disorganized speech) is the clinical evidence from which formal thought disorder is inferred. This is why ICD-11 and DSM-5-TR both phrase the criterion as formal thought disorder "typically manifested as

disorganized speech" (ICD-11 CDDR 2024): the speech is the sign, the thought disorder is the construct.

RULE **Speech is the evidence, thought disorder is the inference.** Disorganised speech is the clinical evidence of formal thought disorder; you rate the disorder only from an actual sample of the patient's speech, never from a global impression.

TRAP **Labelling culturally normal or dialectal speech as thought-disordered.** Speech that is indirect, allusive, code-switched or dialectal in the patient's own linguistic culture, or fluent in a non-native second language, can look loose to an examiner outside that culture; that is a language and register phenomenon, not formal thought disorder.

11.2 Derailment and loosening of associations

The prototype. Derailment, historically loosening of associations and also called tangential or "knight's move" thinking, is the prototype of disorganised speech: the train of thought slips off its track onto an idea that is obliquely related or completely unrelated (Andreasen 1979). Individual derailments may be slight, so the speaker digresses only gradually from the original point, or the links may be plainly obscure. The meaning is typically lost across several sentences, which distinguishes it from incoherence, where the individual sentence itself is already meaningless. Bleuler's original "loosening of associations" was one of his four fundamental symptoms, so this sign sits at the historical centre of the concept of schizophrenia.

11.3 Tangentiality and circumstantiality: the pair to separate

The discriminator. Tangentiality is an oblique or irrelevant reply to a question in which the speaker never returns to the goal, whereas circumstantiality is speech that is very indirect and delayed in reaching its goal, loaded with tedious detail and parenthetical remarks, but which does eventually arrive at the point (Andreasen 1979). The single distinguishing feature is whether the goal idea is ultimately reached: circumstantial speech gets there by a long road, tangential speech never gets there at all. Circumstantiality is not specific to schizophrenia and is common in normal individuals, the obsessional, and organic states, so it carries far less diagnostic weight than derailment.

SIGN	WHAT HAPPENS	DISCRIMINATOR
Circumstantiality	Long, over-detailed, parenthetical route to the answer	**The goal idea is eventually reached**
Tangentiality	Oblique or irrelevant reply that veers away	**The goal idea is never reached**
Derailment	Train of thought slips track across sentences	**Meaning lost over several sentences; links obscure**
Incoherence (word salad)	Individual sentences themselves meaningless	**Breakdown at the single-sentence level**

The disorganised-speech spectrum ordered by severity; the examiner's favourite pair is circumstantiality versus tangentiality, separated by whether the point is ever reached.

11.4 Word salad, incoherence and clang associations

The severe end. Word salad (incoherence, schizophasia) is the severe pole: speech that is essentially incomprehensible, where the individual sentence itself has no meaning because grammar and syntax are ignored or cementing words are dropped (Companion to Psychiatric Studies; Andreasen 1979). Clang associations are a pattern in which word choice is governed by sound, rhyme or pun rather than meaning, so that a word similar in sound drags in a new thought. Clanging is classically emphasised in mania alongside flight of ideas, but it also appears in the disorganised speech of schizophrenia; its presence should therefore prompt a careful look for an affective picture, because diagnosing schizophrenia inside an untreated mood episode is a standard error. Flight of ideas and clang associations as mood-related thought-form disorders, and delusional mood, cross-reference to the Psychometry, Assessment and Descriptive Psychopathology notes.

11.5 Neologisms and word approximations

The invented word. A neologism is a newly formed word or phrase whose derivation cannot be understood, coined to express a concept for which the patient has no dictionary word (Andreasen 1979); classic examples are invented tokens such as "tarn-harn". The term is also loosely applied to existing words used in idiosyncratic ways. A related, milder variant is the word approximation (paraphasia), where an imprecise or old word is substituted for a familiar one, for instance a patient speaking of having "a menu three times a day" instead of three meals a day (Cameron 1938). Neologisms are often found in conjunction with incoherence, so their appearance signals the more severe end of the spectrum.

WORKED EXAMPLE

Asked how she was brought to hospital, a patient replied, "In a convestation, you fool" (Kaplan & Sadock 2024). "Convestation" is a neologism: an invented word with no recoverable dictionary meaning, embedded in speech that is otherwise grammatically intact, which locates the disturbance at the level of word formation rather than whole-discourse derailment.

11.6 Poverty of content of speech: the bridge to the negative domain

The empty message. Poverty of content of speech (alogia of content) is speech that is adequate in amount but conveys little information because it is vague, over-abstract, over-concrete, repetitive or stereotyped; the replies are long enough but the message is empty (Andreasen 1979). It must be separated from *poverty of speech* (reduced amount of speech), which is a negative symptom akin to avolition affecting the domain of speech (Companion to Psychiatric Studies). Poverty of content is conventionally grouped with the disorganisation domain because the disturbance is in the form and informativeness of the message, whereas poverty of speech, blunted affect and avolition belong to the negative domain; the two are easy to confuse and are separated by amount (poverty of speech) versus emptiness (poverty of content).

HOLD THIS
Disorganised speech is the observable evidence of formal thought disorder; you must quote an actual example of the patient's speech, and circumstantiality reaches its goal whereas tangentiality never does.

11.7 Disorganised behaviour: impaired goal-directed activity and bizarre acts

The behavioural face. Disorganised behaviour (disorganized behavior) in ICD-11 is "grossly disorganized behaviour that impedes goal-directed activity", behaviour that appears bizarre or purposeless, unpredictable, or with inappropriate emotional responses that interfere with the ability to organise behaviour (ICD-11 CDDR 2024). It ranges from difficulty performing everyday sequenced tasks and neglect of self-care through to overtly bizarre, purposeless acts. The defining feature is the breakdown of goal-directed activity: the behaviour is not organised toward an end. ICD-11 explicitly separates this from abnormal psychomotor and catatonic behaviour, which is rated in a distinct psychomotor domain, not here.

11.8 Inappropriate affect (incongruity of affect)

The mismatch. Inappropriate affect (incongruity of affect) is emotional expression that is discordant with the thought content or situation, for example laughing while describing a bereavement, and is grouped within the disorganisation picture rather than the negative domain. It is distinct from *blunted or flat affect*, which is a reduction in the range and intensity of emotional expression and is a negative symptom: incongruity is a mismatch of affect, blunting is a loss of affect. Incongruity of affect was, with thought disorder, one of the features Bleuler and later clinicians attached particular significance to as a fundamental disturbance of schizophrenia (Companion to Psychiatric Studies).

TRAP **Confusing inappropriate affect with blunted affect.** Inappropriate (incongruous) affect is a mismatch between emotion and context and sits in the disorganisation domain; blunted or flat affect is an absence of emotional expression and sits in the negative domain.

11.9 Catatonia: flagged here, developed elsewhere

The pointer. Catatonic phenomena, stupor, mutism, negativism, posturing, waxy flexibility, echolalia, echopraxia, stereotypies and excitement, form part of the broader disorganised and psychomotor picture and were historically Kraepelin's catatonic subtype. They are flagged here only as part of that picture; ICD-11 rates them in a separate psychomotor-symptoms domain and treats catatonia as its own entity that can be associated with schizophrenia or arise independently. Catatonia as an entity, its full sign list, its assessment scales and its management, is developed in the Other psychotic disorders, delusional syndromes and catatonia notes, not here. Its management, and the management of schizophrenia as a whole, points forward to the Schizophrenia: management, antipsychotics and adverse effects notes.

GOOD TO REMEMBER

- **Formal thought disorder:** disorder of the form or coherence of thought (the "how" of thinking), inferred from speech; discriminator is that it is the construct, and disorganised speech is its observable evidence.
- **Derailment / loosening of associations:** train of thought slips track onto obliquely or unrelated ideas (Andreasen 1979); discriminator is meaning lost over several sentences, and it was one of Bleuler's fundamental symptoms.
- **Tangentiality:** oblique reply that veers off; discriminator is the goal idea is *never* reached.
- **Circumstantiality:** over-detailed, delayed route to the answer; discriminator is the goal idea *is* eventually reached, and it is non-specific (common in normals and organic states).
- **Incoherence / word salad (schizophasia):** speech incomprehensible at the single-sentence level; discriminator is breakdown within the sentence, versus derailment across sentences.
- **Clang associations:** word choice governed by sound, rhyme or pun; discriminator is its classic link to mania, so it should prompt a search for a mood episode.
- **Neologism:** invented word whose derivation cannot be understood (Andreasen 1979); discriminator is a novel token with no dictionary meaning, versus the milder word approximation (paraphasia).
- **Poverty of content of speech:** adequate amount but empty message (Andreasen 1979); discriminator is amount preserved but informativeness lost, versus poverty of speech (reduced amount, a negative symptom).
- **Disorganised behaviour:** grossly disorganised, bizarre or purposeless behaviour impeding goal-directed activity (ICD-11 CDDR 2024); discriminator is the breakdown of goal direction, rated separately from catatonic psychomotor signs.
- **Inappropriate (incongruous) affect:** emotion discordant with context; discriminator is a mismatch of affect (disorganisation domain), versus blunted affect which is a loss of affect (negative domain).

MNEMONIC

Speech disorganisation "DDT-C-N-P": Derailment, Distractibility/Tangentiality, word-salad (incoherence), Circumstantiality, Neologism, Poverty-of-content

Run the disorganised-speech signs as **D**erailment (loosening of associations), **T**angentiality, word salad / incoherence, **C**lang and **C**ircumstantiality, **N**eologism (with word approximations), and **P**overty of content of speech; then add the two behavioural signs, disorganised behaviour and inappropriate affect.

INDIA

In a multilingual, code-switching setting, an examiner who does not share the patient's language or dialect can over-call formal thought disorder: allusive narration, proverb-heavy speech, or fluent code-switching between languages is a register phenomenon, not disorganised speech. Assess speech form in the language the patient is most fluent in, ideally with an interpreter who can flag what is culturally normal, before rating derailment or tangentiality.

12 · Schneider's first-rank symptoms and Bleuler's fundamental symptoms

Why this matters. Two great phenomenological frameworks shaped how a century of psychiatry decided who has schizophrenia, and examiners love to test whether you can keep them apart. **Eugen Bleuler** asked what lies at the *core* of the illness and answered with his fundamental symptoms, the four A's; **Kurt Schneider** asked which symptoms make the diagnosis *reliable* in the clinic and answered with his first-rank symptoms. The two men were solving different problems, and confusing their lists is the classic exam error. This topic applies both frameworks to schizophrenia and cross-references the raw descriptive definitions of the underlying phenomena, what a delusion, a hallucination or a passivity experience actually is, to the Psychometry, Assessment and Descriptive Psychopathology notes rather than re-defining them here.

The governing tension is one line: Schneider's symptoms are pragmatic diagnostic pointers with no claim to being the essence of the illness, whereas Bleuler's are a theory of what schizophrenia fundamentally *is*. Neither list survives as a diagnostic test in modern nosology, and that loss of status is itself high-yield (Kaplan & Sadock 2024, Gelder et al. 2013).

12.1 Two frameworks, two different questions

Bleuler (1911), renaming Kraepelin's dementia praecox as the "group of schizophrenias", was concerned with the psychological mechanism of the disorder and asked what feature was present in every case. His answer was a splitting or loss of harmonic coordination among thought, emotion and behaviour, captured in the fundamental symptoms. Kurt Schneider (1959), by contrast, made no claim about the essence of schizophrenia; he simply identified a group of symptoms of the first rank that, in the absence of coarse brain disease, made the diagnosis more reliable in everyday practice (Kaplan & Sadock 2024). Older texts write the term as either "first-rank" or "first rank", and both spellings refer to the same Schneiderian set. It is worth noting explicitly that, unlike Bleuler's fundamental symptoms, Schneider's symptoms were never supposed to have any central psychopathological role, merely that they were valuable in making the diagnosis (Gelder et al. 2013).

RULE **Bleuler asks what schizophrenia is; Schneider asks how to spot it reliably.** Fundamental symptoms are a theory of the core; first-rank symptoms are pragmatic diagnostic pointers.

12.2 Schneider's first-rank symptoms: the enumerated list

The Schneiderian first-rank symptoms are a defined set of eleven phenomena, and residents are expected to reproduce them. Their descriptive definitions belong to the Psychometry, Assessment and Descriptive Psychopathology notes; here we enumerate them as applied to schizophrenia (Schneider 1959, Kaplan & Sadock 2024). They fall into three natural families: special auditory hallucinations, disorders of the possession and control of thought, and made experiences of feeling, impulse and act, with delusional perception standing on its own. Somatic passivity and the made experiences together constitute the passivity phenomena, in which the patient experiences his own feelings, impulses or acts as imposed by an external agent.

Audible thoughts (thought echo)
Hearing one's own thoughts spoken aloud, as they are thought or echoed just after (Gedankenlautwerden).

Voices arguing or discussing (third person)
Two or more voices arguing or discussing the patient among themselves, referring to him as "he" or "she".

Voices commenting (running commentary)
A voice giving a continuous commentary on the patient's actions or thoughts as they happen.

Thought withdrawal
The sensation that thoughts are actively removed from the mind by an external agent.

Thought insertion
Thoughts experienced as placed into the mind by an outside agency, not the patient's own.

Thought broadcasting
The sense that one's thoughts escape and are experienced as real by others, made audible or known by telepathy.

Made feelings, impulses and acts
Feelings, impulses or volitional acts experienced as imposed and controlled by an external agent; the patient is a passive participant.

Somatic passivity
Bodily (tactile or visceral) sensations experienced as imposed on the patient by an outside agency.

Delusional perception
A normal percept to which a sudden, unquestionable and idiosyncratic delusional meaning is attached; a two-stage phenomenon.

12.3 The logic of the first-rank list

The list is easier to hold once its structure is clear. Three of the eleven are the special auditory hallucinations (audible thoughts, third-person voices, running commentary). Three are disorders of the possession of thought (thought withdrawal, thought insertion, thought broadcasting). Three are the made experiences of the will (made feelings, made impulses, made acts), which with somatic passivity form the passivity group where the boundary between self and outside agency has broken down. The last, delusional perception, is unique in being a two-stage event: a correctly perceived, normal percept followed instantly by an unshakeable delusional interpretation. This determination of what is part of the self and what is not, lost in passivity, is the thread that unifies most of the list.

WORKED EXAMPLE

A man reports that his own thoughts are spoken back to him a beat after he thinks them (thought echo), that "they lift the thoughts straight out of my head" mid-sentence (thought withdrawal), and that when he raised his arm to drink it was "not me, they moved it for me" (a made act, passivity). Seeing a traffic light turn green, he knew at once and without reasoning that he had been appointed to lead the city (delusional perception: the percept is accurate, only the attached meaning is delusional). Four first-rank symptoms are present, which raises strong suspicion of schizophrenia but, on their own, do not confirm it.

12.4 The modern caveat: first-rank symptoms are not pathognomonic

The single most tested point about Schneider is a corrective one: first-rank symptoms are not pathognomonic of schizophrenia. When first described, the presence of one first-rank symptom in the absence of intoxication, brain injury or clear affective illness was sometimes taken as sufficient for the diagnosis (Kaplan & Sadock 2024). This no longer holds. First-rank symptoms occur in mania, where Schneiderian symptoms have been reported in roughly 10 to 20 percent of manic patients, and in organic psychoses; and they are absent in many people who clearly have schizophrenia (Gelder et al. 2013). It has been clear for decades that no single hallucination or delusion, however carefully specified, confirms or excludes schizophrenia by itself. Nothing about a symptom being pathognomonic can be claimed for any item on the list.

RULE **First-rank symptoms raise suspicion of schizophrenia but are not diagnostic.** They point; they do not prove. Assess form, persistence and mood context before applying the label.

TRAP **Calling first-rank symptoms pathognomonic of schizophrenia.** They occur in mania and organic psychoses and are absent in many with schizophrenia; they are not pathognomonic, and DSM-5 and ICD-11 have removed their privileged diagnostic status.

12.5 Loss of special status in DSM-5 and ICD-11

Both current systems have stripped the first-rank symptoms of their special diagnostic weight. DSM-5-TR and ICD-11 eliminated the special diagnostic importance previously given to Schneiderian symptoms such as running-commentary hallucinations, two or more voices conversing, and bizarre delusions; delusions are now weighed equally toward the diagnosis regardless of their content, and no single symptom is privileged as sufficient (Kaplan & Sadock 2024). DSM-5 raised the symptom threshold from one core symptom to at least two of Criterion A, so that a lone first-rank symptom can no longer carry the diagnosis. The detail of the current criteria, and how ICD-11 runs its symptom items forward with DSM-5-TR cross-mapped and the legacy ICD-10 first-rank weighting, is developed in the criteria topic; the point to hold here is that the Schneiderian era of privileged first-rank symptoms has closed.

INDIA

Where the exit examination and many Indian question banks still test ICD-10, the first-rank symptoms retain their old prominence: ICD-10 weighted thought echo, insertion, withdrawal and broadcasting; passivity and delusional perception; and third-person and running-commentary voices, with one such symptom for one month sufficing. Reproduce the Schneiderian list when the paper asks for ICD-10, but know that ICD-11 and DSM-5 have dropped their special status.

12.6 Bleuler's fundamental symptoms: the four A's

Bleuler divided the symptoms of schizophrenia into fundamental (primary) and accessory (secondary). The fundamental symptoms, present in every case and forming the diagnostic core, are the four A's (Bleuler 1911, Kaplan & Sadock 2024). Their raw descriptive meanings, what loosening of associations or blunted affect actually is, sit in the Psychometry, Assessment and Descriptive Psychopathology notes; here we hold them as Bleuler's account of the essence of schizophrenia. He saw a splitting, a loss of harmonic coordination among thought, emotion and behaviour, as the hallmark, and the four A's are its expression.

Associations (loosening of associations)

Disturbed logical connection between ideas, so that the thread of thought loosens and drifts; Bleuler's central disturbance.

Affect (blunting and incongruity)

Flattening, shallowness or incongruity of emotional response; the outward emotion no longer matches the situation or the thought.

Ambivalence

The simultaneous holding of opposite feelings, wishes or ideas about the same object, without their resolution.

Autism

Withdrawal from external reality into a private inner world, with thought and behaviour dominated by inner life rather than shared reality.

MNEMONIC

The four A's

Associations (loosening), **A**ffect (blunted or incongruous), **A**mbivalence, **A**utism. All 4 A words begin with A and are Bleuler's fundamental symptoms; hallucinations and delusions are conspicuously not among them.

12.7 Bleuler's accessory symptoms and "the schizophrenias"

What most people, patients and clinicians alike, regard as the striking face of schizophrenia, Bleuler regarded as merely secondary. For him hallucinations, delusions, social withdrawal and diminished drive were accessory symptoms: real, often dramatic, but dependent on the individual's adaptive capacity and circumstances, and not the essence of the disorder (Kaplan & Sadock 2024). This inverts the modern intuition, and it is exactly the inversion examiners probe. Bleuler also reframed Kraepelin's single dementia praecox as a group, "the schizophrenias",

holding that these were several related conditions sharing the fundamental disturbance rather than one disease; and he saw the symptoms as lying on a continuum with normal behaviour, a breadth that later contributed to over-diagnosis until formal criteria narrowed the concept.

PEARL

The single cleanest contrast: for Bleuler, hallucinations and delusions are accessory (secondary); the fundamental symptoms are the four A's. For most clinicians and the public, hallucinations and delusions *are* schizophrenia. Holding this reversal straight is what the question is testing.

12.8 Schneider versus Bleuler: setting the two lists side by side

The two frameworks are complementary, not competing, and the table below keeps them apart. Note the near-total non-overlap: Schneider's list is built almost entirely from hallucinations, passivity and delusional perception, the very phenomena Bleuler called accessory; Bleuler's list is built from disturbances of association, affect, volition and relatedness, none of which appears among Schneider's first-rank symptoms. A patient can show florid first-rank symptoms with little of the four A's, or a chronic defect state rich in the four A's with no first-rank symptoms at all.

SCHNEIDER'S FIRST-RANK SYMPTOMS	FAMILY
Audible thoughts (thought echo)	Special auditory hallucination
Voices arguing or discussing in the third person	Special auditory hallucination
Voices commenting (running commentary)	Special auditory hallucination
Thought withdrawal	Disorder of possession of thought
Thought insertion	Disorder of possession of thought
Thought broadcasting	Disorder of possession of thought
Made feelings, made impulses, made acts (passivity)	Made experience of the will
Somatic passivity	Made bodily experience
Delusional perception	Two-stage delusional phenomenon

Schneider's first-rank symptoms grouped by family: three auditory, three thought-possession, the made experiences with somatic passivity, and delusional perception.

BLEULER'S FOUR A'S (FUNDAMENTAL)	NATURE OF THE DISTURBANCE
Loosening of associations	Disturbed linkage of ideas; Bleuler's central sign
Affect (blunting, incongruity)	Emotional response flattened or mismatched
Ambivalence	Opposite feelings or wishes held at once, unresolved
Autism	Withdrawal into a private inner world

Bleuler's four A's, the fundamental symptoms; hallucinations and delusions are accessory and deliberately absent from this list.

COMMON TRAP

Muddling the two lists, for example putting hallucinations or delusions among Bleuler's fundamental symptoms, or listing loosening of associations as a first-rank symptom. Bleuler's four A's contain no hallucination or delusion (those are accessory); Schneider's first-rank symptoms contain no loosening of associations, blunted affect, ambivalence or autism.

GOOD TO REMEMBER

- **Schneider's first-rank symptoms (Schneider 1959):** eleven pragmatic diagnostic pointers, audible thoughts, third-person and running-commentary voices, thought insertion/withdrawal/broadcasting, made feelings/impulses/acts and somatic passivity (passivity), and delusional perception; central claim is that they make the diagnosis reliable, not that they are its essence; the discriminator to hold is that they are not pathognomonic, occurring in roughly 10 to 20 percent of manic patients and in organic psychoses.
- **Delusional perception:** a first-rank symptom in which a normal, correctly perceived percept acquires a sudden unquestionable delusional meaning; the discriminator is that it is two-stage and the perception itself is normal, so it is a disorder of thought, not perception.
- **Passivity (made experiences and somatic passivity):** feelings, impulses, acts or bodily sensations experienced as imposed by an external agent; the discriminator is the loss of the sense of self versus outside agency, the thread uniting most first-rank symptoms.
- **Bleuler's fundamental symptoms (Bleuler 1911):** the four A's, loosening of associations, affect (blunting/incongruity), ambivalence and autism; central claim is that they are the primary core present in every case; the discriminator is that hallucinations and delusions are deliberately excluded from this list.
- **Bleuler's accessory symptoms:** hallucinations, delusions, social withdrawal and diminished drive; central claim is that they are secondary and depend on the person's adaptive capacity; the discriminator is that the modern intuition inverts Bleuler, treating these very symptoms as the face of schizophrenia.
- **"The schizophrenias":** Bleuler's reframing of Kraepelin's single dementia praecox as a group of related conditions sharing the fundamental disturbance; the discriminator is that it introduced both the name schizophrenia (splitting of psychic functions) and a continuum-with-normality view that later widened the diagnosis.

HOLD THIS

Bleuler's four A's (associations, affect, ambivalence, autism) are the fundamental core with hallucinations and delusions merely accessory; Schneider's first-rank symptoms are reliable diagnostic pointers that are not pathognomonic and have lost their special status in DSM-5 and ICD-11.

13 · Cognitive impairment, insight and cognition as a treatment target

Cognition is the part of schizophrenia the examiner most often rewards a resident for taking seriously, because it is the part that decides whether a patient works, lives independently and keeps relationships, yet it appears nowhere in the diagnostic criteria. Two threads run through this topic: the **cognitive impairment** of schizophrenia (its domains, its status as a core feature, its power over function), and the closely related clinical construct of **insight**. Both are separable from positive symptoms, both predict outcome, and both are now framed as things to measure and, where possible, to treat.

Why this is the payoff. Neurocognitive deficits explain work performance and independent living better than positive or negative symptoms do, they are present before onset and in unaffected relatives, and they are the aspect of the illness most tightly correlated with measurable brain dysfunction (Kaplan & Sadock 2024). Dopamine D2 antipsychotics abolish delusions and hallucinations but leave cognition essentially untouched, which is exactly why cognition has become a distinct **treatment target**. The single most examinable move is to hold two facts together: cognition predicts functional outcome, and the drugs that treat psychosis do not fix cognition.

13.1 The neurocognitive impairment of schizophrenia

Magnitude. Patients with schizophrenia perform, on average, one to two standard deviations below healthy controls across a broad range of neurocognition tests, and this cognitive impairment is broad, severe and present in most, if not all, patients (Harvey, in Kaplan & Sadock 2024). It is detectable in unmedicated first-episode patients at a magnitude close to that of established illness, so it is not an artefact of chronicity or of medication. Deficits are also strikingly similar across countries, educational systems and ethnic groups, which argues that they are intrinsic to the disease rather than a product of environment.

1 to 2 SD	~15%	<10%
BELOW CONTROLS ON COGNITION	RATED CLINICALLY "UNIMPAIRED"	VARIANCE SHARED WITH POSITIVE SYMPTOMS

About **~15%** of patients are rated "unimpaired" on clinical neuropsychological testing, but even these individuals perform well below what their premorbid level and parental education would predict, and monozygotic twins discordant for schizophrenia almost always show the affected twin performing worse than the unaffected co-twin (Kaplan & Sadock 2024). In other words, almost every patient is functioning below their own expected baseline.

13.2 The domains affected (the MATRICS seven)

Which functions. The Neurocognition Subcommittee of the MATRICS project (Measurement and Treatment Research to Improve Cognition in Schizophrenia) fixed seven separable domains as the core impaired functions, chosen because they are substantially impaired, distinct from one another and each linked to functional outcome (Green & Nuechterlein; Kaplan & Sadock 2024). These are the domains the MATRICS Consensus Cognitive Battery (MCCB) was built to measure.

Processing speed

Speed of simple information handling (digit symbol, symbol coding, Trail Making A). Often the single strongest discriminator between patients and controls; accounted for more variance than any other measure in the CATIE cognitive data.

Working memory

Holding and manipulating information "online" for seconds (digits backward, spatial span). Described by many authors as a core component of the impairment, tied to prefrontal circuitry and to employment outcome.

Attention / vigilance

Sustained attention over time, tested by the Continuous Performance Test. Moderately-to-severely impaired; underlies difficulty following conversations, instructions and treatment.

Verbal learning and memory

Learning and retaining word lists or stories. Deficit is greater in learning than in retention; unlike Alzheimer disease, patients do not show rapid forgetting of what they did learn.

Visual learning and memory

Learning and reproducing visual material. Fewer sensitive tests exist; correlations with outcome are more modest and mixed.

Reasoning and problem-solving

"Executive function," classically the Wisconsin Card Sorting Test, on which patients perseverate like frontal-lobe patients; drove the frontal-hypoactivation hypothesis.

Social cognition

Theory of mind and facial-affect / social-cue perception. Impaired and, on recent evidence, more strongly tied to social functioning than general neurocognition, largely mediating the link between general cognition and social deficits.

MNEMONIC

Speedy Workers Attend, Verbally and Visually Reasoning Socially

The seven MATRICS domains: **Speed** of processing, **Working** memory, **Attention**/vigilance, **Verbal** learning and memory, **Visual** learning and memory, **Reasoning** and problem-solving, **Social** cognition.

13.3 Cognition as a core feature: the cognitive hypothesis

Core, not consequence. The claim that cognition is a **core feature** of schizophrenia, the framing sometimes called the cognitive hypothesis of schizophrenia, rests on three lines of evidence (Kaplan & Sadock 2024). First, the deficits precede psychosis: in follow-back and high-risk cohorts, low verbal, nonverbal and mathematical test scores are present in childhood and adolescence in those destined to develop the illness, and are prominent during the prodrome. Second, they are heritable and familial: first-degree relatives, including unaffected co-twins, are impaired on cognitive measures (small-to-medium effect sizes), consistent with cognition as an endophenotype. Third, and decisively, they are separable from symptoms: the variance shared between neurocognition and positive symptoms is typically less than **10%**, and when psychosis remits with treatment, cognition does not change with it. Kraepelin and Bleuler both placed cognitive deterioration at the centre of the illness over a century ago.

RULE **Cognition predicts function best.** Neurocognitive deficits explain community functioning, independent living and employment better than positive or negative symptoms, and predict functional status years later.

13.4 Functional impact

Why it matters clinically. The functional impact of cognition is the reason the topic exists. Across the three outcomes most studied, community (social and occupational) function, performance of simulated interpersonal and living skills, and success in psychosocial rehabilitation, every key MATRICS domain shows a significant, medium-sized relationship to outcome (Kaplan & Sadock 2024). Processing speed and verbal memory predict work behaviour and competitive employment; patients in full-time competitive work outperform the unemployed on working memory, attention, problem-solving and episodic memory, with part-time workers in between. Crucially, in patients whose function worsens over time, change in cognition predicts the change while change in negative symptoms does not, another line of evidence that cognition, not symptom fluctuation, carries the disability.

WORKED EXAMPLE

A 26-year-old with stabilised schizophrenia has no delusions or hallucinations on his current antipsychotic, yet cannot hold a supermarket shelf-stacking job: he loses track of instructions mid-task and works too slowly to keep pace. His positive symptoms are controlled; his working memory and processing speed are not. The exam-correct formulation is that residual neurocognitive impairment, not residual psychosis, is driving the occupational failure, which is why cognitive remediation and workplace support, addressed in the Schizophrenia: management, antipsychotics and adverse effects notes, matter more here than a further antipsychotic dose change.

13.5 Why cognition became a treatment target

The gap D2 blockade leaves. Antipsychotics have a pronounced effect on psychotic symptoms but there is currently little pharmacological relief for the neurocognitive impairment of schizophrenia (Kaplan & Sadock 2024). The NIMH CATIE trial compared four second-generation drugs and a first-generation comparator (perphenazine) under randomised, double-blind conditions: cognitive scores improved a little in every arm with none distinguishable from another, and even that small gain was interpreted as practice and expectation effects rather than true drug benefit. High-dose first-generation drugs, and the anticholinergics used to manage their extrapyramidal effects, can actively worsen cognition. The conclusion the examiner wants is blunt: dopamine D2 antipsychotics do not restore cognition, so cognition has to be pursued as a separate, **cognition-targeting** objective.

TRAP **Assuming D2 antipsychotics restore cognition.** They do not. Second-generation drugs give minimal-to-no cognitive benefit over first-generation ones in rigorous trials (CATIE), and high-dose D2 blockade plus anticholinergics can make cognition worse.

The two routes. Because pharmacology alone has failed, the field pursues two complementary strategies. The non-pharmacological route is cognitive remediation therapy: structured strategy-teaching and compensatory training that, in meta-analysis, produces moderate gains in cognitive performance and improves functional outcome when combined with psychosocial rehabilitation (Wykes et al. 2011; Kaplan & Sadock 2024). Its likely mechanism is experience-dependent neuroplasticity, which is why remediation may be a necessary substrate for any pro-cognitive

drug to show effect. The detail of remediation as a therapy, and the drugs below as licensed products, belongs to the Schizophrenia: management, antipsychotics and adverse effects notes; here they are covered only as the rationale for cognition-as-target.

13.6 The muscarinic route: xanomeline and KarXT

A non-dopaminergic mechanism. The most important recent **pro-cognitive** and antipsychotic strategy is the muscarinic agonist route. Xanomeline is a central muscarinic M1/M4 agonist: M4 agonism reduces dopamine cell firing in the ventral tegmental area (theoretically reducing positive symptoms), while M1 agonism increases prefrontal dopamine and is the arm thought most relevant to improving cognition (Stahl 2021). Given alone, xanomeline causes peripheral cholinergic side effects (nausea, vomiting, sweating). It is therefore combined with trospium, a peripherally-restricted anticholinergic that does not cross the blood-brain barrier and blocks the peripheral muscarinic side effects while leaving the central agonism intact. This combination is KarXT (xanomeline-trospium, marketed as Cobenfy).

State the mechanism accurately. The examinable point is mechanistic: unlike every previously approved antipsychotic, KarXT does not directly bind dopamine receptors; its therapeutic effect is mediated through direct agonism of muscarinic acetylcholine receptors (M1 and M4) rather than D2 blockade (Maudsley 15th ed.). A post-hoc analysis of a phase-2 trial reported a signal for benefit on cognitive impairment, particularly in patients who were cognitively impaired at baseline (Sauder et al. 2022), but this is a signal, not established pro-cognitive efficacy, and should be stated as such.

> **COMMON TRAP**
>
> Do not overclaim KarXT as a proven cognition drug or misstate its mechanism. What is verified: xanomeline is a central M1/M4 muscarinic agonist; it acts without direct dopamine-receptor binding; trospium is added purely to block peripheral cholinergic side effects; the primary approved indication is for schizophrenia symptoms, with the cognitive benefit reported so far as a post-hoc signal (Maudsley 15th ed.; Sauder et al. 2022). Licensing and dosing detail live in the Schizophrenia: management, antipsychotics and adverse effects notes.

13.7 Insight as a multidimensional construct

What insight is. In psychopathology, insight is awareness of a morbid change in oneself and a correct attitude to that change, including, where appropriate, recognition that it signifies a mental disorder (Shorter Oxford 2018). It is not simply present or absent, and it is not the same as agreeing with the doctor. The old idea that insight cleanly separates psychosis (absent) from neurosis (present) is no longer held; the "lack of insight" in psychosis is better understood as impaired reality testing. The descriptive definitions of the underlying phenomena that insight is directed at (delusion, hallucination) belong to the Psychometry, Assessment and Descriptive Psychopathology notes.

The three dimensions. The standard model (David 1990) treats insight as three separable, graded components, which map directly onto the classic staged questions (Shorter Oxford 2018): awareness that the phenomena are occurring, relabelling of those phenomena as abnormal or

pathological rather than normal or externally caused, and acceptance of the need for treatment, that is, treatment adherence. Insight is commonly impaired in schizophrenia, is influenced by cultural and cognitive factors, and each dimension can be present to a different degree in the same patient.

DIMENSION (DAVID 1990)	THE CLINICAL QUESTION	WHAT IT PREDICTS
Awareness of illness	Does the patient recognise that a change/phenomenon is occurring?	**Engagement with assessment**
Relabelling of symptoms as pathological	Does the patient attribute it to mental illness rather than to normal life or external cause?	**Acceptance of the clinical frame**
Treatment adherence	Does the patient accept the need for treatment and take it?	**Relapse risk and outcome**

The three-dimensional structure of insight (David 1990); the discriminator is that the three dimensions dissociate, a patient can be aware of an experience yet not relabel it as illness, or relabel it yet still refuse treatment.

Measurement and clinical weight. Insight is quantified by structured scales, notably the Schedule for the Assessment of Insight (SAI, David 1990) and its expanded version (SAI-E), and the Scale to assess Unawareness of Mental Disorder (SUMD, Amador). Poor insight predicts poorer treatment adherence and worse outcome, and is one of the mechanisms linking illness to non-adherence and relapse. Insight relates only weakly to general intelligence but overlaps with executive function, tying it back to the cognitive theme of this topic.

HOLD THIS

Cognition, not positive symptoms, predicts real-world function in schizophrenia; D2 antipsychotics fix psychosis but not cognition, which is why cognition is now a separate treatment target pursued by cognitive remediation and the muscarinic M1/M4 route (xanomeline-trospium, KarXT), a mechanism that acts without direct dopamine-receptor blockade.

GOOD TO REMEMBER

- **Cognitive impairment:** broad neurocognitive deficit ~1 to 2 SD below controls, present pre-onset and in unaffected relatives; core feature though absent from ICD-11/DSM-5-TR criteria; discriminator is that it is separable from and does not track positive symptoms.
- **MATRICS seven domains:** processing speed, working memory, attention/vigilance, verbal learning and memory, visual learning and memory, reasoning and problem-solving, social cognition; the number to know is seven, measured by the MCCB.
- **Processing speed:** often the single strongest cognitive discriminator between patients and controls (digit symbol; CATIE data).
- **Working memory:** a core component tied to prefrontal circuitry; predicts employment and job tenure.
- **Cognitive hypothesis:** central claim that cognition is core, predating onset, familial and separable from symptoms, and the strongest predictor of functional impact; discriminator is that cognition beats positive AND negative symptoms at predicting function.
- **Treatment target:** D2 antipsychotics do not restore cognition (CATIE), so cognition is pursued separately via cognitive remediation therapy (moderate effect, better with rehabilitation) and pharmacology.
- **Xanomeline / KarXT:** central muscarinic M1/M4 agonist (xanomeline) plus peripherally-restricted trospium (KarXT, Cobenfy); acts via muscarinic receptors, NOT direct D2 blockade; cognitive benefit reported so far as a post-hoc signal (Sauder 2022), not established.
- **Insight:** multidimensional (David 1990), awareness of illness, relabelling of symptoms as pathological, treatment adherence; measured by the SAI; commonly impaired and predictive of adherence and outcome; discriminator is that the three dimensions dissociate.

14 · Prodrome, the at-risk mental state and first-episode psychosis

Schizophrenia rarely announces itself with a florid first hallucination. In most patients there is a slow slide of months to years in which function erodes, personality flattens and odd experiences creep in before any frank psychotic symptom crosses threshold. Recognising this window, the **prodrome** and the operationalised **at-risk mental state**, matters because it is the seam where prevention, early intervention and a great deal of contemporary research live. It is also a favourite examiner trap: the whole clinical challenge is to identify risk without over-treating a state that, in most people, will never become schizophrenia.

Exam framing. Expect to be asked to define the prodrome, list the three at-risk (**ultra-high-risk**) subgroups, quote a **transition** rate, and, above all, to state the guideline position on antipsychotics in a high-risk state. Get the last point right and you separate yourself from the candidate who manages an at-risk state as though it were established illness.

14.1 The prodrome: non-specific decline, then attenuated symptoms

Definition. The prodrome is the period of disturbance preceding frank psychosis, typically evolving over months to years, in which non-specific changes appear first and attenuated (subthreshold) psychotic features follow. It is a *retrospective* concept in its classic sense: a prodrome is only certain once psychosis has actually declared, which is why prospective work reframed it as an "at-risk" state (see 14.3). Early features are famously non-specific, depressed mood, anxiety, sleep disturbance, irritability, social withdrawal, falling academic or occupational

performance, and reduced concentration, overlapping heavily with depression and normal adolescence (Yung & McGorry 1996).

Attenuated phase. As the prodrome matures, attenuated psychotic phenomena emerge: ideas of reference, magical or odd beliefs, perceptual distortions and suspiciousness, held with relatively preserved insight and below the intensity, frequency or conviction that would qualify as a delusion or hallucination proper. For the descriptive definitions of what a delusion, a hallucination or formal thought disorder actually *is* as a phenomenon, cross-reference the Psychometry, Assessment and Descriptive Psychopathology notes; here the point is only that these signs appear in a muted, subthreshold form.

TRAP **Prodrome is not a diagnosis.** Non-specific decline plus low mood in a teenager is far more often depression or adjustment than an emerging psychosis; the prodrome is confirmed only in hindsight.

14.2 Basic symptoms: the earliest self-experienced disturbances

Concept. The basic symptoms approach (Huber; Schultze-Lutter) describes the earliest, subtle, self-perceived disturbances of thought, perception, language and attention, for example thought interference, thought pressure, disturbances of receptive speech, and visual perceptual changes, experienced with full insight and often preceding attenuated psychotic symptoms. Cognitive-perceptive basic symptoms (COPER) and a cognitive-disturbances cluster (COGDIS) form one arm of contemporary **clinical high risk** criteria alongside the ultra-high-risk paradigm (Schultze-Lutter 2015).

14.3 The at-risk mental state and the ultra-high-risk criteria

Prospective identification is operationalised through the at-risk mental state (**arms**), assessed on the Comprehensive Assessment of At-Risk Mental States (CAARMS), and the closely equivalent ultra-high-risk (**uhr**) criteria of the Structured Interview for Psychosis-risk Syndromes (SIPS). To meet an ultra high risk / at-risk mental state one must fall into at least one of three **arms** (Yung et al. 2003, 2008):

GROUP	WHAT DEFINES IT	KEY QUALIFIER
Attenuated psychotic symptoms (APS)	Subthreshold positive symptoms present in the past year: below the intensity, frequency or duration of frank psychosis	**The commonest and largest entry route**
Brief limited intermittent psychotic symptoms (BLIPS / BIPS)	Frank psychotic symptoms that resolve spontaneously within a short window (CAARMS: less than 1 week) without treatment	**Highest short-term transition of the three**
Trait-plus-state (genetic risk and deterioration, GRD)	Schizotypal personality disorder or a first-degree relative with psychosis (trait), *plus* a marked decline in functioning (state) over the past year	**Risk comes from vulnerability + functional drop, not current symptoms**

The three ultra-high-risk / at-risk mental state subgroups. Meeting any one arm qualifies; BLIPS carries the highest short-term transition, GRD the lowest.

Terminology. "At-risk mental state", "ultra-high-risk" and "clinical high risk" (**chr**) are used near-synonymously; CHR is the umbrella term now favoured in North American and European literature, encompassing both the ultra high risk positive-symptom paradigm and the basic-symptom paradigm. The state is a help-seeking, symptomatic status, not a benign trait label.

RULE **Three arms, one qualifies.** Attenuated psychotic symptoms, brief limited intermittent psychotic symptoms, or trait-plus-state (genetic risk plus functional decline): any single arm meets the at-risk mental state.

14.4 Attenuated psychosis syndrome: the DSM-5 condition for further study

What it is. DSM-5 (and DSM-5-TR) placed attenuated psychosis syndrome among the conditions for further study, not in the main text, precisely to flag risk without minting a premature disorder (Fusar-Poli & Heckers). It describes at least one attenuated positive symptom (delusions, hallucinations or disorganised speech) that is present at least weekly for the past month, has begun or worsened in the past year, causes distress or disability, and, crucially, is held with *relatively intact reality testing*, that is, below the threshold for frank psychosis. It maps closely onto the attenuated psychotic symptoms arm of the ultra-high-risk criteria.

Its deliberate relegation to "for further study" reflects the core tension of this whole area: most who meet it will not transition, so naming it a disorder risks stigma and over-treatment (see 14.6). It is a research and staging construct, not a licence to prescribe.

14.5 Transition to psychosis: the numbers

Rate. Across ultra-high-risk cohorts, **transition** to a frank psychotic disorder accumulates with follow-up: about **18%** at 6 months, **22%** at 1 year, **29%** at 2 years and **36%** at 3 years, the risk rising steadily across that window. Early single-cohort studies reported higher short-term figures (about **37%** at 12 months) than the pooled one-year estimate of **22%**, partly because broader ascertainment and earlier detection dilute the sample (Fusar-Poli et al. 2012; New Oxford Textbook of Psychiatry 2020).

~22%	~36%	~1/3
POOLED TRANSITION AT 1 YEAR	POOLED TRANSITION BY 3 YEARS	RECOVER, ~1/3 STABLE SUBTHRESHOLD

Gradient. Transition is not uniform across the three arms: it is highest with brief limited intermittent psychotic symptoms and with more intense, frequent or persistent attenuated symptoms, and lowest in the trait-plus-state (genetic risk plus deterioration) group. Put simply, the closer the presentation already sits to frank psychosis, the higher the conversion. A useful rule of thumb from at-risk follow-up: roughly one-third convert to a psychotic disorder, one-third remain stably subthreshold, and one-third improve or fully recover (Kaplan & Sadock 2024). Importantly, when transition occurs the outcome is a spectrum, schizophrenia, schizoaffective, bipolar or psychotic depression, not schizophrenia alone.

TRAP **Do not quote a single "conversion to schizophrenia" figure.** At-risk states convert to a range of psychoses, and most at-risk individuals never transition at all.

14.6 Board steer: antipsychotics in the prodrome and at-risk state

This is the highest-yield point in the topic. Guidelines do **not routinely** recommend antipsychotics for a clinical-high-risk / at-risk state with the aim of preventing transition (NICE CG178; EPA guidance, Schmidt et al. 2015). The rationale is a simple risk-benefit calculation: because only a minority actually transition, most at-risk individuals treated with an antipsychotic would be exposed to weight gain, metabolic harm, sedation and extrapyramidal effects for no benefit, and the evidence that antipsychotics prevent (rather than merely delay) transition is weak.

What is preferred instead. The recommended stance is to offer cognitive behavioural therapy (individual CBT, for which the evidence in this group is strongest), active monitoring / regular review of mental state, and to *treat the comorbidity that is actually present*: depression, anxiety and substance use. Antipsychotics are reserved for frank psychosis, or for a severe, rapidly deteriorating or dangerous picture where the clinical situation itself, not a preventive rationale, warrants them. For the drugs themselves, their adverse-effect profiles and the management of established illness, cross-reference the Schizophrenia: management, antipsychotics and adverse effects notes.

RULE **No antipsychotic to prevent transition.** In a clinical-high-risk patient, offer CBT, active monitoring and treatment of comorbid depression, anxiety and substance use; reserve antipsychotics for frank psychosis or a severe, deteriorating picture.

TRAP **Managing an at-risk state as schizophrenia.** Starting a maintenance antipsychotic in an at-risk mental state purely to prevent transition medicalises a group most of whom will never develop psychosis.

14.7 First-episode psychosis and the duration of untreated psychosis

Definition. First-episode psychosis (**fep**) denotes the first frank psychotic episode, before diagnosis is stabilised: it is a syndromal, not a nosological, label, because the eventual diagnosis (schizophrenia, schizoaffective disorder, bipolar disorder, psychotic depression, substance-induced or organic psychosis) is often not yet clear. It is the target of dedicated early-intervention services (for example the EPPIC model), which combine low-dose antipsychotics with psychosocial and vocational support.

DUP. The interval between the onset of frank psychotic symptoms and the start of adequate antipsychotic treatment is the duration of untreated psychosis (DUP). A longer DUP is associated with poorer symptomatic and functional outcome and slower, less complete remission, which is the central argument for early detection and rapid treatment in first-episode psychosis (first episode psychosis) services. For how DUP and first-episode outcome fit into the natural history and prognosis of the illness, cross-reference the course topic within these notes. First-episode

patients are notably antipsychotic-sensitive, so the treatment principle is "low and slow"; the drug detail belongs in the Schizophrenia: management, antipsychotics and adverse effects notes.

DUP ↑	Low & slow
WORSE OUTCOME, SLOWER REMISSION	FEP ANTIPSYCHOTIC SENSITIVITY

14.8 Endophenotypes: heritable markers between genotype and phenotype

Concept. An endophenotype (intermediate phenotype; Gottesman & Gould 2003) is a heritable, quantifiable, state-independent trait marker lying on the causal pathway *between* genotype and the clinical phenotype, more proximal to gene action than the diagnosis itself and therefore more tractable for genetic and progression research. The classic Gottesman criteria: the marker is associated with the illness in the population, is heritable, is state-independent (present whether or not the person is currently ill), co-segregates with illness within families, and is found in unaffected relatives at higher rates than in the general population.

Candidate markers in schizophrenia. Well-studied examples include smooth-pursuit eye-movement abnormality (impaired pursuit gain with catch-up saccades), the P50 sensory-gating deficit (failure to suppress the P50 auditory evoked response to the second of paired clicks), prepulse inhibition deficits (reduced attenuation of the startle response by a preceding weak stimulus), and working-memory (and broader neurocognitive) deficits. These are found in patients and, at intermediate frequency, in their unaffected relatives, and are studied as markers of vulnerability and of progression across the at-risk to first-episode continuum (Kaplan & Sadock 2024). For the underlying twin, family and adoption methods that make a trait "heritable", cross-reference the Psychiatric Genetics notes.

HOLD THIS

Do not start an antipsychotic in a clinical-high-risk / at-risk mental state purely to prevent transition: only about 22 percent transition by 1 year and about 36 percent by 3 years, so offer CBT, active monitoring and treatment of comorbid depression, anxiety and substance use, and reserve antipsychotics for frank psychosis or a severe, deteriorating picture.

MNEMONIC

A-B-T for the three arms

Attenuated psychotic symptoms, **B**rief limited intermittent psychotic symptoms, **T**rait-plus-state (genetic risk plus deterioration). Any one arm meets the ultra-high-risk / at-risk mental state.

GOOD TO REMEMBER

- **Prodrome:** the disturbance preceding frank psychosis, non-specific decline first then attenuated symptoms; core point is that it is confirmed retrospectively, so prospective work uses the at-risk mental state instead.
- **At-risk mental state / ultra-high-risk / clinical high risk:** an operationalised help-seeking risk status; the discriminator is that it needs only ONE of three arms (attenuated psychotic symptoms, brief limited intermittent psychotic symptoms, or trait-plus-state).
- **BLIPS (brief limited intermittent psychotic symptoms):** frank psychotic symptoms that remit spontaneously within about a week; discriminator is that it carries the HIGHEST short-term transition of the three arms.
- **Trait-plus-state (GRD):** genetic risk (schizotypal PD or first-degree relative with psychosis) PLUS a marked functional decline over the past year; discriminator is that risk comes from vulnerability + drop, with no current subthreshold symptoms required.
- **Attenuated psychosis syndrome:** DSM-5 condition for further study, at least one attenuated positive symptom, weekly for a month, with relatively intact reality testing; discriminator is its deliberate placement OUTSIDE the main manual to avoid over-diagnosis.
- **Transition to psychosis:** pooled about 22 percent at 1 year and about 36 percent by 3 years, higher with more intense attenuated symptoms and with BLIPS; discriminator is that conversion is to a SPECTRUM of psychoses, not schizophrenia alone.
- **First-episode psychosis (FEP):** the first frank psychotic episode, diagnosis not yet stabilised; discriminator is that a longer duration of untreated psychosis predicts worse outcome, the rationale for early intervention.
- **Endophenotype:** a heritable, state-independent, quantifiable trait marker between genotype and phenotype (smooth-pursuit eye-movement abnormality, P50 sensory-gating deficit, prepulse-inhibition and working-memory deficits); discriminator is that it must appear in unaffected relatives, not just in patients.

PEARL

The single best "positive" predictor of transition is not any biomarker but the clinical severity of the presenting attenuated symptoms plus a steep functional decline; this is why staging models weight symptom intensity and function so heavily, and why active monitoring (not medication) is the default at-risk intervention.

Classification, subtypes and nosological change

15 · The diagnostic criteria: ICD-11, DSM-5-TR and the legacy ICD-10

Why this matters. A resident is expected to reproduce the operational criteria for schizophrenia from both current systems, and to know precisely what changed when **ICD-11** and **DSM-5-TR** replaced their predecessors. Examiners test three things: the two duration thresholds, the symptom set with its "at least two" rule, and the nosological shift away from subtypes and from privileged first-rank symptoms toward a dimensional, specifier-based description. This topic runs the criteria forward, cross-maps them, and closes with a labelled legacy box for ICD-10, which many Indian question banks still use.

The raw descriptive definitions of the underlying phenomena, what a delusion, a hallucination, formal thought disorder or a first-rank symptom actually is, belong to the Psychometry,

Assessment and Descriptive Psychopathology notes; here we apply and enumerate them within the operational criteria (Kaplan & Sadock 2024, Gaebel 2020). Management, antipsychotics and adverse effects are developed in the Schizophrenia: management, antipsychotics and adverse effects notes and are not taught here.

15.1 ICD-11: the core symptom set and the "at least two" rule

The current ICD-11 requirement is at least two of a defined set of core symptoms, present most of the time for at least one month (Gaebel 2020, Kaplan & Sadock 2024). The seven symptom groups are persistent delusions, persistent hallucinations, disorganised thinking (formal thought disorder), experiences of influence, passivity or control, negative symptoms, grossly disorganised behaviour, and psychomotor disturbance. Critically, at least one of the two must come from the first four groups, the core positive or disorganisation cluster, so a picture built only from negative symptoms and psychomotor disturbance does not meet the threshold. ICD-11 does not impose a separate functional-decline criterion in the way DSM-5-TR does, resting the diagnosis on the symptom set and the duration instead.

Persistent delusions

Fixed false beliefs, weighed equally toward the diagnosis regardless of bizarreness or content (core positive; one of the first four).

Persistent hallucinations

Perceptions without a stimulus, most often auditory (core positive; one of the first four).

Disorganised thinking

Formal thought disorder inferred from disorganised speech, from tangentiality to word salad (disorganisation; one of the first four).

Experiences of influence, passivity or control

The old Schneiderian passivity and thought-interference phenomena, now one item among several (one of the first four).

Negative symptoms

Blunted affect, alogia, avolition, asociality, anhedonia (not among the first four).

Grossly disorganised behaviour

Purposeless, bizarre or context-inappropriate behaviour impairing goal-directed activity.

Psychomotor disturbance

Catatonic phenomena: stupor, posturing, waxy flexibility, excitement, mutism.

RULE **ICD-11 needs two core symptoms for one month, and at least one must be a core positive or disorganisation symptom.** Negative and psychomotor items alone cannot carry the diagnosis.

15.2 ICD-11 symptom-domain qualifiers and course specifiers

Having replaced subtypes, ICD-11 asks the clinician to rate a set of symptom-domain qualifiers describing the cross-sectional profile of the current episode, plus course specifiers describing the longitudinal pattern (Gaebel 2020). Each domain qualifier is rated as present or absent and, where relevant, by severity, so that two patients with the same diagnosis can be described dimensionally rather than forced into one categorical box. The six symptom domains are positive

symptoms, negative symptoms, depressive mood symptoms, manic mood symptoms, psychomotor symptoms, and cognitive symptoms. The course specifiers capture stage and pattern: first episode, multiple episodes, or continuous, each further qualified as currently symptomatic, in partial remission, or in full remission.

Symptom-domain qualifiers

Six ratable domains, positive, negative, depressive, manic, psychomotor, cognitive, describing the current cross-sectional profile.

Course specifiers

First episode / multiple episodes / continuous, each as currently symptomatic, partial remission or full remission.

15.3 ICD-11 and the abolition of subtypes

The single most examined nosological point is the abolition of subtypes: ICD-11 deleted the classical paranoid, hebephrenic, catatonic, undifferentiated, residual and simple subtypes that ICD-10 had retained (Gaebel 2020). The stated grounds were their poor inter-rater reliability, their marked temporal instability, so that a patient labelled paranoid at one admission was frequently hebephrenic or undifferentiated at the next, and their low predictive validity for course, treatment response or outcome. In their place ICD-11 substitutes the symptom-domain qualifiers and course specifiers of the preceding subtopic, a dimensional description intended to capture the same clinical variation with far better reliability. Catatonia is now coded separately rather than as a schizophrenia subtype; its detail belongs to the Other psychotic disorders, delusional syndromes and catatonia notes.

> **PEARL**
>
> The subtypes fell for the same three reasons in both systems: poor reliability, temporal instability, and low predictive validity. Whenever an examiner asks why paranoid, hebephrenic and catatonic schizophrenia disappeared, those three phrases are the answer, and the replacement is a dimensional symptom-domain and course-specifier scheme.

15.4 DSM-5-TR Criterion A: two of five active-phase symptoms

The DSM-5 family defines the active-phase symptoms in Criterion A, which requires two of five symptoms, each present for a significant portion of a one-month period (or less if successfully treated), with at least one being a core positive symptom (American Psychiatric Association 2022, Kaplan & Sadock 2024). The five are delusions, hallucinations, disorganised speech, grossly disorganised or catatonic behaviour, and negative symptoms. The "at least one core positive" constraint means the qualifying pair must include one of delusions, hallucinations or disorganised speech; a diagnosis cannot rest on, for example, catatonic behaviour plus negative symptoms alone.

1. Delusions

A qualifying core positive symptom (any content, weighed equally).

2. Hallucinations

A qualifying core positive symptom.

3. Disorganised speech

The observable index of formal thought disorder; a qualifying core positive symptom.

4. Grossly disorganised or catatonic behaviour

Not counted as a core positive symptom for the "at least one" rule.

5. Negative symptoms

Diminished emotional expression or avolition; not a core positive symptom.

RULE **DSM-5-TR Criterion A is two of five, and the pair must include at least one core positive symptom.** Core positives are delusions, hallucinations or disorganised speech.

15.5 DSM-5-TR: the six-month duration, dysfunction and the exclusions

DSM-5-TR wraps Criterion A in three further requirements. First, a total six month duration: continuous signs of disturbance for at least six months, of which at least one month must be active-phase (Criterion A) symptoms, the remainder being prodromal or residual phases. This is the pivotal contrast with ICD-11's single month, and it is why an illness of five months meeting Criterion A is coded as schizophreniform disorder, not schizophrenia, until it crosses six months. Second, social or occupational dysfunction: functioning in work, relationships or self-care is markedly below the level achieved before onset. Third, the exclusion criteria (American Psychiatric Association 2022).

Six-month duration

Continuous disturbance for at least six months including at least one month of active Criterion A symptoms.

Functional criterion

Marked decline in work, interpersonal relations or self-care below the premorbid level.

Schizoaffective and mood exclusion

Excluded if a major depressive or manic episode has been present for the majority of the total active and residual illness, or if mood episodes are absent only briefly.

Substance and medical exclusion

The disturbance must not be attributable to a substance or another medical condition.

COMMON TRAP

Applying the schizophrenia label during an untreated mood episode. If a full depressive or manic syndrome is present alongside the psychosis, the mood-disorder exclusion must be worked through first: psychotic symptoms confined to mood episodes point to a mood disorder with psychotic features or to schizoaffective disorder, not to schizophrenia. Treat and re-assess the mood before committing to the diagnosis.

TRAP **Diagnosing schizophrenia inside an untreated mood episode without applying the exclusion.** Mood-congruent psychosis confined to depressive or manic episodes is a mood or schizoaffective disorder until proven otherwise.

15.6 What changed from DSM-IV: threshold, subtypes and first-rank de-prioritisation

Three changes from DSM-IV are high-yield (American Psychiatric Association 2022, Kaplan & Sadock 2024). First, the raised threshold and de-prioritisation of first-rank symptoms: DSM-IV allowed a single Criterion A symptom to suffice if it was a bizarre delusion or a Schneiderian hallucination (a running commentary, or two or more voices conversing). DSM-5 abolished this special weighting, so that two symptoms are always required and no bizarre delusion or first-rank hallucination counts double; this de-prioritization reflects evidence that first-rank symptoms are neither pathognomonic nor of superior diagnostic value. Second, subtype removal: the paranoid, disorganised, catatonic, undifferentiated and residual subtypes were deleted for the same reliability, stability and validity failings that led ICD-11 to drop its own subtypes. Third, DSM-5 introduced dimensional severity ratings across eight domains and moved catatonia to a cross-cutting specifier.

WORKED EXAMPLE

A 24-year-old has four months of persistent persecutory delusions and running-commentary auditory hallucinations, with a clear decline in work and self-care and no mood episode or substance cause. Under ICD-11 he already meets schizophrenia: two core symptoms, both from the first four, beyond one month. Under DSM-5-TR he meets Criterion A (two of five, including core positives) but the total illness is under six months, so the correct DSM-5-TR label is schizophreniform disorder; it converts to schizophrenia only once continuous disturbance reaches six months. The one lone running-commentary voice that would have sufficed under DSM-IV no longer carries the diagnosis by itself.

15.7 The legacy ICD-10 criteria: what changed

Because the exit examination and many Indian question banks still test ICD-10, its criteria remain worth holding, framed as a legacy standard against which to see what changed. ICD-10 required symptoms for at least one month, the same threshold ICD-11 retains, but differed in two decisive ways: it gave first-rank symptoms special weight, so that one clear first-rank symptom (thought echo, insertion, withdrawal or broadcasting; passivity or delusional perception; third-person or running-commentary voices) for one month sufficed for the diagnosis; and it retained the full list of subtypes (paranoid, hebephrenic, catatonic, undifferentiated, post-schizophrenic depression, residual, simple). The two current systems have removed both features.

INDIA

For an ICD-10 answer, reproduce the first-rank weighting and the subtype list; for a modern answer, state that ICD-11 keeps the one-month threshold but abolished subtypes and stripped first-rank symptoms of their special status, and that DSM-5-TR requires six months total. Where a paper is silent, note which system you are using.

15.8 The three systems side by side

The comparison below sets the current and legacy criteria against each other across the five axes examiners probe: duration, the core symptom rule, the status of first-rank symptoms, subtypes, and the functional criterion. It maps directly onto the criteria map (Fig 8.1).

AXIS	ICD-11	DSM-5-TR	ICD-10 (LEGACY)
Minimum duration	**1 month of symptoms**	**6 months total (>=1 month active)**	1 month of symptoms
Core symptom rule	>=2 of seven groups, >=1 from the first four (positive/disorganisation)	**Criterion A: 2 of 5, >=1 core positive**	1 first-rank OR 2 of a lower-rank set for 1 month
First-rank symptoms	De-prioritised; one item among several, no special weight	De-prioritised; no single symptom sufficient	**Special weight; one alone can suffice**
Subtypes	**Abolished; replaced by domain qualifiers + course specifiers**	**Removed; replaced by dimensional severity ratings**	**Retained (paranoid, hebephrenic, catatonic, etc.)**
Functional criterion	Not a separate mandatory criterion	**Required: marked social/occupational decline**	Not a separate mandatory criterion
Mood / substance exclusion	Present	Present (schizoaffective, mood, substance, medical)	Present

Criteria comparison: ICD-11 versus DSM-5-TR versus the legacy ICD-10 across duration, core symptoms, first-rank status, subtypes and the functional criterion; the pivotal contrast is one month (ICD-11, ICD-10) against six months total (DSM-5-TR).

GOOD TO REMEMBER

- **ICD-11 schizophrenia:** at least two of seven core symptoms with at least one from the first four (positive or disorganisation cluster), present for at least one month; central change is the abolition of subtypes for symptom-domain qualifiers plus course specifiers; the discriminator is the one-month duration and the "one from the first four" rule.
- **DSM-5-TR schizophrenia:** Criterion A two of five (>=1 core positive), plus six months total duration with at least one month active, social or occupational dysfunction, and the mood and substance/medical exclusions; the discriminator is the six-month total duration, distinguishing it from schizophreniform disorder (under six months).
- **Criterion A (DSM-5-TR):** delusions, hallucinations, disorganised speech, grossly disorganised or catatonic behaviour, negative symptoms; central rule is two of five with at least one core positive; the discriminator is that no single symptom, first-rank or bizarre, now suffices.
- **Symptom-domain qualifiers and course specifiers (ICD-11):** six ratable domains (positive, negative, depressive, manic, psychomotor, cognitive) and a course axis (first / multiple episodes / continuous, each symptomatic / partial / full remission); central claim is dimensional description replacing subtypes; the discriminator is that these are rated per-episode, not fixed categories.
- **Abolition of subtypes (both systems):** paranoid, hebephrenic/disorganised, catatonic, undifferentiated, residual and simple subtypes deleted; central reason is poor reliability, temporal instability and low predictive validity; the discriminator is that ICD-10 alone still retains them.
- **Legacy ICD-10:** one-month duration, but first-rank symptoms carried special weight (one alone could suffice) and the classical subtypes were retained; the discriminator, what changed, is that both current systems keep the month but drop first-rank privilege and subtypes.

HOLD THIS

ICD-11 needs at least two core symptoms (one from the first four) for one month; DSM-5-TR needs Criterion A two of five plus a six-month total duration with dysfunction and the exclusions; both abolished subtypes and de-prioritised first-rank symptoms, while legacy ICD-10 kept the month, the subtypes and the first-rank weighting.

16 · History and the abolition of the subtypes

The classification of schizophrenia is the most historically loaded topic in the whole chapter, and the modern examiner tests two things: whether you can trace the **historical evolution** from Kraepelin through Bleuler to Schneider, and whether you know that both current systems have deleted the classical subtypes. The disorder has been renamed and re-carved twice, from a unitary deteriorating dementia to a group of syndromes to a symptom-domain construct, and each turn left a residue that still surfaces in short-answer questions. Reading the history forward makes sense of why the ICD-10 subtypes existed at all and why they were retired.

How to use this page. Fix the three-name lineage first, because a single line on each of Kraepelin, Bleuler and Schneider answers most history questions. Then hold the six ICD-10 subtypes as a list you can reproduce, with simple schizophrenia as the odd, controversial one. Finally, learn the abolition argument as a four-point causal chain, because the shift from categorical subtypes to a dimensional specifier model is the single highest-yield nosology point in the chapter and the one most likely to be marked wrong. The descriptive definitions of the individual signs, what a delusion, a hallucination or formal thought disorder *is* as a phenomenon, are not re-derived here; they belong to the Psychometry, Assessment and Descriptive Psychopathology notes.

16.1 Kraepelin and dementia praecox: the unitary deteriorating illness

The founding separation. Emil Kraepelin, across the successive editions of his textbook, drew the great divide of modern psychiatric nosology: he separated two major primary psychotic illnesses, dementia praecox and manic-depressive insanity, using long-term course and outcome as the defining feature rather than any cross-sectional symptom (Kaplan & Sadock 2024). Dementia praecox, a term he borrowed from Morel meaning a dementia of the young, was conceived as a single, unitary illness with an early-adult onset and a characteristically *poor, deteriorating* outcome, set against manic-depressive insanity with its better, episodic, remitting prognosis (Companion to Psychiatric Studies). This prognosis-based dichotomy, deterioration versus recovery, is the Kraepelinian principle examiners want named.

What he folded into it. Kraepelin unified into dementia praecox three older descriptive syndromes that had been described separately: hebephrenia (Hecker 1871), catatonia (Kahlbaum 1874), and his own dementia paranoides, treating them as manifestations of one disorder with a common early onset and poor outcome (Companion to Psychiatric Studies). Those three descriptive strands are the ancestors of the later paranoid, hebephrenic and catatonic subtypes, which is why the subtype scheme reads as a fossil of nineteenth-century syndrome-spotting.

RULE **Kraepelin split psychosis by course, not by symptom.** Dementia praecox versus manic-depressive insanity was a prognosis-based dichotomy, poor deteriorating outcome versus better episodic outcome, and that longitudinal logic still underlies the schizophrenia/mood divide today.

16.2 Bleuler and the schizophrenias: a group, splitting, and the four A's

The renaming. Eugen Bleuler renamed dementia praecox **schizophrenia** in 1908, and, crucially, pluralised the concept: his 1911 monograph was titled *Dementia Praecox or the Group of Schizophrenias*, deliberately calling it "**the schizophrenias**", a *group* of related disorders rather than one disease (Bleuler 1911). He challenged Kraepelin on two counts: the outcome need not be a relentless dementia, so the prognosis was better and more variable than Kraepelin allowed, and the core disturbance was not memory loss but a *splitting* (schizo-) of the mind (-phrenia), a loosening of the associative threads between thought, emotion and volition.

Fundamental versus accessory symptoms. Bleuler distinguished the *fundamental* symptoms, which he held to be pathognomonic and always present, from the *accessory* symptoms (delusions and hallucinations), which he considered secondary and non-specific because they also occur in other disorders. The fundamental symptoms are memorised as the four A's.

MNEMONIC

THE FOUR A's: Association (loosening), Affect (blunted or incongruous), Ambivalence, Autism.

Bleuler's fundamental symptoms: loosening of **A**ssociations (the primary "splitting", disconnected thought), disturbance of **A**ffect (flattened or incongruous emotion), **A**mbivalence (simultaneous contradictory impulses or feelings), and **A**utism (withdrawal into an inner private world, detachment from reality). The accessory symptoms he demoted, delusions and hallucinations, are the very features the four A's are contrasted against. A common exam trap is to list delusions among the four A's; they are accessory, not fundamental.

16.3 Schneider and the symptom emphasis: first-rank symptoms

The pendulum swings back to cross-section. Where Kraepelin defined by course and Bleuler by an inferred core disturbance, Kurt Schneider defined by readily elicited cross-sectional symptoms. He proposed a set of first-rank symptoms, audible thoughts, voices arguing or commenting, thought withdrawal, insertion and broadcasting, made feelings, impulses and acts, somatic passivity and delusional perception, whose presence in the absence of organic disease he held to be strongly suggestive of schizophrenia (Kaplan & Sadock 2024). His contribution was pragmatic and reliability-driven: symptoms a clinician could observe and agree on, which is why first-rank symptoms dominated ICD-10. Their descriptive definitions as phenomena are cross-referenced to the Psychometry, Assessment and Descriptive Psychopathology notes; the point here is only the historical role. First-rank symptoms were later shown to be neither specific nor pathognomonic and were stripped of their privileged diagnostic weight in both ICD-11 and DSM-5.

FIGURE	NAMED THE DISORDER	DEFINING PRINCIPLE	PROGNOSTIC VIEW
Kraepelin (1890s)	Dementia praecox (from Morel)	**Longitudinal course and outcome; a unitary deteriorating illness**	Poor, deteriorating; separated from manic-depressive insanity
Bleuler (1908 to 1911)	The schizophrenias (a group)	**Splitting of psychic functions; four fundamental symptoms (four A's)**	Better and more variable than Kraepelin allowed
Schneider (1959)	(retained "schizophrenia")	**Cross-sectional first-rank symptoms, chosen for reliability**	Not a prognostic scheme; a diagnostic-symptom emphasis

The historical evolution on one row each: the discriminator is the defining principle, course (Kraepelin) to inferred core disturbance (Bleuler) to observable symptom (Schneider).

GOOD TO REMEMBER

- **Kraepelin:** coined the modern concept of dementia praecox as a unitary illness of the young with a deteriorating course; core claim is prognosis-based separation from manic-depressive insanity; discriminator is that he defined by long-term course, not symptom.
- **Dementia praecox:** Kraepelin's unitary, early-onset, poor-outcome psychosis that folded in hebephrenia (Hecker), catatonia (Kahlbaum) and dementia paranoides; discriminator is the poor deteriorating prognosis versus manic-depressive insanity.
- **Bleuler:** renamed it "the schizophrenias", a group with a better and more variable prognosis, with the core lesion a splitting of psychic functions; discriminator is the four fundamental symptoms (four A's: Association, Affect, Ambivalence, Autism), with delusions and hallucinations demoted to accessory.
- **Schneider:** defined schizophrenia by reliable cross-sectional first-rank symptoms; discriminator is that these were later found non-specific and lost their special diagnostic status in ICD-11 and DSM-5.

16.4 The ICD-10 subtypes: the six-way scheme

The legacy categorical scheme. ICD-10 (F20) carved schizophrenia into categorical clinical subtypes, assigned on the predominant symptom picture at presentation. Because many Indian examinations and case records still run on ICD-10, the list must be reproducible. The main types are paranoid (F20.0), hebephrenic (F20.1), catatonic (F20.2), undifferentiated (F20.3), residual (F20.5) and simple schizophrenia (F20.6), with post-schizophrenic depression (F20.4) sitting alongside as a course category rather than a symptom subtype.

Paranoid (F20.0)

Dominated by relatively stable, often systematised delusions (persecution, reference, grandeur, control, jealousy) and hallucinations, usually persecutory; affect, volition and speech relatively preserved. The commonest subtype, later and more insidious onset, least personality deterioration.

Hebephrenic (F20.1)

The disorganised subtype: prominent thought disorder and disorganisation, shallow, inappropriate or fatuous affect, mannerisms, aimless disinhibited behaviour, fragmentary delusions and hallucinations. Early onset (teens to early twenties), poor prognosis, one of the worst outcomes.

Catatonic (F20.2)

Dominated by psychomotor disturbance: stupor, mutism, negativism, rigidity, posturing, waxy flexibility, excitement or command automatism. Catatonia as an entity is cross-referenced to the Other psychotic disorders, delusional syndromes and catatonia notes.

Undifferentiated (F20.3)

Meets the general criteria for schizophrenia but fits no single subtype cleanly, or shows features of more than one without one predominating. A very common category, which is precisely part of the problem.

Residual (F20.5)

A chronic stage: enduring, prominent negative symptoms (social withdrawal, blunted affect, poverty of speech, psychomotor slowing) following at least one clear psychotic episode, with the florid positive symptoms now attenuated.

Simple schizophrenia (F20.6)

An insidious, progressive decline in functioning with negative symptoms and behavioural oddities but *without* a preceding florid psychotic episode (see 16.5).

16.5 Simple schizophrenia (simplex): the concept and the controversy

What it claims to be. **Simple schizophrenia**, the **simplex** form, describes an insidious but progressive decline, loss of drive and interest, aimlessness, social withdrawal, self-neglect and a shallow, odd affect, developing over years in the absence of frank delusions, hallucinations or any clear-cut psychotic episode. It is, in effect, a purely negative-symptom deteriorating course without positive psychosis, arriving at a residual-like state without ever passing through an acute one.

Why it is contentious. Simple schizophrenia is the most controversial subtype, and the **controversy** is a favourite exam point. Because it lacks the positive symptoms that make schizophrenia recognisable and reliably diagnosable, the diagnosis rests almost entirely on inferred decline, which is hard to distinguish from schizoid or schizotypal personality, an insidious depressive or negative-symptom prodrome, or simple demoralisation. Its inter-rater reliability is poor and its boundaries ill-defined; for this reason DSM never accepted it as a formal diagnosis (it appeared only as a research proposal, simple deteriorative disorder, in a DSM appendix), even while ICD-10 retained it.

> **COMMON TRAP**
>
> Do not equate simple schizophrenia with residual schizophrenia. Both are negative-symptom, deteriorated pictures, but residual schizophrenia *requires* a documented prior florid psychotic episode, whereas simple schizophrenia is defined by never having had one. The presence or absence of a past acute psychotic episode is the discriminator.

16.6 Why both systems abolished the subtypes

The nosological change. This is the currency point. Both DSM-5 (2013, unchanged in DSM-5-TR 2022) and ICD-11 (2019) achieved the **abolition of subtypes**: the classical categorical subtypes were deleted from both systems (Kaplan & Sadock 2024). The **subtype removal** rested

on a convergent, four-part evidence base, and reproducing the four reasons is what earns the mark.

WORKED EXAMPLE

Consider a patient labelled "paranoid schizophrenia" at first presentation who, over five years, loses the systematised delusions and settles into a withdrawn, blunted, amotivated state. On the old scheme the label would have to migrate from paranoid to residual, and had they been disorganised in between, to hebephrenic. The subtype changes while the patient does not have a different *disease*, illustrating the temporal instability that helped sink the scheme: a "subtype" that reclassifies the same person over time is not carving a real category.

1. **Poor inter-rater reliability.** Different clinicians assigned different subtypes to the same patient; the categories were not reliably distinguishable, especially at the boundaries (simple, undifferentiated).
2. **Temporal instability within a patient.** The subtype a given patient met changed across the course of their illness, so the label was not a stable trait of the person but a snapshot of the current cross-section (Linscott et al. 2010).
3. **Low predictive validity.** The subtypes had a weak relationship to biological variables, to treatment response and to long-term outcome, so knowing the subtype did not usefully predict prognosis or guide management (Kaplan & Sadock 2024).
4. **Most patients fell into undifferentiated.** A large share of real presentations did not fit any single clean subtype and defaulted to undifferentiated, which drains a classification of its point.

What replaced them. In place of categorical subtypes, both systems adopted a dimensional approach: the same patient is now described by rating the *severity* of a set of symptom domains and specifiers (for example positive, negative, cognitive, disorganisation, and mood symptoms in DSM-5's dimensional assessment; and course specifiers such as first-episode, multiple-episode, continuous). The clinical reality that a patient is "more negative-symptom-predominant" is captured as a position on continua rather than forced into a box. This categorical-to-dimensional shift is the high-yield nosology statement of the topic.

RULE **Subtypes out, dimensions in.** The schizophrenia subtypes were dropped from both DSM-5 and ICD-11 for poor reliability, temporal instability and low predictive validity, and replaced by a dimensional symptom-domain and specifier approach.

TRAP **Recording "paranoid schizophrenia" as a current formal subtype.** "Paranoid schizophrenia" is not a valid DSM-5-TR or ICD-11 subtype; both systems abolished the subtypes. It survives only as legacy ICD-10 terminology, and using it as a formal current diagnosis is a marked error.

HOLD THIS

Both DSM-5 (2013) and ICD-11 (2019) deleted the schizophrenia subtypes, paranoid, hebephrenic, catatonic, undifferentiated, residual and simple, because they showed poor inter-rater reliability, temporal instability within a patient, and low predictive validity, replacing them with a dimensional symptom-domain and specifier assessment.

GOOD TO REMEMBER

- **ICD-10 subtypes:** paranoid (delusions/hallucinations, best-preserved, commonest), hebephrenic (disorganised, early-onset, worst prognosis), catatonic (psychomotor), undifferentiated (fits none cleanly), residual (chronic negative state after a prior episode), simple (insidious negative decline, no florid episode); discriminator to memorise is that paranoid is the commonest and best-preserved while hebephrenic carries the worst prognosis, and that ICD-11 abolished the subtypes altogether.
- **Simple schizophrenia (simplex):** insidious progressive negative-symptom decline without a frank psychotic episode; central claim is deterioration without positive psychosis; discriminator and source of controversy is the absence of any acute episode, which makes it unreliable and led DSM to reject it as a formal diagnosis.
- **Abolition of subtypes:** both DSM-5 and ICD-11 removed all subtypes; central reasons are poor reliability, temporal instability, low predictive validity, and most patients being undifferentiated; discriminator is the replacement by a dimensional symptom-domain and specifier model.
- **Dimensional model:** rates severity across symptom domains (positive, negative, cognitive, disorganisation, affective) plus course specifiers; central claim is that schizophrenia is better described on continua than in categories; discriminator is that it is the direct successor to the deleted subtypes.

17 · The schizophrenia spectrum and the dimensional debate

Why this matters. Schizophrenia does not sit alone. It is the anchor of a **spectrum** of related psychotic conditions and, on a wider view, the severe end of a **psychosis continuum** that reaches down into the general population. Examiners use this topic to test whether a resident can hold two ideas at once: that our manuals still make a **categorical** diagnosis, and that the underlying phenomena are almost certainly **dimensional**. The high-yield payoff is being able to name the spectrum neighbours, place them by their boundary rule, and then explain how ICD-11 and DSM-5 fuse a categorical label with dimensional specifiers.

Two scope notes. First, the neighbouring disorders are named here only as the boundary of the spectrum around schizophrenia; each as a full diagnostic entity, with its own criteria and management, is developed in the Other psychotic disorders, delusional syndromes and catatonia notes, and the work of separating each from schizophrenia is done in the differential topic. Second, the raw descriptive definitions of the underlying phenomena, what a delusion, a hallucination, formal thought disorder or a first-rank symptom actually is, belong to the Psychometry, Assessment and Descriptive Psychopathology notes; here those signs are applied, not redefined (Kaplan & Sadock 2024).

17.1 What the schizophrenia spectrum is

The schizophrenia spectrum is the family of disorders sharing psychotic phenomenology and, to varying degrees, a genetic and neurodevelopmental relationship with schizophrenia, grouped

together in DSM-5-TR as the "Schizophrenia Spectrum and Other Psychotic Disorders" chapter and in ICD-11 as the "Schizophrenia or other primary psychotic disorders" grouping (American Psychiatric Association 2022, Gaebel 2020). The organising idea is that these conditions differ from schizophrenia not in kind but along measurable axes: the severity and breadth of psychotic symptoms, the duration for which they persist, and how far they are loaded with mood symptoms. Schizophrenia occupies the position of a full, sustained, mood-free psychotic syndrome; its neighbours sit at defined distances from it along those axes.

RULE **The spectrum is a continuum of severity, duration and mood-loading, not a set of unrelated boxes.** Each neighbour of schizophrenia is defined by where it sits on one of those three axes.

17.2 The boundary neighbours: how each is placed on the spectrum

Five conditions form the immediate spectrum boundary around schizophrenia. Each is best remembered by the single axis that separates it from schizophrenia. Schizotypal disorder marks the attenuated, personality-level lower boundary: enduring odd beliefs, perceptual distortions and eccentric behaviour that never reach frank, sustained psychosis (ICD-11 places it within the spectrum; DSM-5 lists schizotypal personality disorder in this chapter but also among the personality disorders). Schizophreniform disorder is a pure duration boundary: it is schizophrenia-like psychosis of less than the six-month total DSM-5 threshold, converting to schizophrenia if it persists. Brief psychotic disorder is the shortest-duration boundary: psychosis lasting more than a day but remitting within one month, with full return to premorbid function. Schizoaffective disorder is the mood boundary: a concurrent mood-plus-psychosis picture in which a mood episode and Criterion-A psychosis coincide, yet psychosis also occurs for at least two weeks without prominent mood symptoms. Delusional disorder is the circumscribed-content, preserved-function boundary: sustained delusions without the fuller symptom set or the functional collapse of schizophrenia.

SPECTRUM NEIGHBOUR	BOUNDARY AXIS	DISCRIMINATOR FROM SCHIZOPHRENIA
Schizotypal disorder	Severity (attenuated)	**Odd/eccentric but no frank, sustained psychosis**
Brief psychotic disorder	Duration (shortest)	**Psychosis >1 day, remits within 1 month, full recovery**
Schizophreniform disorder	Duration (intermediate)	**Full picture but total illness <6 months (DSM-5)**
Schizoaffective disorder	Mood-loading	**Mood episode concurrent with psychosis, plus >=2 weeks of psychosis without prominent mood**
Delusional disorder	Severity/breadth	**Circumscribed delusions, function otherwise preserved**

The five spectrum neighbours placed by their single defining boundary axis; each is developed as a full entity in the Other psychotic disorders, delusional syndromes and catatonia notes.

TRAP **Confusing schizophreniform with schizoaffective disorder.** Schizophreniform is a duration boundary (a full picture that has simply not lasted six months); schizoaffective is a mood-plus-psychosis boundary (a concurrent mood episode). One is about the clock, the other about mood.

17.3 The categorical model and its limits

The categorical model treats schizophrenia as a discrete disease entity, present or absent by criteria, qualitatively distinct from health and from other disorders. This is the working assumption of every operational manual and it has real virtues: it communicates in one word, guides treatment thresholds, and organises services. Its weakness is that nature has stubbornly refused to draw the lines the categories require. There is no biological test, no pathognomonic sign, no discontinuity in the distribution of symptoms that marks a clean boundary between schizophrenia and health or between schizophrenia and its neighbours. The categories carve a continuous landscape at conventional, and to some degree arbitrary, thresholds, which is why the same patient can shift diagnostic label across episodes and why comorbidity between "distinct" spectrum entities is so high (Kaplan & Sadock 2024).

17.4 The dimensional model and the psychosis continuum

The dimensional alternative holds that psychotic experience is distributed continuously in the population and that clinical psychosis is the severe, persistent, impairing tail of that distribution rather than a categorically separate state. This is the psychosis continuum: psychotic phenomena "lay on a continuum from mild subthreshold psychotic phenomena to frank and florid psychosis," with no discrete demarcation "other than severity, breadth, and persistence" (Kaplan & Sadock 2024). On this view the final categorical diagnosis is the endpoint of a longitudinal pathway, from asymptomatic, to subthreshold psychotic experiences, to infrequent frank symptoms, to persistent psychosis, with the transition governed by an accumulating interplay of genetic and environmental load. Subthreshold symptoms are read as indicators of proneness to psychosis, not as a disease in themselves.

PEARL

The continuum is the reason the same three axes recur everywhere: severity, persistence (duration), and mood-loading. They define the spectrum neighbours in 17.2 and they define the psychosis continuum here. Hold "severity, duration, mood" as the master key to the whole topic.

17.5 Psychotic-like experiences in the general population

The empirical engine of the dimensional case is that psychotic-like experiences (PLEs, also called psychotic experiences) are common in people who carry no psychiatric diagnosis and never seek care: isolated ideas of reference, magical thinking, unusual perceptual experiences, fleeting hallucination-like phenomena. Prevalence estimates vary widely with the instrument used, but converge on the message that these experiences are far commoner than psychotic disorders. The WHO World Mental Health Survey across 18 countries reported a mean lifetime psychotic-experience rate of **5.8%**, higher in high-income (6.8%) than low- and low-middle-income (3.2%) countries; a replication of the US National Comorbidity Survey found **9.1%** reporting at least one such experience, and the WHO World Health Survey across 52 countries found **12.5%**

endorsing at least one over the past year (Kaplan & Sadock 2024, McGrath 2015). The great majority of these individuals meet no diagnostic criteria and remain stable; only a modest proportion ever convert to a psychotic illness.

~5.8%	~9.1%	~12.5%
LIFETIME PE, WHO WMH (18 COUNTRIES)	>=1 PE, US NCS REPLICATION	>=1 PE PAST YEAR, WHO WORLD HEALTH SURVEY

COMMON TRAP

Reading a high general-population rate of psychotic-like experiences as a high rate of schizophrenia. The two are separated by an order of magnitude: schizophrenia lifetime risk is about one percent, while psychotic experiences run to several percent or more. The whole point of the continuum is that most people with a psychotic experience never develop a psychotic disorder; the experience marks proneness, not disease.

17.6 The extended psychosis phenotype and the proneness-persistence-impairment model

Van Os and colleagues formalised the continuum into the extended psychosis phenotype: the observable spread of psychotic experience from transient, non-clinical phenomena in the general population, through the attenuated and at-risk states, to full clinical psychosis, all seen as expressions of the same underlying liability (van Os & Linscott 2012). Their meta-analysis proposed the proneness-persistence-impairment model: subclinical psychotic experiences are common and mostly transitory (proneness); in a minority they persist rather than fade (persistence), driven by the accumulation of environmental and genetic risk; and only when persistence is joined by distress and functional impairment does the experience become clinically relevant and liable to cross into disorder (van Os 2009). The model reframes the diagnostic threshold as a point on a graded liability rather than a natural kind.

WORKED EXAMPLE

A 19-year-old with no illness reports occasional sensed presences and the feeling that song lyrics carry personal messages, without conviction, distress or dysfunction. This is a psychotic-like experience on the proneness end of the extended phenotype; base rates say it will most likely remit and never become a disorder. Contrast a 19-year-old whose similar experiences have hardened over a year into held delusions, daily voices, withdrawal and failing studies: persistence plus impairment has moved him along the continuum toward the clinical, categorical diagnosis. Same phenomenology, different position on severity, persistence and impairment.

17.7 How ICD-11 and DSM-5 blend categorical diagnosis with dimensional specifiers

The manuals did not choose between the two models; they blended them. Both retain a categorical diagnosis of schizophrenia made by threshold criteria, but both bolt on a dimensional layer that describes the individual patient beyond the label. DSM-5 introduced the Clinician-Rated Dimensions of Psychosis Symptom Severity, an eight-item scale rating hallucinations, delusions, disorganised speech, abnormal psychomotor behaviour, negative symptoms and the three associated domains of impaired cognition, depression and mania, each on a 0 to 4 scale

(American Psychiatric Association 2022). ICD-11 does the parallel thing through its six symptom-domain qualifiers, positive, negative, depressive, manic, psychomotor and cognitive, rated per episode, plus course specifiers (Gaebel 2020). Both did this in the same move that abolished the classical subtypes: the paranoid, hebephrenic and catatonic subtypes were dropped for poor reliability, temporal instability and low predictive validity, and a dimensional symptom-domain description was put in their place. The result is a hybrid: a categorical diagnosis carrying a dimensional profile.

INDIA

Where the exit examination or a question bank still uses ICD-10, remember that the dimensional specifier layer is a feature of ICD-11 and DSM-5, not of ICD-10, which retained the subtypes and offered no symptom-domain rating. For a modern answer, state the blend explicitly: categorical diagnosis plus dimensional specifiers, subtypes abolished. Note which system you are answering in.

GOOD TO REMEMBER

- **Schizophrenia spectrum:** the DSM-5 "Schizophrenia Spectrum and Other Psychotic Disorders" / ICD-11 "primary psychotic disorders" family sharing psychotic phenomenology with schizophrenia; central claim is that its members differ by degree along severity, duration and mood-loading; discriminator is that schizophrenia is the full, sustained, mood-free anchor.
- **Schizotypal disorder:** attenuated, enduring odd beliefs and perceptual distortions; central claim is a personality-level, subclinical psychosis phenotype genetically linked to schizophrenia; discriminator is that it never reaches frank, sustained psychosis.
- **Schizophreniform disorder:** a schizophrenia-like picture; central claim is that it is a duration boundary; discriminator is total illness under six months (DSM-5), converting to schizophrenia if it persists.
- **Brief psychotic disorder:** acute psychosis; central claim is the shortest-duration boundary; discriminator is onset over a day, remission within one month, and full return to premorbid function.
- **Schizoaffective disorder:** concurrent mood-plus-psychosis; central claim is the mood boundary; discriminator is a mood episode concurrent with Criterion-A psychosis plus at least two weeks of psychosis without prominent mood symptoms.
- **Delusional disorder:** sustained circumscribed delusions; central claim is a narrow, function-preserving boundary; discriminator is intact functioning outside the delusional theme without the fuller schizophrenia syndrome.
- **Psychosis continuum:** psychosis distributed continuously from subthreshold experiences to florid illness; central claim is no discrete demarcation other than severity, breadth and persistence; discriminator is that most population-level psychotic experiences never become disorder.
- **Extended psychosis phenotype (van Os & Linscott 2012):** the population-to-clinic spread of psychotic experience as one liability; central claim is the proneness-persistence-impairment model; discriminator is that clinical relevance requires persistence plus impairment, not the experience alone.
- **Categorical-dimensional blend (ICD-11 / DSM-5):** a threshold diagnosis carrying a symptom-domain rating; central claim is that both manuals kept the category but added dimensional specifiers and dropped subtypes; discriminator is that the dimensional layer is absent from legacy ICD-10.

HOLD THIS

Schizophrenia is the anchor of a spectrum whose neighbours are placed by severity (schizotypal, delusional), duration (brief, schizophreniform) and mood-loading (schizoaffective), and the severe end of a psychosis continuum on which psychotic-like experiences run to several percent of the healthy population; ICD-11 and DSM-5 keep a categorical diagnosis but add dimensional symptom-domain specifiers and abolish the subtypes.

18 · Discriminate: schizophrenia versus its mimics

Why this matters. Schizophrenia is a diagnosis of pattern and of exclusion. The whole point of the classification band is that it hands you a decision procedure: before the label is allowed to settle, every psychosis that could be mistaken for it must be walked past and ruled out. Examiners test this as a **differential diagnosis**, and they reward the candidate who can name, for each mimic, the single discriminator that separates it from schizophrenia rather than reciting six full criteria sets. This topic builds one interleaved **differential** decision tree, one discriminator per rival, and closes on the mandatory organic and substance workup of a first episode.

The raw descriptive definitions of the phenomena being weighed, what a delusion, a hallucination or formal thought disorder actually is, belong to the Psychometry, Assessment and Descriptive Psychopathology notes; here we only sort the disorders. The other psychotic disorders as entities in their own right, with their full criteria, belong to the Other psychotic disorders, delusional syndromes and catatonia notes; they appear below only as points on the differential diagnosis tree. Nothing about treatment is taught here (Kaplan & Sadock 2024, American Psychiatric Association 2022).

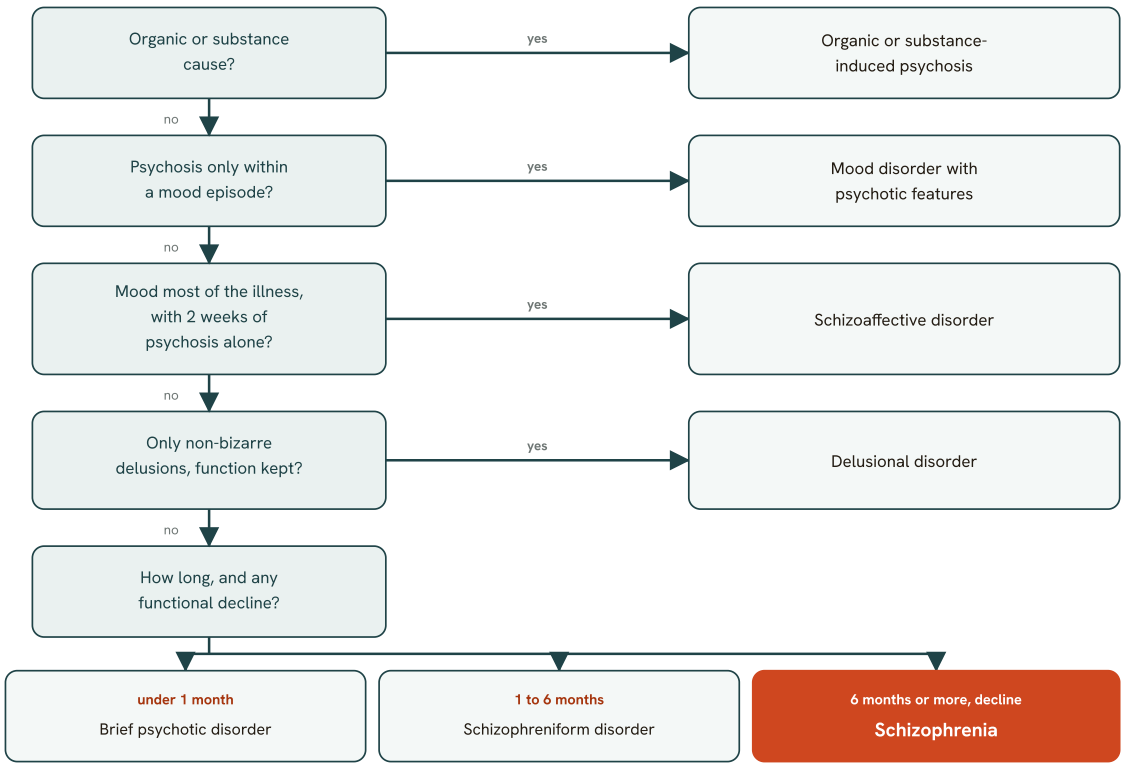


Fig 8.12 The differential decision tree that separates schizophrenia from its mimics. Working down from a first episode of psychosis, each question turns on a single discriminator: rule out an organic or substance cause first, then a mood-confined psychosis, then schizoaffective disorder, then a preserved-function delusional disorder, and finally sort the remainder by duration and decline. Only the six-month picture with functional decline is schizophrenia.

18.1 The order of operations: organic and substance first, then mood, then time

The differential is not a flat list; it has an order. First strip out the psychoses that are not primary at all, the organic and substance-induced ones, because missing them is the most dangerous error and the cause is treatable. Next apply the mood exclusion: a psychosis confined to a mood episode is a mood disorder, and one that overlaps a mood illness in a defined way is schizoaffective. Only once both of those are cleared does the picture become a *primary, non-affective* psychosis, at which point the remaining discriminator is time: less than one month is brief psychotic disorder, one to six months is schizophreniform, and six months or more (with dysfunction) is schizophrenia. Delusional disorder sits to the side as the picture built from non-bizarre delusions alone. This ordering is the tree in Fig 8.6.

RULE **Exclude secondary causes, then mood, then read the clock.** Organic and substance-induced psychosis are ruled out first, the mood exclusion next, and duration decides among the remaining primary non-affective psychoses.

18.2 Mood disorder with psychotic features: psychosis lives inside the mood episode

The first affective rival is a mood disorder with psychotic features, a major depressive or manic episode severe enough to carry delusions or hallucinations. The single discriminator is *temporal confinement*: the psychotic symptoms are present **only** during the mood episode and remit when

the mood resolves, never standing alone in euthymia (American Psychiatric Association 2022). A supporting clue, not a rule, is that the content is often **mood-congruent**: nihilistic, guilt-laden or poverty delusions in depression; grandiose or special-powers delusions in mania. In schizophrenia, by contrast, psychosis persists across mood states and outside any full mood episode.

RULE **Psychosis confined to mood episodes is a mood disorder, not schizophrenia.** If it is only ever present when the patient is depressed or manic, and it clears when the mood clears, the diagnosis is a mood disorder with psychotic features.

18.3 Schizoaffective disorder: the two rules that box it in

Schizoaffective disorder is the overlap zone, and it is defined by two rules that must both hold (DSM-5-TR Criteria B and C; American Psychiatric Association 2022). First, at some point in the lifetime illness there is a period of at least two weeks of delusions or hallucinations *in the absence* of a major mood episode; this is what separates it downward from a pure mood disorder with psychotic features, in which psychosis never outlives the mood. Second, symptoms meeting criteria for a major mood episode are present for the majority of the total duration of the active and residual illness; this is what separates it upward from schizophrenia, in which mood episodes, if they occur at all, are present only for a *minority* of the illness. Schizoaffective therefore sits precisely between the two: enough standalone psychosis to exclude a mood disorder, enough mood to exclude schizophrenia.

WORKED EXAMPLE

A patient has, over a two-year illness, roughly fourteen months in which a major depressive or manic episode is present and, within that, a clear three-week stretch of persecutory delusions while euthymic. The standalone psychotic fortnight (well over two weeks) rules out a pure mood-with-psychosis label; the mood burden occupying the majority of the illness rules out schizophrenia. The answer is schizoaffective disorder. Shrink the mood component to a couple of brief episodes and the same psychosis becomes schizophrenia with intercurrent mood symptoms.

18.4 Delusional disorder: non-bizarre delusions, otherwise intact

Delusional disorder is the picture built from one or more *non-bizarre* delusions (persecutory, jealous, erotomanic, grandiose, somatic) that could conceivably be true, with functioning outside the direct impact of the delusion largely *preserved* and behaviour not obviously odd (American Psychiatric Association 2022; Marneros 2020). The discriminator from schizophrenia is the *absence of the other core symptoms*: there are no prominent hallucinations, no formal thought disorder, no negative symptoms and no grossly disorganised behaviour; if any of these is prominent, the diagnosis moves toward schizophrenia. In short, schizophrenia is a broad, multi-domain psychosis with functional decline; delusional disorder is a narrow, encapsulated delusional system on an otherwise working person.

18.5 Schizophreniform disorder: the schizophrenia picture, one to six months

Schizophreniform disorder is, symptomatically, schizophrenia: it meets the same active-phase (Criterion A) symptom set. It is separated by *duration alone*, an episode lasting at least one month but less than six months, and, unlike schizophrenia, it does **not** require a marked functional decline (American Psychiatric Association 2022). If the illness is still ongoing when the diagnosis is made, it is labelled "provisional"; should it fail to remit and cross six months, the diagnosis converts to schizophrenia. It is therefore best read as schizophrenia caught before the six-month duration line, or as a good-prognosis episode that resolves before it.

TRAP **Calling a four-month schizophrenia-like psychosis "schizophrenia" under DSM-5-TR.** Below six months total it is schizophreniform disorder (provisional if ongoing); it becomes schizophrenia only once continuous disturbance reaches six months.

18.6 Brief psychotic disorder: under one month, often post-stressor, full recovery

Brief psychotic disorder is the shortest of the primary psychoses: at least one day but *less than one month*, with *eventual full return* to the premorbid level of function (American Psychiatric Association 2022). It frequently, though not necessarily, follows a marked psychosocial *stressor* (the "with marked stressor(s)" specifier; the peripartum-onset specifier captures the postpartum form). The two discriminators from schizophrenia are the sub-one-month duration and the complete recovery to baseline; schizophrenia neither resolves within a month nor reliably returns the patient to premorbid function. Note the tidy duration ladder across the primary non-affective psychoses: under one month is brief psychotic, one to six months is schizophreniform, six months or more is schizophrenia.

<1 month	1 to 6 months	≥6 months
BRIEF PSYCHOTIC DISORDER	SCHIZOPHRENIFORM DISORDER	SCHIZOPHRENIA (DSM-5-TR)

18.7 Organic and substance-induced psychosis: the mandatory first-episode workup

Before any of the primary psychoses can be diagnosed, a psychosis that is *secondary*, driven by a medical illness or a substance, must be excluded. A psychosis attributable to a general medical condition is an organic psychosis (a secondary psychosis); one driven by intoxication, withdrawal or a prescribed agent is a substance-induced psychosis. This is why every first-episode psychosis (a **first episode psychosis**, fep) carries a mandatory organic-and-substance workup: the purpose of the first-episode psychosis assessment is to catch the treatable secondary cause before committing to a lifelong primary label.

Organic causes to exclude. The high-yield secondary causes are autoimmune and infective *encephalitis* (the classic being anti-NMDA receptor encephalitis, NMDARE, driven by antibodies to the NMDA-receptor GluN1 subunit, presenting with new-onset psychosis plus seizures, movement disorder and autonomic instability; Kaplan & Sadock 2024), *temporal-lobe pathology* (temporal-lobe epilepsy, tumour), and *delirium* (an acute, fluctuating confusional state with clouded consciousness, the single most important bedside separator from a primary psychosis, in which the sensorium is clear). Red flags that mandate a hunt for an organic cause include acute or subacute onset, clouding or fluctuation of consciousness, seizures, focal neurology, abnormal

movements, and prominent visual (rather than auditory) hallucinations. **Substances to exclude.** Cannabis, stimulants (amphetamine, cocaine, methamphetamine), hallucinogens, and withdrawal states must be cleared by history and a urine drug screen; a substance-induced psychosis by definition resolves once the agent and a reasonable washout have passed, whereas schizophrenia does not. For the neurochemical pathways and the imaging principles (CT, MRI) that underlie this workup, cross-reference the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

TRAP **Missing an organic or substance cause in a first episode of psychosis.** Diagnosing schizophrenia at a first-episode psychosis without a completed organic and substance-induced psychosis workup is the classic and dangerous exam error; anti-NMDA encephalitis and stimulant psychosis both mimic it and both are treatable.

18.8 The differential at a glance

The table below sets each mimic against the one discriminator that separates it from schizophrenia and the key feature that anchors it, running the affective rivals, the duration-defined rivals, the encapsulated-delusion rival and the two secondary psychoses in the same order as the decision tree (Fig 8.12).

MIMIC	THE ONE DISCRIMINATOR FROM SCHIZOPHRENIA	KEY FEATURE
Mood disorder with psychotic features	**Psychosis present ONLY within a mood episode, remits with the mood**	Often mood-congruent (nihilistic in depression, grandiose in mania)
Schizoaffective disorder	**≥2 weeks of psychosis WITHOUT a mood episode, AND mood present for the MAJORITY of the illness**	The overlap zone: too much standalone psychosis for a mood disorder, too much mood for schizophrenia
Delusional disorder	**Non-bizarre delusion(s) with function otherwise preserved and NO other prominent core symptoms**	Encapsulated delusional system; no prominent hallucinations, thought disorder or negative symptoms
Schizophreniform disorder	**Duration 1 to 6 months; NO functional-decline requirement**	Symptomatically schizophrenia caught before the 6-month line ("provisional" if ongoing)
Brief psychotic disorder	**Duration <1 month with FULL return to baseline; often post-stressor**	Shortest primary psychosis; complete recovery is definitional
Organic / secondary psychosis	**A medical cause (encephalitis, temporal-lobe pathology, delirium) is demonstrable**	Clouded/fluctuating consciousness, seizures, focal signs, visual hallucinations; anti-NMDA encephalitis is the classic
Substance-induced psychosis	**Onset and offset track a substance; resolves after the agent and washout**	Cannabis, stimulants, hallucinogens, withdrawal; cleared by history and urine drug screen

Interleaved differential of schizophrenia against its mimics: each row gives the single discriminator and the anchoring feature, in the order of the decision tree, secondary causes first, then mood, then the duration ladder, with delusional disorder to the side.

GOOD TO REMEMBER

- **Mood disorder with psychotic features:** a major depressive or manic episode carrying delusions or hallucinations; central claim is that psychosis is confined to the mood episode and is often mood-congruent; the discriminator is that it is present only during the mood episode and remits when the mood resolves.
- **Schizoaffective disorder:** a psychosis with a heavy mood burden; core criteria are at least two weeks of psychosis without a mood episode PLUS mood episodes present for the majority of the total illness; the discriminator is the two-week standalone-psychosis rule (excludes mood disorder) with the majority-of-illness mood rule (excludes schizophrenia).
- **Delusional disorder:** non-bizarre delusion(s) on an otherwise intact person; central claim is preserved function outside the delusion with no other prominent core symptoms; the discriminator is the absence of prominent hallucinations, thought disorder, negative symptoms or disorganisation.
- **Schizophreniform disorder:** the full schizophrenia symptom picture; core criterion is a duration of one to six months with NO required functional decline; the discriminator is duration, it converts to schizophrenia at six months.
- **Brief psychotic disorder:** an acute psychosis, often after a stressor; core criteria are duration under one month with full return to premorbid function; the discriminator is the sub-one-month duration plus complete recovery to baseline.
- **Organic (secondary) and substance-induced psychosis:** psychoses driven by a medical illness (autoimmune or infective encephalitis such as anti-NMDA receptor encephalitis, temporal-lobe pathology, delirium) or by a substance; central claim is that they are secondary, not primary; the discriminator is a demonstrable medical or substance cause, which the mandatory first-episode psychosis workup is designed to catch before schizophrenia is diagnosed.

HOLD THIS

Rule out organic and substance-induced psychosis first, then apply the mood exclusion (confined-to-episode is a mood disorder, two-weeks-standalone plus majority-mood is schizoaffective), then read the clock: under one month is brief psychotic, one to six months is schizophreniform, six months or more with dysfunction is schizophrenia, and a non-bizarre delusion on an intact person is delusional disorder.

Course, prognosis and outcome

19 · The phases, natural course and duration of untreated psychosis

Schizophrenia is not a single event but a trajectory. Long before the first frank hallucination there are subtle differences in cognition and social function, then a symptomatic decline, then the first acute episode, and for many patients a chronic course of recurrent episodes on a background of persisting deficit. Being able to name the **phases**, describe the **natural course** and the pattern of **relapse**, and quote the classical outcome data is a staple of both long cases and vivas. The single most examinable modern fact in this topic is that a longer **duration of untreated psychosis** predicts a worse outcome, which is the whole rationale for early intervention.

Exam framing. Expect to be asked to lay out the phases from premorbid to residual, to state the **rule of thirds** and attribute it honestly as an approximation, to name the three WHO cross-cultural **outcome study** generations (International Pilot Study of Schizophrenia, Determinants of Outcome, International Study of Schizophrenia), and to define the duration of untreated psychosis and state its prognostic significance. The classic examiner trap here is to reproduce the Kraepelinian picture of a uniformly deteriorating illness; the modern data show heterogeneous, frequently non-deteriorating outcomes.

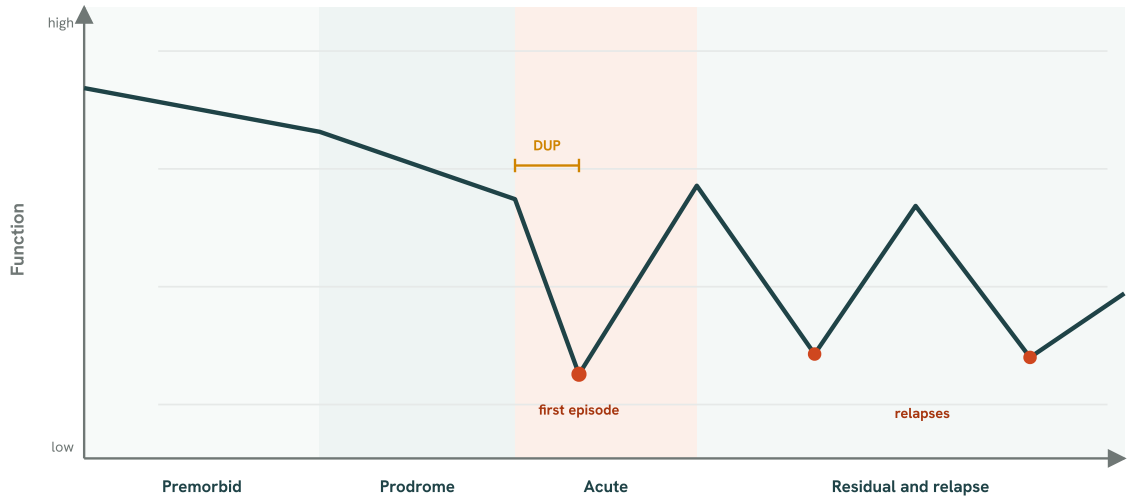


Fig 8.13 The phases and natural course of schizophrenia, plotted as function against time. A near-normal premorbid level declines through the prodrome, drops at the first episode after a duration of untreated psychosis, and then follows a relapsing course with incomplete recovery to a residual baseline. The course is heterogeneous rather than uniformly deteriorating, and a longer duration of untreated psychosis predicts a worse outcome.

19.1 The premorbid phase: subtle differences long before illness

What it is. The premorbid phase is the long period, often reaching back to childhood, in which individuals who will later develop schizophrenia differ subtly from their peers, before any prodromal symptom appears. These **premorbid** differences are typically mild and non-specific: slightly delayed developmental milestones, poorer motor coordination, lower average childhood IQ and academic attainment, more social withdrawal and fewer friendships, and a tendency to solitary or "schizoid" traits (Kaplan & Sadock 2024). They are detectable at a population level in birth-cohort and follow-back studies but are far too non-specific to identify an individual case prospectively. Conceptually this phase is where the neurodevelopmental account of the illness is anchored; for the developmental mechanisms themselves, cross-reference the neurodevelopment material within these notes.

The key point for exams is that these premorbid features are *trait-like* and present well before psychosis, distinguishing them from the prodrome, which is a symptomatic *change* from the person's own baseline.

19.2 The prodromal phase: symptomatic decline before frank psychosis

What it is. The prodromal phase is the period of symptomatic disturbance preceding frank psychosis, evolving over months to years, in which non-specific changes appear first (depressed mood, anxiety, sleep disturbance, irritability, social withdrawal, falling academic or occupational performance) and attenuated subthreshold psychotic features follow (ideas of reference, odd beliefs, perceptual distortions, suspiciousness), held with relatively preserved insight (Yung & McGorry 1996). Classically the **prodromal phase** is a retrospective concept, certain only once psychosis has declared, which is why prospective research reframes it as an at-risk mental state. The detailed operational at-risk criteria and transition data are developed in the prodrome and first-episode topic within these notes; here it sits simply as the second phase of the natural history.

19.3 The acute phase: the first episode and active psychosis

What it is. The acute phase is the period of florid, active psychosis in which positive symptoms (delusions, hallucinations, disorganisation) dominate the picture and typically bring the patient to psychiatric attention. The first such episode is the **acute** first-episode presentation, usually in late adolescence or early adult life, and it is the point at which diagnosis is provisionally made and treatment begun. For the descriptive definitions of what a delusion, a hallucination or formal thought disorder actually *is* as a phenomenon, cross-reference the Psychometry, Assessment and Descriptive Psychopathology notes; here the acute phase is defined by the prominence and activity of those positive symptoms rather than by their form.

Onset may be acute (developing over days to weeks, often with a better prognosis) or insidious (evolving over months to years out of a long prodrome, carrying a worse prognosis). Following the acute episode most patients enter partial or full remission, but a substantial proportion do not return fully to their premorbid level.

19.4 The residual phase: chronic negative and defect states

What it is. The residual phase is the chronic phase that follows one or more acute episodes, in which florid positive symptoms have subsided but attenuated symptoms and, above all, persistent negative symptoms and cognitive impairment remain. The **residual phase** is the substrate of long-term disability: blunted affect, poverty of speech, avolition, social withdrawal and functional decline, often with relatively few active positive symptoms. In this phase deterioration in social role tends to be established rather than progressing; much of the loss of social function occurs during the first two years after diagnosis rather than accruing steadily over decades (Shorter Oxford Textbook of Psychiatry 2018). For the enduring primary negative-symptom construct (the deficit syndrome) as an entity, cross-reference the negative-symptoms topic within these notes.

19.5 The natural course: episodic relapse on a variable background

Pattern. The natural course of schizophrenia in most patients is one of recurrent acute episodes separated by inter-episode periods of variable recovery, superimposed on the phase structure above. Some patients have a single episode with full recovery; some have recurrent episodes with full inter-episode recovery; many have recurrent episodes with incomplete recovery and a

stepwise accumulation of residual deficit; a minority run a continuous, unremitting course. The classic clinical observation is that each **relapse** tends to be followed by slower and less complete remission, and that inter-episode functioning may ratchet downward, though this is far from universal.

ICD-10 course specifiers. The natural course was formally captured in ICD-10 by a set of longitudinal specifiers applied when the illness had been observed for at least a year: continuous; episodic with progressive deficit; episodic with stable deficit; episodic remittent; incomplete remission; and complete remission. Where exams still use ICD-10, these course specifiers remain fair game. ICD-11 and DSM-5-TR have moved away from this scheme toward course qualifiers keyed to episode number and current state (first episode, multiple episodes, continuous), each specified as currently in acute episode, in partial remission or in full remission; both current systems also dropped the classical subtypes in favour of a dimensional symptom-domain approach.

TRAP **Not a uniformly deteriorating Kraepelinian course.** Dementia praecox implied inevitable decline; the natural course is in fact heterogeneous, and a large fraction of patients stabilise or recover rather than deteriorate relentlessly.

19.6 Relapse and its drivers

Relapse. A relapse is the recurrence or marked worsening of active psychotic symptoms after a period of remission or stability. The strongest and most modifiable driver of **relapse** is discontinuation of antipsychotic medication: relapse risk is high when maintenance treatment is stopped after an episode. High expressed emotion in the family environment (critical, hostile or over-involved attitudes), substance misuse (notably cannabis and stimulants) and psychosocial stress are further recognised precipitants. The management levers that reduce relapse (maintenance pharmacotherapy, family intervention, adherence support) belong to treatment and are developed in the Schizophrenia: management, antipsychotics and adverse effects notes; here relapse matters as the engine of the recurrent natural course.

RULE **Stopping the drug is the commonest cause of relapse.** After a first episode, relapse risk is substantially higher once maintenance antipsychotic medication is discontinued.

19.7 Long-term outcome and the rule of thirds

The heterogeneity. The long-term outcome of schizophrenia is strikingly heterogeneous. Long-term follow-up cohorts (including the classic European studies by Manfred Bleuler and by Ciompi) converged on the message that a substantial proportion of patients achieve social recovery or a favourable outcome, contradicting the fatalistic Kraepelinian view. This clinical shorthand is the rule of thirds: as an approximation, roughly one-third of patients have a good **long-term outcome** (recovery or mild residual symptoms with reasonable function), roughly one-third an intermediate outcome (persisting symptoms but some function), and roughly one-third a poor outcome (chronic, severely disabling illness).

RULE **Rule of thirds, quote it as an approximation.** Roughly a third good outcome, a third intermediate, a third poor; a memory aid for heterogeneity, not a precise statistic, and the exact proportions vary by cohort and outcome definition.

Attribution honesty. The rule of thirds is a teaching heuristic distilled from several outcome cohorts rather than the finding of one definitive study, and the precise proportions depend heavily on how "outcome" is defined and on the era, treatment access and length of follow-up. Quote it as an approximate, illustrative figure and name it as a heuristic; do not present it as a precise, source-anchored statistic.

19.8 The WHO cross-cultural outcome studies: IPSS, DOSMED and ISoS

The most important body of **outcome study** evidence comes from three linked generations of a World Health Organization **who study** programme, which followed large cohorts across many countries with standardised instruments.

STUDY	WHAT IT WAS	CENTRAL FINDING
ipss (International Pilot Study of Schizophrenia)	WHO collaborative study, patients ascertained across nine countries from the late 1960s, using standardised structured interviews (Present State Examination, CATEGO)	**Schizophrenia could be reliably identified across diverse cultures; outcomes were variable and often better than expected**
dosmed (Determinants of Outcome of Severe Mental Disorders)	WHO incidence-based follow-up across ten countries, designed to sidestep the sampling bias of prevalence cohorts by studying first-contact cases	**Confirmed a broadly comparable incidence but a heterogeneous, frequently non-deteriorating course**
isos (International Study of Schizophrenia)	WHO long-term (roughly 15 to 25 year) follow-up of the earlier IPSS and DOSMED cohorts	**A large proportion of patients were recovered or substantially improved at very long follow-up; outcomes were not uniformly deteriorating**

The three generations of the WHO cross-cultural outcome programme. Their unifying message is that long-term outcome is heterogeneous and often non-deteriorating, not the inevitable decline implied by dementia praecox (Jablensky 2000).

The much-cited finding that outcomes were *better in developing than in developed countries* came out of this same programme; that specific finding, its size and the debate over whether it is real or an artefact of ascertainment and follow-up, is worked through in the prognosis and prognostic-factors topic within these notes rather than repeated here. For the purposes of the natural course, the load-bearing conclusion is heterogeneity: the WHO data are the empirical refutation of a single deteriorating trajectory.

19.9 The duration of untreated psychosis

Definition. The duration of untreated psychosis (DUP) is the interval between the onset of frank psychotic symptoms and the start of adequate antipsychotic treatment. It is distinct from the duration of untreated *illness*, which reaches back further to the onset of the prodrome. Across

first-episode cohorts a longer DUP is associated with a poorer symptomatic and functional outcome and with slower, less complete remission (Penttila et al. 2014; Fraguas et al. 2014).

Why it matters. Two explanations are advanced for the association between a longer period of **untreated psychosis** and worse outcome (Shorter Oxford Textbook of Psychiatry 2018). The first is confounding: a prolonged, insidious onset is itself a marker of a more severe, treatment-resistant form of the illness, so a long **dup** may be an *index* of severity rather than a cause of poor outcome. The second is the "neurotoxicity" hypothesis: that untreated active psychosis is itself harmful and renders the illness progressively less responsive to treatment. Whichever mechanism dominates, a long DUP flags a worse prognosis, and shortening it is the explicit target of early-intervention and early-detection services. Note the honest caveat that whether early-intervention teams actually reduce DUP, and whether that translates into better long-term outcome, remains debated.

DUP ↑	~2 yr	~1/3
WORSE OUTCOME, SLOWER REMISSION	MOST SOCIAL DECLINE IS EARLY	GOOD LONG-TERM OUTCOME (RULE OF THIRDS)

RULE **Longer DUP predicts worse outcome.** A longer duration of untreated psychosis is associated with poorer symptomatic and functional outcome, which is the central argument for early detection and prompt treatment.

TRAP **Do not read DUP as purely causal.** Part of the association may be confounding: an insidious, prolonged onset is itself a marker of severe, treatment-resistant illness, so a long DUP may index severity rather than cause the poor outcome.

WORKED EXAMPLE

A 19-year-old with a year of falling grades, withdrawal and odd magical beliefs (prodromal phase) develops florid persecutory delusions and voices over three weeks (acute first episode) but is only brought to services eight months later. That eight-month interval from frank psychosis to adequate treatment is the duration of untreated psychosis. Following treatment the positive symptoms remit but blunted affect and avolition persist (residual phase), and after he stops medication he relapses within the year. This single vignette carries the whole natural course: premorbid to prodromal to acute to residual, with relapse on drug discontinuation and a prognostically important long DUP.

HOLD THIS

The natural course runs premorbid to prodromal to acute to residual with relapsing episodes; long-term outcome is heterogeneous (rule of thirds, and the WHO IPSS, DOSMED and ISoS studies show frequently non-deteriorating outcomes), and a longer duration of untreated psychosis predicts a worse outcome.

MNEMONIC

PPARR

Premorbid, **P**rodromal, **A**cute, **R**esidual, **R**elapse: the four phases plus the relapsing pattern that defines the natural course.

GOOD TO REMEMBER

- **Premorbid phase:** trait-like subtle differences (mild motor, cognitive/IQ and social differences) present from childhood, well before any symptom; discriminator is that it is a stable baseline trait, not a change, and is too non-specific to identify an individual case.
- **Prodromal phase:** symptomatic change from the person's own baseline, non-specific decline then attenuated psychotic features over months to years; discriminator is that it is classically a retrospective concept, reframed prospectively as the at-risk mental state.
- **Acute phase:** florid active psychosis dominated by positive symptoms, containing the first episode; discriminator is that acute onset carries a better prognosis than an insidious one.
- **Residual phase:** chronic phase with persisting negative symptoms and cognitive impairment after positive symptoms subside; discriminator is that most social decline is established within the first two years, not accrued steadily over decades.
- **Natural course and relapse:** recurrent acute episodes with variable inter-episode recovery; discriminator is that the commonest and most modifiable driver of relapse is antipsychotic discontinuation.
- **Rule of thirds:** roughly a third good, a third intermediate, a third poor long-term outcome; discriminator is that it is an approximate teaching heuristic, not a precise single-study statistic.
- **WHO outcome studies (IPSS, DOSMED, ISoS):** IPSS showed schizophrenia is identifiable across cultures, DOSMED was the incidence-based ten-country follow-up, ISoS the very long-term follow-up; discriminator/central claim is that outcomes are heterogeneous and frequently non-deteriorating, refuting a uniform Kraepelinian decline (Jablensky 2000).
- **Duration of untreated psychosis (DUP):** interval from onset of frank psychosis to adequate treatment; discriminator is that a longer DUP predicts worse outcome (partly causal "neurotoxicity", partly a marker of insidious severe illness) and is the target of early intervention.

PEARL

The examiner's favourite pivot is from Kraepelin to the WHO data: dementia praecox framed schizophrenia as inevitably deteriorating, but IPSS, DOSMED and ISoS, together with the long-term European cohorts, show a heterogeneous course in which a large minority recover. Lead with heterogeneity, then hang the rule of thirds and the prognostic weight of duration of untreated psychosis off it.

20 · Prognostic factors, cross-cultural outcome and recovery

The course of schizophrenia is heterogeneous and, in the individual case, still largely unpredictable, so what an examiner tests here is not a single verdict but three separable things: which features at first presentation shift the odds toward a better or worse outcome, why the WHO cross-cultural programme found the counterintuitive result that outcome was on average better in the developing world, and what modern operational definitions of remission and recovery actually require. Each of these is a discrete answer with its own evidence, and the

commonest error is to blur them, above all to treat a patient who is symptom-free as though they have recovered.

How to hold it. Learn the good-versus-poor **prognostic factor** lists as paired opposites, keep the three WHO studies (IPSS, DOSMeD, ISoS) as one story with a critique attached, and treat symptomatic **remission** and functional **recovery** as two different thresholds. The raw descriptive definitions of the psychotic phenomena themselves belong to the Psychometry, Assessment and Descriptive Psychopathology notes; antipsychotic treatment, its effect on outcome and rehabilitation belong to the Schizophrenia: management, antipsychotics and adverse effects notes; this topic states them only as far as prognosis requires.

Feature	Good prognosis	Poor prognosis
Onset	Acute, sudden	Insidious, gradual
Precipitant	Clear stressor	None identified
Symptoms	Positive, affective	Negative, deficit
Premorbid	Good adjustment	Poor, withdrawn
Demographics	Female, married, later onset	Male, single, early onset
Untreated psychosis	Short DUP, treated early	Long DUP
Support	Good social support	Poor support, high EE

Weigh the balance of features; no single factor decides the outcome.

Fig 8.14 Good against poor prognostic factors in schizophrenia. The good-prognosis column reads as an acute, affective, well-supported presentation treated early; the poor-prognosis column as an insidious, negative-symptom illness with a long duration of untreated psychosis. The prognosis is the balance across features, not any one of them.

20.1 Good versus poor prognostic factors as paired opposites

Why learn them paired. The predictors of outcome are best held as a single axis with a favourable and an unfavourable pole, because almost every good prognosis feature has a mirror-image poor prognosis feature, and an examiner who gives you one expects the other. The good pole describes an illness that looks reactive, affective and abrupt on a healthy premorbid substrate; the poor pole describes an illness that looks endogenous, negative-symptom-laden and creeping on an already-compromised substrate (Kaplan & Sadock 2024).

The favourable set. A good prognosis is predicted by an acute onset, an identifiable precipitant, prominent mood or affective symptoms, good premorbid functioning, being married or female, and a short duration of untreated psychosis with early treatment (Puri & Hall). Later age of onset, the presence of confusion or perplexity in the acute phase, a family history of mood disorder,

predominant positive symptoms and good treatment concordance sit on the same favourable pole.

The unfavourable set. A poor prognosis is predicted by an insidious onset, prominent negative symptoms, poor premorbid functioning, early onset, male sex, a long duration of untreated psychosis and no identifiable precipitant (an der Heiden & Hafner 2011). Cognitive impairment at presentation, a family history of schizophrenia, chronic course beyond two years, social isolation and structural change such as ventricular enlargement on imaging cluster on this pole. The parsed reviews stress that the predictive value of any single factor is modest, so these shift the odds rather than fix the outcome (Shorter Oxford / an der Heiden & Hafner 2011).

DIMENSION	GOOD PROGNOSIS	POOR PROGNOSIS
Onset	**Acute or abrupt**	Insidious, creeping
Precipitant	**Identifiable stressor present**	No precipitant
Affective symptoms	**Prominent mood component**	Absent; flat or blunted affect
Symptom profile	Predominantly positive symptoms	**Predominant negative symptoms**
Premorbid functioning	**Good premorbid adjustment**	Poor premorbid functioning
Age of onset	Later onset	**Early onset**
Sex and marital status	Female; married	Male; unmarried
Duration of untreated psychosis	**Short DUP, early treatment**	Long DUP, delayed treatment
Family history	Mood disorder	Schizophrenia

The favourable pole reads as reactive, affective and abrupt on a healthy substrate; the poor pole reads as endogenous, negative and insidious on a compromised one. Drawn as Fig 8.8.

RULE **Acute, affective, short DUP predicts better.** An acute onset with an affective component and a short duration of untreated psychosis is the single most reliable favourable triad; treat it as your first-line answer to "what predicts a better outcome".

20.2 Duration of untreated psychosis as a modifiable predictor

Why DUP is special. Most prognostic factors are fixed at presentation and cannot be changed; the duration of untreated psychosis is the one major predictor that is potentially modifiable, which is why it carries such clinical weight. A longer DUP is associated, across cohorts, with a worse symptomatic and functional outcome, and this association is the epidemiological engine behind the early-intervention and first-episode-service movement (Kaplan & Sadock 2024). The causal direction is debated, since an insidious, negative-symptom illness both lengthens DUP and worsens outcome independently, but the working exam position is that shortening DUP through early detection is a legitimate target because at least part of the effect appears causal.

20.3 The WHO cross-cultural programme: IPSS, DOSMeD and ISoS

The three studies as one story. The claim that outcome is better in the developing world rests on a linked WHO cross-cultural programme of three studies. The International Pilot Study of Schizophrenia (IPSS), begun in 1968-69, interviewed patients with psychotic disorders across nine countries using the Present State Examination, and its first achievement was to show that schizophrenia presents in recognisably similar ways across very diverse cultures (WHO 1973; Kaplan & Sadock 2024). Its follow-up then produced the surprise: two-year course and outcome were better in patients from developing centres such as India, Nigeria and Colombia than in developed centres, particularly for the proportion reaching complete remission (WHO 1973; Shorter Oxford / Harrison et al. 2001).

DOSMeD and ISoS. Because IPSS could be criticised for how cases were ascertained, WHO mounted the Determinants of Outcome of Severe Mental Disorders study (DOSMeD), an incidence-based design across ten countries intended to capture first-contact cases and reduce selection bias, which broadly replicated the better developing-country outcome (Jablensky et al. 1992; Jablensky 2000). The International Study of Schizophrenia (ISoS) then reassembled these cohorts for very long-term follow-up at 15 and 25 years, confirming the geographical stability of the difference while also showing that late recovery in a significant minority was more common than therapeutic pessimism had assumed (Harrison et al. 2001; Hopper & Wanderling 2000).

INDIA

India was a centre in all three WHO studies, and the Indian data anchored the better-developing-country finding: in the IPSS follow-up the Indian centres showed a high proportion reaching complete remission. The complementary Indian ICMR study, SOFACOS (Study of Factors Associated with Course and Outcome of Schizophrenia), followed 386 patients across Vellore, Madras and Lucknow and reported a favourable outcome in about two-thirds, higher than the roughly one-half seen in Ciompi's long European cohort (Verghese et al. 1989). Cite India as the exemplar centre for the cross-cultural outcome claim, not as a separate finding.

20.4 The modern critique of the developing-country finding

Why the finding is now contested. The better outcome in developing countries from the WHO cross-cultural studies is one of the most cited results in social psychiatry, but its interpretation is genuinely controversial, and an examiner rewards the critique as much as the finding. Four methodological concerns recur (Cohen et al. 2008; Kaplan & Sadock 2024; Shorter Oxford / an der Heiden & Hafner 2011).

Case-mix and diagnostic non-equivalence

Developing-country samples may have contained more acute, remitting and organically tinged psychoses that would fare better whatever the setting, so like was not compared with like.

Acute-onset over-representation

An excess of acute-onset cases in the developing centres inflates apparent outcome, because acute onset is itself a good prognostic factor, confounding the country comparison.

Follow-up and attrition

Differential loss to follow-up, higher early mortality in some sites, and the difficulty of tracing patients across decades can bias which patients remain to be counted as recovered.

Outcome-definition heterogeneity

Outcome was measured with varying instruments and thresholds across sites and eras, and social outcome, which was often worse than symptomatic outcome, was not always separated from symptom outcome.

Where the debate rests. The subsequent WHO analyses argued that a real difference in the severity and type of illness at first presentation contributed, so the effect is not purely artefactual; but the strong "better outcome in the developing world" headline should be delivered with these caveats, not as a settled truth (Harrison et al. 2001; Cohen et al. 2008). The safe examination line is that the finding is robust in the WHO data yet its explanation, whether social, familial (lower expressed emotion, greater community reintegration) or methodological, remains unresolved.

COMMON TRAP

Reciting "outcome is better in developing countries (WHO)" as a bare fact without the critique. The strong claim rests on IPSS, DOSMeD and ISoS but is undercut by case-mix, an over-representation of acute-onset cases, follow-up and attrition problems, and heterogeneous outcome definitions; the marks are in naming those concerns.

20.5 Remission: the Andreasen operational criteria

Why an operational definition was needed. Before 2005 "remission" in schizophrenia was used loosely, which made trials and cohorts incomparable. The Remission in Schizophrenia Working Group, led by Nancy Andreasen, produced a standard, consensus remission criteria definition to fix this (Andreasen et al. 2005). The definition has two limbs: a severity threshold and a time threshold.

The two limbs. The *severity* limb requires that a defined set of core schizophrenia symptoms across the three domains, positive, negative and disorganised, be rated no higher than mild, operationalised as a score of mild or less on the relevant PANSS or SAPS/SANS items. The *duration* limb requires that this low-severity state be sustained for a minimum period of at least **six months** (Andreasen et al. 2005). Meeting a low symptom score at a single visit is therefore not remission; the six-month persistence is what distinguishes remission from a transient response, and this durational rule is the single most examinable point in the definition.

MNEMONIC

MILD for SIX

Remission (Andreasen 2005) is core symptoms rated MILD or less across positive, negative and disorganised domains, sustained for at least SIX months. Both limbs are needed; the six-month persistence is the discriminator from mere symptomatic response.

20.6 Remission versus functional outcome versus recovery

Three ascending thresholds. These three terms name three different and increasingly demanding states, and conflating them is the classic outcome error. Symptomatic remission (Andreasen) is a low symptom burden sustained for six months. Functional outcome is a separate axis entirely, describing role performance in work, study, independent living and relationships, and it can be poor even when symptoms are in remission, because negative symptoms and cognitive impairment, rather than psychosis, are the chief drivers of disability. Recovery is the most demanding operationalised construct, typically requiring improvement in *both* symptoms and social or functional role, sustained for a longer window, usually at least two years (Shorter Oxford / Jaaskelainen et al. 2013; Harrison et al. 2001).

What the recovery numbers say. A widely cited meta-analysis defining recovery as combined symptomatic and functional improvement sustained for at least two years found that only about **14%** of patients met the criterion, and this figure had not clearly improved over decades (Jaaskelainen et al. 2013). The long-term ISoS and Harrison cohorts found roughly one-sixth in full recovery, with late recovery in a meaningful minority, and studies such as AESOP repeatedly showed that social outcomes were worse than symptomatic ones (Harrison et al. 2001; Morgan et al. 2014). The recovery-movement point, developed further in the management notes, is that recovery in its fullest sense is more than symptom control: it includes agency, meaning and a life the person values, not merely a low PANSS score.

TRAP **Equating symptomatic remission with functional recovery.** A patient in Andreasen remission can remain occupationally and socially disabled; remission is a symptom threshold, recovery requires sustained functional improvement too, and negative symptoms and cognition, not psychosis, drive the residual disability.

HOLD THIS

Good prognosis is acute onset, a precipitant, prominent mood symptoms, good premorbid functioning, married or female and short DUP; the WHO cross-cultural studies (IPSS, DOSMeD, ISoS) found better outcome in developing countries but the finding is undercut by case-mix and acute-onset over-representation; and Andreasen remission is core symptoms mild or less for at least six months, which is not the same as functional recovery.

GOOD TO REMEMBER

- **Good prognostic factors:** features shifting the odds toward better outcome; acute onset, identifiable precipitant, prominent mood symptoms, good premorbid functioning, married or female, short duration of untreated psychosis; discriminator is that they describe a reactive, affective, abrupt illness and predict only probabilistically.
- **Poor prognostic factors:** features shifting the odds toward worse outcome; insidious onset, prominent negative symptoms, poor premorbid functioning, early onset, male sex, long duration of untreated psychosis, no precipitant; discriminator is that negative symptoms and long DUP are the heaviest-weighted of the set.
- **Duration of untreated psychosis (DUP):** time from psychosis onset to first effective treatment; longer DUP predicts worse outcome; discriminator is that it is the one *modifiable* major predictor, hence the target of early-intervention services.
- **IPSS (WHO 1973):** nine-country cross-cultural study using the PSE; showed schizophrenia presents similarly across cultures and, on follow-up, better outcome in developing centres; discriminator is that it was the origin of the cross-cultural outcome claim.
- **DOSMeD (Jablensky et al. 1992):** ten-country incidence-based WHO study of first-contact cases; replicated the better developing-country outcome with reduced selection bias; discriminator is its incidence-based, first-contact design answering the case-ascertainment critique of IPSS.
- **ISoS (Harrison et al. 2001):** 15-to-25-year follow-up reassembling the IPSS/DOSMeD cohorts; confirmed geographical stability of outcome and documented late recovery; discriminator is that it is the very-long-term arm showing recovery can occur late.
- **Andreasen remission criteria (2005):** Remission in Schizophrenia Working Group definition; core symptoms across positive, negative and disorganised domains rated mild or less, sustained at least six months; discriminator is the six-month duration limb, absent from mere symptomatic response.
- **Recovery:** combined symptomatic and functional improvement sustained (typically at least two years); met by roughly 14% in meta-analysis (Jaaskelainen et al. 2013); discriminator is that it requires functional outcome, not symptom control alone, and is more than a low symptom score.

PEARL

Three answers carry every prognosis viva: the favourable triad is acute onset plus affective symptoms plus short DUP; the cross-cultural headline is "better in developing countries (IPSS, DOSMeD, ISoS), but case-mix and acute-onset over-representation cloud it"; and the remission-versus-recovery line is "Andreasen remission is mild symptoms for six months, recovery adds sustained functional improvement".

Figure. The good-versus-poor prognostic-factor grid, favourable and unfavourable poles set against each other across onset, precipitant, affect, symptom profile, premorbid functioning, sex and DUP, is drawn as Fig 8.8.

21 · Suicide, the mortality gap and physical comorbidity

Schizophrenia is not only a disorder of psychosis; it is a disorder of **shortened life**. Two facts anchor the outcome story that examiners return to again and again: patients are at high suicide risk, and, separately, they die many years earlier than the general population from ordinary physical disease. The trap the exam is built to catch is conflating the two. Suicide is the dramatic, early, and preventable killer, but it accounts for a minority of the total lost years. The bulk of the

mortality gap is cardiometabolic, and it is under-recognised and under-treated (Kaplan & Sadock 2024, De Hert 2011).

Why this matters clinically. Framing schizophrenia as a physical-health condition as much as a psychiatric one reorganises what you do at every review: you screen the heart and the metabolism, not just the mental state. The excess deaths are largely from causes that are measurable, modifiable, and shared with primary care, which is exactly why metabolic screening and physical-health monitoring in serious mental illness are now core competencies rather than an afterthought.

21.1 The suicide figure to hold

Lifetime risk. Older texts quote a suicide rate of 10 percent; contemporary meta-analyses put the lifetime suicide risk at roughly **~5%** (Palmer 2005, Popovic 2014; Kaplan & Sadock 2024, Semple & Smyth). The 10 percent figure is a classic exam relic and should be quoted as historical, not current. Non-fatal behaviour is far commoner: suicide attempts and suicidal ideation are frequent, with attempt rates in some series approaching 50 percent (Kaplan & Sadock 2024).

~5%	~15–20 yr	2–4×
LIFETIME SUICIDE RISK	LIFE-EXPECTANCY GAP IN SMI	ALL-CAUSE SMR VS GENERAL POPULATION

RULE **Quote ~5 percent, not 10 percent.** The lifetime suicide risk in schizophrenia is about five percent on modern meta-analysis; the historical 10 percent figure is not supported by contemporary data.

21.2 When and in whom suicide risk is highest

Temporal pattern. Risk is front-loaded. It is greatest early in the illness, including the prodrome and first years, in patients with frequent relapses, and around the time of admission and in the period immediately after discharge (Kaplan & Sadock 2024). The post-discharge window is the single most testable high-risk period: the patient is out of the containing environment, insight may be returning, and follow-up may be loose.

Risk factors. Young age, male sex, and high premorbid function with preserved or emerging insight into the decline (a fear of mental deterioration) all raise risk, as do depression, hopelessness, agitation, prior suicide attempts, substance misuse, and prominent paranoid delusions (Cassidy 2018, Popovic 2014; Kaplan & Sadock 2024). Note the paradox that examiners like: *good* premorbid function and returning insight are risk-raising here, because they let the patient grasp what has been lost. Persistent primary negative symptoms, by contrast, are associated with a lower suicide risk.

WORKED EXAMPLE

A 22-year-old man, previously a high-achieving engineering student, is discharged after a first admission for schizophrenia. His positive symptoms have resolved on medication and he now speaks lucidly about how far behind his peers he has fallen. On paper he looks well. In fact he sits in the highest-risk band: young, male, high premorbid function, emerging insight into decline, and freshly post-discharge. Insight resolving is not the same as risk resolving.

TRAP **Assuming returning insight means falling risk.** Preserved or emerging insight with high premorbid function is a suicide-*risk* factor in schizophrenia, not a reassurance; the early post-discharge period is peak risk.

21.3 The mortality gap: the headline number

Premature death. People with schizophrenia and other serious mental illness (SMI) die prematurely. The commonly cited figure is a reduction in life expectancy of about **15 to 20 years** in serious mental illness (Firth 2019 Lancet Psychiatry Commission). Schizophrenia-specific registry estimates are a little narrower, on the order of 10 to 15 years, with men losing more years than women (Kaplan & Sadock 2024). One influential textbook quotes men dying approximately 20 years and women approximately 15 years prematurely (Semple & Smyth, citing Saha 2007). The direction of travel is the exam point: the gap has, if anything, widened even as general-population mortality has fallen (Saha 2007).

Standardised mortality ratio. Population cohorts consistently find all-cause mortality two to four times that of the general population, that is a standardised mortality ratio of roughly two to four (Olfson 2015, Osby; Kaplan & Sadock 2024). This is a **relative** risk, observed over expected deaths, not an absolute one.

PEARL

The mortality gap is *widening*, not closing. As the general population lives longer, medical gains have largely bypassed people with schizophrenia, so the standardised mortality ratio has drifted upward over recent decades (Saha 2007). It is a marker of a health system failing a population, not of the illness alone.

21.4 Suicide versus cardiometabolic causes: what really drives the gap

The core distinction. Suicide accounts for a good part of the excess mortality early in the course, but across the whole lifespan it is a minority of the lost years. In the Global Burden of Disease framing, chronic physical disease is the primary cause of premature death in schizophrenia, with cardiovascular disease alone accounting for more than a third of premature deaths, while suicide, homicide and accidents together account for under fifteen percent of the excess (Kaplan & Sadock 2024, citing GBD). Registry work agrees: in one 25-year cohort, around eighty percent of patients died of medical disease (Brown; Kaplan & Sadock 2024).

A caveat to hold honestly. Some texts, counting the proportion of specifically *early* excess deaths, put unnatural causes (suicide and accidents) as high as around sixty percent (Semple &

Smyth). The reconciliation is that suicide dominates the *early* years and the *relative* risk in the young, whereas cardiometabolic disease dominates the *total* years of life lost across the lifespan. For a whole-population, whole-lifespan statement, cardiometabolic causes win.

RULE **Cardiometabolic, not suicide.** Most of the mortality gap in serious mental illness is cardiometabolic (chiefly cardiovascular disease), not suicide; suicide dominates the early and relative risk, physical disease dominates the total years lost.

TRAP **Blaming the whole excess mortality on suicide.** Attributing the premature death of people with schizophrenia only to suicide misses the two-thirds-plus that is cardiometabolic and preventable, and it is the classic wrong answer.

21.5 Physical comorbidity: the pattern of illness

Comorbidity is the rule. Physical comorbidity in schizophrenia is the norm, not the exception, and as many as two-thirds of patients carry more than one physical disease, that is multimorbidity (Kaplan & Sadock 2024). The **physical comorbidity** cluster that matters for the mortality gap is cardiometabolic and respiratory.

Metabolic syndrome

Clustered central obesity, dyslipidaemia, hypertension and hyperglycaemia; prevalent even in unmedicated first-episode psychosis (about 10 percent) and rising steeply with treatment and chronicity (Mitchell 2013).

Cardiovascular disease

The leading single cause of death in schizophrenia; pooled relative risk on the order of 1.5, higher for stroke and heart failure, with markedly worse outcomes after acute coronary events (Correll, Fan; Kaplan & Sadock 2024).

Type 2 diabetes

Prevalence roughly two to four times the general population (pooled around 10 to 13 percent), part of it predating antipsychotics, most of it amplified by them; low glucose and lipid screening rates persist (Stubbs, Vancampfort; Kaplan & Sadock 2024).

Smoking

Rates far above the general population, driving the elevated COPD, pneumonia and lung-cancer mortality; a major, modifiable contributor to the excess (Kaplan & Sadock 2024).

DOMAIN	SIGNAL IN SCHIZOPHRENIA	WHY IT MATTERS
Cardiovascular disease	**Leading cause of death; RR ~1.5, worse post-ACS outcomes**	Largest slice of the mortality gap
Type 2 diabetes	**~2–4× prevalence; low screening rates**	Screen glucose/HbA1c; often missed
Metabolic syndrome	~10% at first episode, unmedicated; rises with treatment	Present before drugs, worsened by them
Smoking / respiratory	**High smoking prevalence; raised COPD, pneumonia, lung cancer**	Modifiable; drives respiratory excess
Infections	Raised HIV, hepatitis B/C, TB, severe COVID-19	Contributory, often neglected

The physical-comorbidity map behind the mortality gap: cardiometabolic and respiratory disease carry the excess deaths, and screening is where the gains sit.

21.6 The antipsychotic contribution, in proportion

Two truths at once. Antipsychotics, especially some second-generation agents, contribute materially to the cardiometabolic burden through weight gain and metabolic change, and this is a real driver of **physical comorbidity**. Yet moderate antipsychotic exposure is associated with the *lowest* mortality in schizophrenia, and even higher doses carry lower mortality than no treatment at all (Torniainen 2015; Semple & Smyth). The metabolic liability of individual agents, the monitoring schedules, and how to mitigate them belong to the Schizophrenia: management, antipsychotics and adverse effects notes and are cross-referenced there rather than repeated here.

COMMON TRAP

Concluding that because antipsychotics cause metabolic harm they should be minimised or stopped to protect physical health. The mortality data point the other way: untreated schizophrenia carries the highest mortality, and moderate treatment the lowest. The answer is to treat *and* screen, not to withhold treatment.

21.7 Physical-health and metabolic screening in serious mental illness

The clinical response. Because the excess deaths are cardiometabolic and modifiable, structured physical-health monitoring is now standard care in **serious mental illness**. Metabolic screening means tracking weight and waist circumference, blood pressure, fasting glucose or HbA1c, and a lipid profile, at baseline and at defined intervals after starting or changing an antipsychotic, alongside smoking-cessation support and attention to diet and activity (De Hert 2011, Kaplan & Sadock 2024). The recurring failure the exam probes is that these patients are screened *less*, not more, than the general population despite being at higher risk, so the abnormalities go undetected and untreated (Solmi; Kaplan & Sadock 2024).

INDIA

Very high background smoking and smokeless-tobacco use, rising type 2 diabetes prevalence, and limited integration between psychiatric and general medical services make the physical-health gap especially stark in Indian practice. Baseline weight, blood pressure, fasting glucose and a lipid profile before and during antipsychotic treatment are low-cost, high-yield, and often the only physical-health contact these patients get.

MNEMONIC

SAD PERSONS meets the METABOLIC review

For suicide, remember risk loads onto the young, male, insightful, recently-discharged patient with depression and prior attempts. For the body, run the metabolic review every time: weight/waist, blood pressure, glucose or HbA1c, lipids, and smoking. One patient, two screens: the mind and the metabolism.

HOLD THIS

Roughly five percent lifetime suicide risk (highest early and post-discharge), a 15 to 20 year mortality gap in serious mental illness, and most of that gap cardiometabolic rather than suicide.

GOOD TO REMEMBER

- **Suicide risk in schizophrenia:** lifetime risk about five percent (not the old 10 percent); highest early in illness and just after discharge; discriminating risk factors are young age, male sex, high premorbid function with insight into decline, depression, and prior attempts.
- **Mortality gap:** premature death of roughly 15 to 20 years in serious mental illness (schizophrenia-specific registry figures ~10 to 15 years, more in men); standardised mortality ratio two to four times the general population; discriminator is that it is *widening*, not closing.
- **Physical comorbidity:** cardiovascular disease, type 2 diabetes, metabolic syndrome and heavy smoking; the number to know is that cardiometabolic disease, chiefly cardiovascular, causes the majority of premature deaths, more than a third from cardiovascular disease alone, while suicide/accidents are under fifteen percent of the excess.
- **Antipsychotic contribution:** a real driver of metabolic burden, yet moderate treatment carries lower mortality than none; details of agent-specific risk and monitoring are in the Schizophrenia: management, antipsychotics and adverse effects notes.
- **Metabolic screening in SMI:** weight/waist, blood pressure, fasting glucose or HbA1c, lipids at baseline and intervals, plus smoking cessation; the failure to know is that these patients are screened less than the general population despite higher risk.

Apply and consolidate

22 · Apply: four worked clinical vignettes

Everything in the preceding topics converges on four repeatable clinical moves, and the fastest way to fix them is to watch each one run once on a patient. This topic is that rehearsal: four short worked clinical vignettes, each a brief scenario, then the reasoning, then the read. They are deliberately the four that examiners return to, the workup of a first-episode psychosis, the

schizophrenia-versus-mood-with-psychosis differential, the primary-versus-secondary negative-symptom split, and a prognosis weighing, because between them they exercise the criteria, the differential, the phenomenology and the course in the exact order a viva demands.

How to use it. Read each vignette as a decision procedure, not a story: identify the discriminator the scenario turns on, state it, and only then commit to the label. The raw descriptive definitions of what a **delusion**, a **hallucination** or formal thought disorder actually is belong to the Psychometry, Assessment and Descriptive Psychopathology notes; the full criteria are set out in the criteria and discriminate topics above and are only applied here. Treatment is never decided in these vignettes; the drugs belong to the Schizophrenia: management, antipsychotics and adverse effects notes.

22.1 Vignette one: the first-episode workup

The move. A first frank psychosis is not a diagnosis until the treatable secondary causes are excluded; the first worked example runs that organic and substance workup before any primary label is allowed to settle. A first-episode psychosis (fep) is a syndromal label precisely because the eventual diagnosis is not yet fixed, so the whole exercise is to catch a reversible cause before committing (Kaplan & Sadock 2024).

WORKED EXAMPLE

Case: A 21-year-old man is brought by his family after roughly four months of change. It began with social withdrawal, dropping grades and odd, over-read meaning in ordinary events (attenuated, subthreshold ideas of reference); over the last six weeks it hardened into a fixed persecutory delusion that a neighbour is poisoning him and a running-commentary auditory hallucination. Consciousness is clear, there is no fluctuation, no seizure, no fever and no focal neurology; a urine drug screen is negative and there is no history of cannabis or stimulant use. **The reasoning:** because this is a first episode, the mandatory workup comes first, rule out an organic psychosis (a clear, non-fluctuating sensorium with no seizures, focal signs, abnormal movements or prominent visual hallucinations makes anti-NMDA-receptor encephalitis and temporal-lobe pathology unlikely, though basic screening bloods and imaging are still done) and rule out a substance-induced psychosis (negative screen, no use history, so no offset-on-washout to expect). Only now is a primary non-affective psychosis on the table, and the picture must be run through both current systems. **The read:** under ICD-11 he already qualifies, two core symptoms (persistent delusion plus persistent hallucination), both from the first four groups, present well beyond the one-month threshold. Under DSM-5-TR he meets Criterion A (two of five, including core positives) with a clear functional decline, but the total continuous disturbance is about four months, under the six-month line, so the correct DSM-5-TR label is schizophreniform disorder (provisional, since ongoing), converting to schizophrenia only once continuous disturbance reaches six months.

RULE **Exclude organic and substance causes before naming a primary psychosis.** Every first episode gets an organic-and-substance workup; only then do you apply the criteria and read the clock.

TRAP **Calling this "schizophrenia" under DSM-5-TR at four months.** The same picture is ICD-11 schizophrenia (one month) but DSM-5-TR schizophreniform disorder until six months; the two systems disagree here by design.

22.2 Vignette two: schizophrenia versus mood with psychosis

The move. The second worked example turns entirely on one discriminator, temporal confinement of the psychosis to mood episodes. A psychosis present *only* during a mood episode is a mood disorder; a psychosis that also stands alone, on a heavy mood background, is schizoaffective; a psychosis that persists across mood states with mood present only briefly is schizophrenia (American Psychiatric Association 2022).

WORKED EXAMPLE

Case: Two patients, same presenting complaint of "hearing voices", opposite answers. *Patient A* has had two discrete depressive episodes; in each, at the depth of the low mood, she developed nihilistic and guilt-laden delusions and a derogatory voice, and each time the psychosis cleared completely as the mood lifted, never appearing while she was euthymic. *Patient B*, over a two-year illness, has had a major mood episode present for roughly fourteen of the twenty-four months, but within that span there was a clear three-week stretch of persecutory delusions while fully euthymic. **The reasoning:** for Patient A the psychosis is *confined to the mood episode* and is mood-congruent, and it remits when the mood remits, so it never outlives the affective illness. For Patient B two rules must both be checked: is there at least a two-week period of psychosis in the *absence* of a mood episode (yes, the three euthymic weeks, which excludes a pure mood-with-psychosis label), and is a mood episode present for the *majority* of the total active and residual illness (yes, fourteen of twenty-four months, which excludes schizophrenia). **The read:** Patient A is a major depressive disorder with psychotic features, the discriminator being that psychosis is present only during the mood episode. Patient B is schizoaffective disorder, the discriminator being standalone psychosis of at least two weeks plus mood for the majority of the illness. Shrink Patient B's mood component to a couple of brief episodes and the same psychosis becomes schizophrenia with intercurrent mood symptoms.

RELATIONSHIP OF PSYCHOSIS TO MOOD	DIAGNOSIS	THE DISCRIMINATOR
Present ONLY during a mood episode; remits with the mood	Mood disorder with psychotic features	**Temporal confinement to the mood episode**
≥2 weeks standalone psychosis, AND mood present for the majority of the illness	Schizoaffective disorder	**Two-week standalone rule PLUS majority-mood rule**
Persists across mood states; mood present only for a minority	Schizophrenia	**Psychosis outlives and outweighs the mood**

The mood-versus-schizophrenia decision, one axis: how much of the psychosis stands outside a mood episode, and how much of the illness the mood occupies.

TRAP **Diagnosing schizophrenia inside an untreated mood episode.** Mood-congruent psychosis confined to depressive or manic episodes is a mood or schizoaffective disorder until the mood is treated and re-assessed.

22.3 Vignette three: primary versus secondary negative symptoms

The move. The third worked example never asks "are there negative symptoms"; it asks "what is producing them". A secondary negative symptom is produced by a removable driver, untreated positive symptoms, depression, extrapyramidal side effects or understimulation, and reverses when that driver is treated; a primary negative symptom is intrinsic and is only the residue after every secondary cause is stripped out (Tasman 2024; Kaplan & Sadock 2024).

WORKED EXAMPLE

Case: A 30-year-old man with schizophrenia is flat, near-mute and does almost nothing, hour after hour. Three details decide the read. First, he is on a high dose of a high-potency antipsychotic and has masked facies, a resting tremor and cogwheel rigidity. Second, his mood, sleep and appetite are unremarkable and he denies pervasive low mood or guilt. Third, when the dose is reduced and the parkinsonism settles, his facial expressivity and spontaneous activity partly return, but a core of blunted affect, poverty of speech and avolition remains, and has been present continuously for over a year, including through periods when his delusions were quiescent and he was clinically stable. **The reasoning:** the initial flatness was substantially *secondary*, a drug-induced parkinsonism (the neuroleptic-induced deficit syndrome) mimicking the disease's own negative symptoms; that part reversed with dose reduction, which is the definitional test of a secondary symptom. Depression was excluded as a driver. What survives the reversal is *primary*: it persists between episodes, outside depression and off the offending dose. This enduring primary picture, at least two negative symptoms sustained through the preceding year during clinical stability, meets the deficit syndrome as defined by Carpenter and operationalised by the Schedule for the Deficit Syndrome. **The read:** primary, enduring negative symptoms of the deficit syndrome, not drug-induced parkinsonism, once the reversible layer is removed. Its functional weight is the whole point, because negative symptoms, not psychosis, predict long-term social disability, and the deficit subgroup carries the poorer functional prognosis.

~15%	25 to 30%	≥2
DEFICIT SYNDROME, FIRST-EPISODE	DEFICIT SYNDROME, CHRONIC	NEGATIVE SYMPTOMS IN PAST YEAR (SDS)

RULE **Strip out the reversible causes before calling negative symptoms primary.** Treat positive symptoms, depression, extrapyramidal effects and understimulation first; only the enduring residue between episodes is the deficit syndrome.

TRAP **Labelling drug-induced parkinsonism "primary negative symptoms."** Masked facies and bradykinesia on a high antipsychotic dose are a reversible mimic; question the dose before you commit a patient to a deficit label.

22.4 Vignette four: the prognosis weighing

The move. The fourth worked example lays a patient's features on the two-poled prognostic axis and weighs the favourable against the unfavourable to state a likely course. Almost every good prognosis feature has a mirror-image poor prognosis feature, and the task is not to find one but to weigh the balance, remembering that any single factor only shifts the odds (Kaplan & Sadock 2024).

WORKED EXAMPLE

Case: Two contrasting first presentations. *Patient X*, a 32-year-old married woman, develops an abrupt psychosis over two weeks following a clear bereavement, with prominent affective colouring and perplexity, on a background of good premorbid work and social function; she is brought to care within days, so the duration of untreated psychosis is short. *Patient Y*, a 17-year-old unmarried man, has an insidious two-year slide of deepening social withdrawal, blunting and avolition with no identifiable precipitant, a schizoid premorbid personality, a family history of schizophrenia, and reaches care only after a long duration of untreated psychosis. **The reasoning:** Patient X sits almost entirely on the favourable pole, acute onset, an identifiable precipitant, prominent mood symptoms, good premorbid functioning, married and female, and a short DUP, the reactive, affective, abrupt-onset pattern that predicts better. Patient Y sits on the unfavourable pole, insidious onset, prominent negative symptoms, poor premorbid functioning, early onset, male, no precipitant, a family history of schizophrenia and a long DUP, and negative symptoms plus a long DUP are the heaviest-weighted of the poor set. **The read:** Patient X's balance points to a better-than-average course with a good chance of substantial remission; Patient Y's balance points to a poorer course with higher risk of chronicity and functional disability. The one modifiable lever in either case is the DUP, which is why early detection is the actionable message rather than a fixed verdict.

FEATURE	PATIENT X (FAVOURABLE)	PATIENT Y (UNFAVOURABLE)
Onset	**Acute (2 weeks)**	Insidious (2 years)
Precipitant	**Clear bereavement**	None
Affective symptoms	**Prominent**	Absent; blunted
Premorbid function	**Good**	Poor (schizoid)
Age and sex	32; female; married	**17; male; unmarried**
Duration of untreated psychosis	**Short**	Long
Family history	None stated	**Schizophrenia**

The same seven prognostic dimensions weighed for two presentations; X reads reactive-affective-abrupt (better course), Y reads endogenous-negative-insidious (poorer course), with DUP the one modifiable lever.

RULE **Weigh both poles, do not count one factor.** Prognosis is the balance of favourable against unfavourable features; the acute-affective-short-DUP triad is the strongest favourable signal and negative-symptoms-plus-long-DUP the strongest unfavourable one.

PEARL

The four vignettes share a single grammar: find the discriminator, name it, then read. Workup discriminator is a demonstrable organic or substance cause; mood discriminator is temporal confinement of psychosis to mood episodes; negative-symptom discriminator is reversibility on treating the driver; prognosis discriminator is the balance of the two poles with DUP as the one modifiable lever.

HOLD THIS

Every psychosis case runs the same four moves in order: exclude organic and substance causes first, then apply the mood exclusion (psychosis confined to mood episodes is a mood disorder, not schizophrenia), then read the duration clock, and finally weigh the prognostic poles with the duration of untreated psychosis as the one modifiable lever.

GOOD TO REMEMBER

- **First-episode workup (vignette one):** a first frank psychosis needing organic and substance exclusion before a primary label; core move is rule out encephalitis, temporal-lobe pathology, delirium and substance causes, then apply criteria; the discriminator is that the same picture is ICD-11 schizophrenia at one month but DSM-5-TR schizophreniform disorder until six months.
- **Mood-with-psychosis versus schizophrenia (vignette two):** the affective differential; core move is to ask whether psychosis is confined to mood episodes; the discriminator is temporal confinement (mood disorder if psychosis only ever appears within a mood episode, schizoaffective if there is at least two weeks of standalone psychosis plus mood for the majority of the illness).
- **Primary versus secondary negative symptoms (vignette three):** the negative-symptom split; core move is to strip out positive symptoms, depression, extrapyramidal effects and understimulation; the discriminator is reversibility, and the enduring residue between episodes meeting at least two negative symptoms for the preceding year is the deficit syndrome (Carpenter), roughly 15 percent first-episode and 25 to 30 percent chronic, carrying the greatest functional weight.
- **Prognosis weighing (vignette four):** the course estimate; core move is to lay features on the favourable-versus-unfavourable axis and weigh the balance; the discriminator is the balance itself (acute onset, precipitant, affective symptoms, good premorbid function, married or female, short DUP for a better course; the opposite pole for a worse one), with DUP the single modifiable lever.

23 · Consolidate: mnemonic, retrieval and synthesis

Everything in this chapter has been laid out in bands: the causes, the phenomenon, the criteria and nosological change, and the course. This closing topic does not add facts; it fuses them. The examinable payoff of the whole note is the ability to unpack one seed cue into the entire chapter, to recall each band cold under viva pressure, and to redraw the structure of the disorder from a blank page. Consolidation is the step that turns a read note into a retrievable one, and it is where marks are won or lost in the examination.

How to use this page. Three tools, in order. First, the master **mnemonic** that chains the four bands so a single cue unpacks the whole chapter, the payoff of the seed planted in the orientation topic. Second, a set of **answer-free recall prompts**: the single highest-yield revision technique for this material is **active recall**, so test yourself against these before you re-read anything. Third,

a **synthesis map** to redraw from memory, the four-branch skeleton on which every fact hangs. Do not treat this as a summary to skim; treat it as a set of exercises to perform.

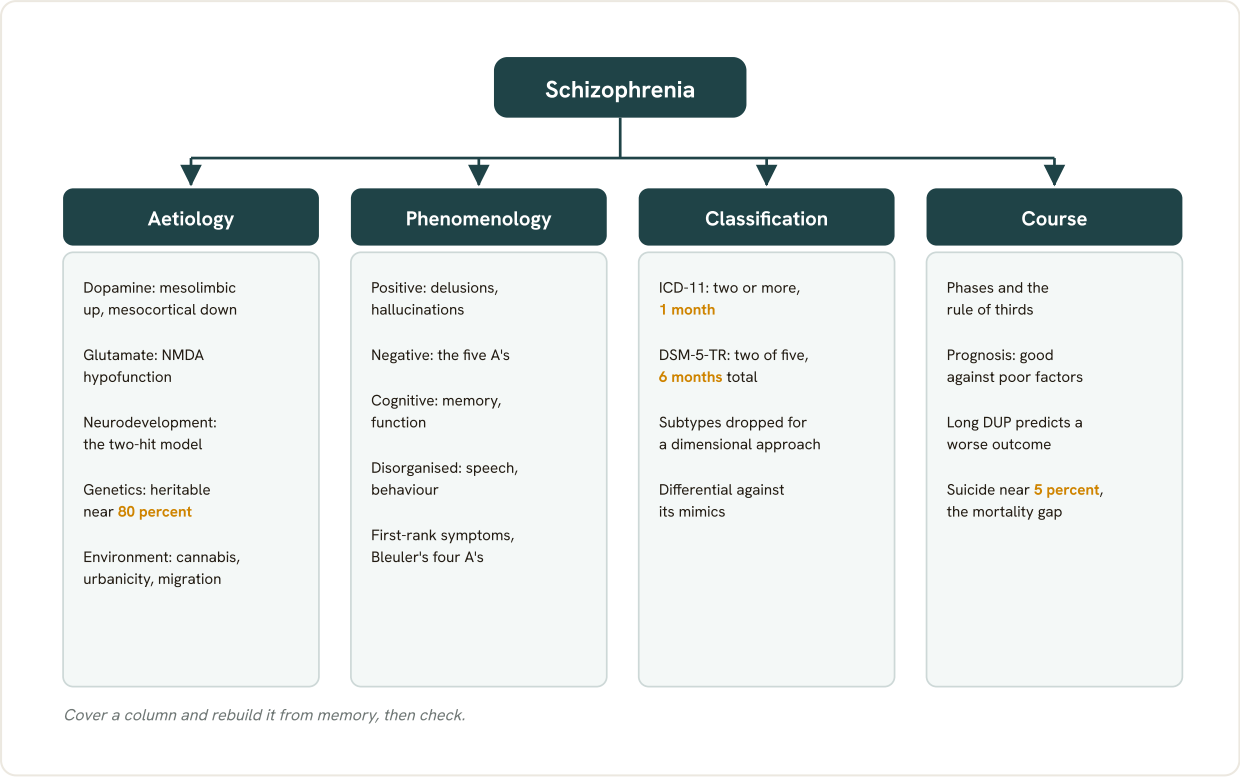


Fig 8.15 The whole chapter as one map, four branches from a single node: aetiology, phenomenology, classification and course. Redraw it from memory, then cover each column and rebuild its contents. The chain runs from cause to phenomenon to criteria to outcome, and holding the four branches together is what turns a list of facts into an understanding of the illness.

23.1 The master mnemonic: the whole chapter on one seed

The seed unpacked. The chapter runs in four bands, and one master mnemonic chains them so that a single cue delivers the entire note: *cause*, then *phenomenon*, then *criteria*, then *course*. This is the payoff of the seed set at orientation: *CAUSE, PHENOMENON, CRITERIA, COURSE*, in reading order. Fix the four Cs and each later topic slots onto its band; the criteria map is the hinge in the middle, the schema the cause bands build toward and the course bands read forward from. The box below unpacks every letter of the chain, chaining the causes, the phenomenon with its domains and first-rank symptoms, the criteria with the nosological change, and the course with its prognosis and outcome.

MNEMONIC

"CAUSE, PHENOMENON, CRITERIA, COURSE": the four bands. CAUSE = "D-G-N-G" (Dopamine, Glutamate, Neurodevelopment, Genes). PHENOMENON = "P-N-C-D-A" (the five domains) + FRS (first-rank symptoms). CRITERIA = ICD-11 forward, DSM-5-TR mapped, subtypes dropped. COURSE = "PPARR" + rule of thirds + suicide/mortality.

Unpack it letter by letter. **CAUSE**, held on **D-G-N-G**, is the aetiology climb: **D**opamine (mesolimbic hyperdopaminergia drives positive symptoms, mesocortical hypodopaminergia the negative and cognitive, reframed as aberrant salience; Howes & Kapur 2009, Kapur 2003), **G**lutamate (NMDA-receptor hypofunction on parvalbumin interneurons, argued from ketamine and PCP), **N**eurodevelopment (the neurodevelopmental and two-hit models: a primed brain plus an adolescent second hit), and **G**enes (heritability **~80%**, MZ concordance **~40-50%** versus DZ **~10-15%**, polygenic plus rare high-penetrance CNVs; Sullivan et al. 2003). No single lesion, a convergence. **PHENOMENON** is the five-domain picture on **P-N-C-D-A**, a **P**ositive symptom (delusion, hallucination), a **N**egative symptom (the deficit, the 5 As), the **C**ognitive impairment, the **D**isorganisation (formal thought disorder, disorganised behaviour) and the **A**ffective disturbance, with Schneider's first-rank symptoms (FRS) suggestive but not pathognomonic laid over the positive and disorganisation domains. **CRITERIA** is the map: ICD-11 (6A20) run forward, DSM-5-TR cross-mapped on the six-month total-duration contrast, ICD-10 flagged legacy, and the nosological change, both systems dropping the subtypes for a dimensional symptom-domain approach. **COURSE** is the natural history on **PPARR** (Premorbid, Prodromal, Acute, Residual, Relapse), the good-versus-poor prognostic poles, the rule of thirds and the WHO cross-cultural outcome data, and the outcome band: suicide **~5%** lifetime and a mortality gap of **~15 to 20 years**. One seed, four bands, the whole chapter.

RULE **One cue, four bands.** If you can say "CAUSE, PHENOMENON, CRITERIA, COURSE" and unpack each into its sub-mnemonic, you can rebuild the entire chapter without notes; that is the whole point of the seed.

TRAP **Memorising the acronym without the unpacking.** A mnemonic you cannot expand is a dead cue; drill the expansion (D-G-N-G, P-N-C-D-A, ICD-11-forward, PPARR) until each letter opens its own paragraph, or the chain buys you nothing in the viva.

23.2 Retrieval practice across the four bands

Why testing beats re-reading. The evidence on studying is unambiguous: **active recall** and spaced **retrieval practice** outperform passive re-reading and highlighting for durable memory. Use the prompts below as your first pass, not your last. **Cover the answers** that live in the topics above, attempt each prompt aloud or on paper from memory, and only then check yourself against the relevant topic. The prompts span all four bands so that a single sitting exercises the whole chapter.

RETRIEVAL PRACTICE, COVER THE ANSWERS

These are answer-free recall prompts. This is **active recall**: **retrieval practice** works only if you attempt each one from memory before checking, so **cover the answers** in the topics above and write your own before you look.

1. State the four generational forms of the dopamine hypothesis and say which pathway drives positive versus negative symptoms.
2. Explain, in one line each, the glutamate hypothesis and why the ketamine model beats a pure dopamine account.
3. Define the two-hit model: name the first hit and the second hit.
4. Give the heritability of schizophrenia and the monozygotic versus dizygotic twin concordance figures.
5. List the five symptom domains and the five negative-symptom As.
6. Distinguish Bleuler's fundamental symptoms (the four As) from Schneider's first-rank symptoms, and state whether first-rank symptoms are pathognomonic.
7. State the ICD-11 symptom-and-duration criteria for schizophrenia and name at least one core qualifying symptom.
8. Give the single decisive difference between the ICD-11 and DSM-5-TR duration requirements.
9. Name the change ICD-11 made to the status of first-rank symptoms relative to ICD-10.
10. Explain why both DSM-5 and ICD-11 dropped the classical subtypes, and what replaced them.
11. Name the four phases of the natural course in order, plus the relapsing pattern.
12. List the favourable-triad good prognostic factors and the single most modifiable predictor of outcome.
13. Name the three WHO cross-cultural outcome studies and their unifying message.
14. Give the lifetime suicide risk figure and state whether suicide or cardiometabolic disease drives the larger share of the mortality gap.
15. Define the duration of untreated psychosis and state its prognostic significance.

RULE **Attempt before you check.** The learning is in the effortful retrieval, not in reading the answer; a prompt you look up without trying teaches almost nothing.

23.3 The synthesis map: redraw the chapter from memory

One skeleton, four branches. The final consolidation exercise is to draw the synthesis map of the whole chapter on a blank page: a central node, schizophrenia, with four branches, aetiology, phenomenology, classification and course. Off *aetiology* hang dopamine, glutamate, neurodevelopment and genes; off *phenomenology* hang the five domains and the first-rank symptoms; off *classification* hang the ICD-11-forward, DSM-5-TR-mapped, ICD-10-legacy criteria and the dropped subtypes; off *course* hang the phases, prognostic factors, WHO outcome data, suicide and the mortality gap. Rebuild this map from memory, redraw from memory each week until the four branches and their twigs come without prompting, and you own the chapter; the mnemonic in 23.1 is the verbal form of this same map, and each recall prompt in 23.2 tests one twig of it.

HOLD THIS

The whole chapter is one seed, "CAUSE, PHENOMENON, CRITERIA, COURSE", unpacking into four branches, aetiology, phenomenology, classification and course; recall it by active retrieval and redraw the four-branch synthesis map from memory until every twig comes unprompted.

GOOD TO REMEMBER

- **Master mnemonic (CAUSE, PHENOMENON, CRITERIA, COURSE):** the four bands of the chapter in reading order; central claim is that one seed cue unpacks the entire note; discriminator is that each band carries its own sub-mnemonic (D-G-N-G, P-N-C-D-A, ICD-11-forward, PPARR) that must be drilled, not just the top-level acronym.
- **Active recall and retrieval practice:** testing yourself from memory, with answers covered, before re-reading; central claim is that effortful retrieval produces more durable memory than passive review; discriminator is that the benefit depends on attempting each prompt before checking, so answer-free prompts are the correct format.
- **Synthesis map:** a central schizophrenia node with four branches, aetiology, phenomenology, classification and course, each with its twigs; central claim is that redrawing it from memory proves the structure is held, not just the facts; discriminator is that it is the visual twin of the master mnemonic and of the recall-prompt set, so all three tools test the same skeleton.

Figure. The whole-chapter synthesis map, the central schizophrenia node with its four branches, aetiology (dopamine, glutamate, neurodevelopment, genes), phenomenology (five domains, first-rank symptoms), classification (ICD-11 forward, DSM-5-TR mapped, subtypes dropped) and course (phases, prognosis, WHO outcome, suicide and mortality), to be redrawn from memory, is drawn as Fig 8.9.

Previously asked

Schizophrenia is one of the most heavily examined topics of the clinical paper, and it is tested **whole**: as full long essays on aetiopathogenesis and on the different types, and as a steady stream of short notes on the neurobiology, the phenomenology, the prodrome and the outcome. The essays often carry a management tail, and that part is developed in the Schizophrenia: management, antipsychotics and adverse effects notes; the other psychotic disorders and catatonia, which sit in the differential here, are their own chapter. The genuine questions below are grouped by the four bands of these notes.

? HOW THIS TERRITORY IS ACTUALLY TESTED

Q **Aetiology and neurobiology.** The commonest long essay asks you to discuss the etiopathogenesis of schizophrenia (with a drug-management tail that belongs to the management notes); the neurobiology also comes as "describe the neuroanatomical studies in schizophrenia" and "MRI in schizophrenia," and the perennial "recent advances in schizophrenia" is asked again and again. long essay and short note, recurring

Q **Clinical features and phenomenology.** Short notes single out "cognition in schizophrenia," the "prodrome of schizophrenia," and the "need, clinical implications and problems of the psychiatric rating scales of schizophrenia." short note

Q **Classification and nosological change.** The classic long essay to "discuss the etiology, clinical features and management of the different types of schizophrenia in detail" now turns on the reason both systems abolished those types. long essay

Q **Course, prognosis and outcome.** The outcome is tested directly as "predictors of schizophrenia," "prognosis in schizophrenia," "disability assessment in schizophrenia," and even "marriage in schizophrenia." short note

Prepare this material to be argued, not just recited: the criteria map, the differential decision tree and the four worked vignettes in these notes are built to the way the topic is examined. Antipsychotic pharmacotherapy, adverse effects and psychosocial rehabilitation are developed in the Schizophrenia: management, antipsychotics and adverse effects notes; schizoaffective disorder, delusional disorder and catatonia as entities are developed in the Other psychotic disorders, delusional syndromes and catatonia notes; these notes own the aetiology, the phenomenology, the classification and the course.

Quick review

The whole subject in one table	
ORIENTATION AND THE CRITERIA MAP	Schizophrenia is a chronic, multifactorial psychotic disorder of the young adult, defined by a syndrome not a test. The diagnosis needs two or more core symptoms, at least one from the positive or disorganisation cluster, for the required duration: ICD-11 asks one month, DSM-5-TR a six-month total with functional decline, after a mood, substance and organic cause are excluded.
EPIDEMIOLOGY	Lifetime risk near one percent; incidence roughly fifteen per hundred thousand per year with real geographic variation. Onset is earlier in men (early-to-mid twenties) than women (late twenties, with a second peri-menopausal peak). Life expectancy is reduced by about fifteen to twenty years, most of it cardiometabolic.
GENETICS	Heritability is about eighty percent, the strongest risk being an affected first-degree relative. Monozygotic concordance is roughly forty to fifty percent against ten to fifteen percent for dizygotic twins; adoption studies separate genes from rearing. The architecture is polygenic (over a hundred GWAS loci, the C4 signal) with rare high-penetrance copy number variants, above all the 22q11.2 deletion.
DOPAMINE HYPOTHESIS	From excess dopamine to a regional model: mesolimbic hyperdopaminergia drives the positive symptoms, mesocortical hypofunction the negative and cognitive ones. Kapur's aberrant salience reframes psychosis as dysregulated dopamine assigning undue salience to neutral stimuli, with delusions and hallucinations the attempt to explain it.
GLUTAMATE AND OTHER SYSTEMS	NMDA receptor hypofunction, argued from the ketamine and PCP model that reproduces positive, negative and cognitive symptoms, is the strongest challenge to a pure dopamine account. Parvalbumin GABA interneuron deficits, the 5-HT2A serotonin model, cholinergic contributions and neuroinflammation (microglia, the kynurenine pathway) complete the picture.
NEURODEVELOPMENT AND ENVIRONMENT	An early static lesion expressed at adolescent maturation: the two-hit model pairs a genetic and prenatal first hit (obstetric complications, maternal infection, winter or spring birth) with an adolescent second hit (excess synaptic pruning, cannabis, psychosocial stress). Cannabis is a dose- and age-dependent component cause; social drift explains the low-socioeconomic association.
NEUROIMAGING AND NEUROPATHOLOGY	Lateral ventricular enlargement is the most replicated structural finding, with grey-matter and hippocampal reduction and functional hypofrontality. Neuropathology shows reduced neuropil, excess synaptic pruning and, crucially, an absence of gliosis, which argues for a

The whole subject in one table	
	neurodevelopmental rather than a neurodegenerative process.
THE SYMPTOM DOMAINS	Five semi-independent domains, positive, negative, cognitive, disorganised and affective, describe a profile rather than a subtype. Crow's type I (positive, reversible) versus type II (negative, structural) and Liddle's three syndromes (reality distortion, disorganisation, psychomotor poverty) are the dimensional models.
POSITIVE SYMPTOMS	Delusions (persecutory, referential, grandiose, control and passivity, bizarre) and hallucinations (third-person and running-commentary auditory voices most characteristic), with formal thought disorder inferred from disorganised speech. No positive symptom is specific; prominent visual hallucinations should prompt an organic search.
NEGATIVE SYMPTOMS	The five A's: affective flattening, alogia, avolition, anhedonia and asociality. Separate primary (intrinsic, enduring) from secondary (from positive symptoms, depression, extrapyramidal effects or understimulation, and reversible). The deficit syndrome is enduring primary negative symptoms; assess with the SANS and the PANSS negative subscale.
DISORGANISATION	Disorganised speech is the clinical face of formal thought disorder (derailment, tangentiality, word salad, neologism), with disorganised behaviour and inappropriate affect. The catatonic phenomena are flagged here but developed as an entity in the Other psychotic disorders, delusional syndromes and catatonia notes.
FIRST-RANK AND FUNDAMENTAL SYMPTOMS	Schneider's first-rank symptoms (thought insertion, withdrawal and broadcast, passivity, third-person and commentary voices, delusional perception) are not pathognomonic and have lost their special status in DSM-5 and ICD-11. Bleuler's four A's (loosened associations, blunted affect, ambivalence, autism) are fundamental, against the accessory hallucinations and delusions.
COGNITION	Impaired processing speed, working memory, attention, verbal learning, executive function and social cognition are a core feature, present before onset and the strongest predictor of function. D2 antipsychotics do not restore cognition, so cognition is a treatment target through cognitive remediation and newer agents such as the muscarinic xanomeline-trospium (detail in the management notes). Insight is multidimensional and predicts adherence.
PRODROME AND FIRST EPISODE	The prodrome and the at-risk mental state (ultra-high-risk and clinical high risk) precede frank psychosis, with transition about twenty-two percent at one year and thirty-six percent by three years. Antipsychotics are not routinely recommended in the at-risk state to prevent transition; use cognitive behavioural therapy, monitoring and treatment of

The whole subject in one table	
	comorbidity. Endophenotypes (smooth-pursuit, P50 gating, working memory) mark risk.
DIAGNOSTIC CRITERIA	ICD-11: two or more core symptoms, at least one a core positive or disorganisation symptom, for one month, with domain qualifiers and course specifiers. DSM-5-TR: two of five, a six-month total with one month active, plus functional decline and exclusions. Legacy ICD-10 required one month, weighted first-rank symptoms and kept the subtypes.
CLASSIFICATION AND NOSOLOGICAL CHANGE	Kraepelin's dementia praecox became Bleuler's schizophrenias. Both ICD-11 and DSM-5 dropped the historical subtypes (paranoid, hebephrenic, catatonic, simple, residual, undifferentiated) for poor reliability, temporal instability and low predictive validity, replacing them with a dimensional symptom-domain approach.
THE SPECTRUM	The neighbours of schizophrenia, schizotypal, schizophreniform, brief psychotic, schizoaffective and delusional disorder, sit on a psychosis continuum. Psychotic-like experiences occur in the general population; the extended phenotype supports a dimensional over a purely categorical view.
DISCRIMINATE: THE DIFFERENTIAL	Rule out an organic or substance cause first, then a mood-confined psychosis (a mood disorder), then schizoaffective disorder (two weeks of psychosis without mood, mood most of the illness), then delusional disorder (non-bizarre, function preserved). Sort the remainder by duration: under one month brief psychotic, one to six months schizophreniform, six months with decline schizophrenia.
COURSE	Premorbid, prodromal, acute and residual phases with a relapsing course. The rule of thirds (roughly a third good, a third intermediate, a third poor) and the WHO cross-cultural studies (IPSS, DOSMeD, ISoS) show heterogeneous, often non-deteriorating outcomes. A longer duration of untreated psychosis predicts a worse outcome.
PROGNOSIS	Good prognosis with acute onset, a precipitant, affective symptoms, good premorbid function, female sex, marriage, a short duration of untreated psychosis; poor prognosis with insidious onset, negative symptoms, poor premorbid function, early onset, male sex and a long duration. The WHO better-outcome-in-developing-countries finding is read with its modern critique. Remission uses the Andreasen criteria; symptomatic remission is not functional recovery.
OUTCOME AND MORTALITY	Lifetime suicide risk about five percent, highest early and after discharge. The mortality gap of fifteen to twenty years is mostly cardiometabolic, driven by metabolic syndrome, cardiovascular disease, diabetes and smoking, so physical-health and metabolic screening are essential in serious mental illness.

The whole subject in one table	
APPLY AND CONSOLIDATE	Four worked vignettes: a first-episode workup, a schizophrenia versus mood-with-psychosis differential, a negative-symptom-predominant picture, and a prognosis assessment. Then the master mnemonic (cause to phenomenon to criteria to course), answer-free retrieval prompts, and the four-branch synthesis map to redraw from memory.

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The material is grounded in the standard psychiatry texts (the source hierarchy below), which anchor the settled facts on aetiology, phenomenology, classification and course; the descriptive-phenomenology definitions follow the specialist symptom texts. The historical framing of the disorder rests on the foundational sources, and every landmark, contested or numeric claim carries a PubMed-verified journal citation. Each PMID here was checked against PubMed this build, matched on title, first author and year; any citation whose identifier did not resolve to the cited paper was corrected or dropped rather than guessed. A small number of inline references (for example Jablensky's Dialogues in Clinical Neuroscience review and a few society-guideline and monograph items) are not carried in the journal list because they have no stable PubMed record; the claims they support are also covered by the verified citations retained here.

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PART II

II

Schizophrenia: Management, Antipsychotics and Adverse Effects

Treating schizophrenia: the antipsychotics, how they are chosen and combined, and the adverse effects to watch for.

01 Antipsychotic pharmacotherapy and the management plan

02 Psychosocial rehabilitation and psychological treatment

03 Antipsychotic adverse effects and emergencies

04 Apply and consolidate

PAPER II

Schizophrenia: management, antipsychotics and adverse effects

Four sections · one complete notes document

This material gathers the treatment of schizophrenia into one document, the counterpart to the chapter on the illness itself. The first band is **antipsychotic pharmacotherapy and the management plan**: the biopsychosocial plan and the treatment-phase algorithm that orient every case, the receptor pharmacology that explains both the benefit and the harm of these drugs, the first-generation and second-generation and newer agents, the management of the first episode and of maintenance, the depot and long-acting injectables, and then the hard end of the algorithm, treatment resistance and clozapine and the management of the negative symptoms that respond least. The second band is **psychosocial rehabilitation and psychological treatment**: the rehabilitation, family and skills-based work, the psychological therapies, and the community models, including those of Indian practice, that carry the recovery a prescription cannot. The third band is **adverse effects and emergencies**: the extrapyramidal effects and tardive dyskinesia, the metabolic, prolactin and cardiac burden and its monitoring, and the emergencies, neuroleptic malignant syndrome and the differential that separates it from its mimics. The examinable skill is judgement across all three: to build a phase-based plan, to choose the right drug against its adverse-effect cost, to reach for clozapine at the right point, and to recognise and manage the emergencies the drugs create.

HOW TO USE THESE NOTES

Read the three bands as one argument that runs from the plan to its cost. The **pharmacotherapy** band builds the management spine, where the patient is treated, what is targeted in each phase, and every mode of treatment available, then works down the algorithm from the first episode to clozapine; each named drug ends with a **Good to remember** box giving its class and mechanism, its dose range, and the one monitoring parameter to hold. The **rehabilitation** band carries the psychosocial half of recovery, the family, skills, psychological and community work that medication alone cannot deliver. The **adverse-effects** band closes on the harm the drugs create and the emergencies to recognise, each effect ending with a box giving its feature, its discriminator, and the first management step. Figures declare one axis and code it in colour: **petrol** marks structure and the neutral case, **coral** marks the trap or the danger, and **marigold** highlights the number to hold. Four boundaries are worth stating up front: the phenomenology, aetiology, criteria and course of the illness are taught in the Schizophrenia: aetiology, phenomenology, classification and course notes and are not repeated here; the receptor and pathway mechanics and the CYP metabolism belong to the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the technique of electroconvulsive therapy for augmentation and resistance lives in the ECT and neurostimulation notes; and malignant catatonia and the other psychotic disorders as entities live in the Other psychotic disorders, delusional syndromes and catatonia notes, needed here only inside the emergency differential. This is doctor-facing revision, so the full technical vocabulary is used, and every dose, range and monitoring threshold is verified against a source.

Antipsychotic pharmacotherapy and the management plan

1 · Orientation: the biopsychosocial plan and the treatment algorithm

These notes turn from what schizophrenia *is* to what you *do* about it, and the whole of that doing is organised by one schema: the **treatment algorithm**. Schizophrenia is treated, not cured. The realistic aim is symptom control, restored function and recovery over the long run, and the backbone of every phase is an antipsychotic, prescribed inside a wider **biopsychosocial** plan (Maudsley 2021, APA 2020). The examiner on a management question is never testing whether you can name a drug; they are testing whether you can place a given patient on the algorithm, choose a locus of care, target the right symptoms for the phase, and defend the choice against the guideline.

How to use this page. Fix three orienting frames before any drug detail arrives. First, the biopsychosocial **management plan** as a spine with three limbs, the **locus** (where care happens), the **focus** (which symptoms, set by the phase) and the **modus** (every mode of treatment on the table). Second, the treatment algorithm run forward across the **phases of treatment**: acute, stabilisation and maintenance, then the branch to clozapine when two adequate trials fail. Third, the master mnemonic that chains the whole chapter so one cue unpacks the note. The illness itself, its phenomenology, aetiology, criteria and course, is not re-taught here; it belongs to the Schizophrenia: aetiology, phenomenology, classification and course notes, and this chapter

applies management to it. The receptor pharmacology and CYP metabolism behind the drugs belong to the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

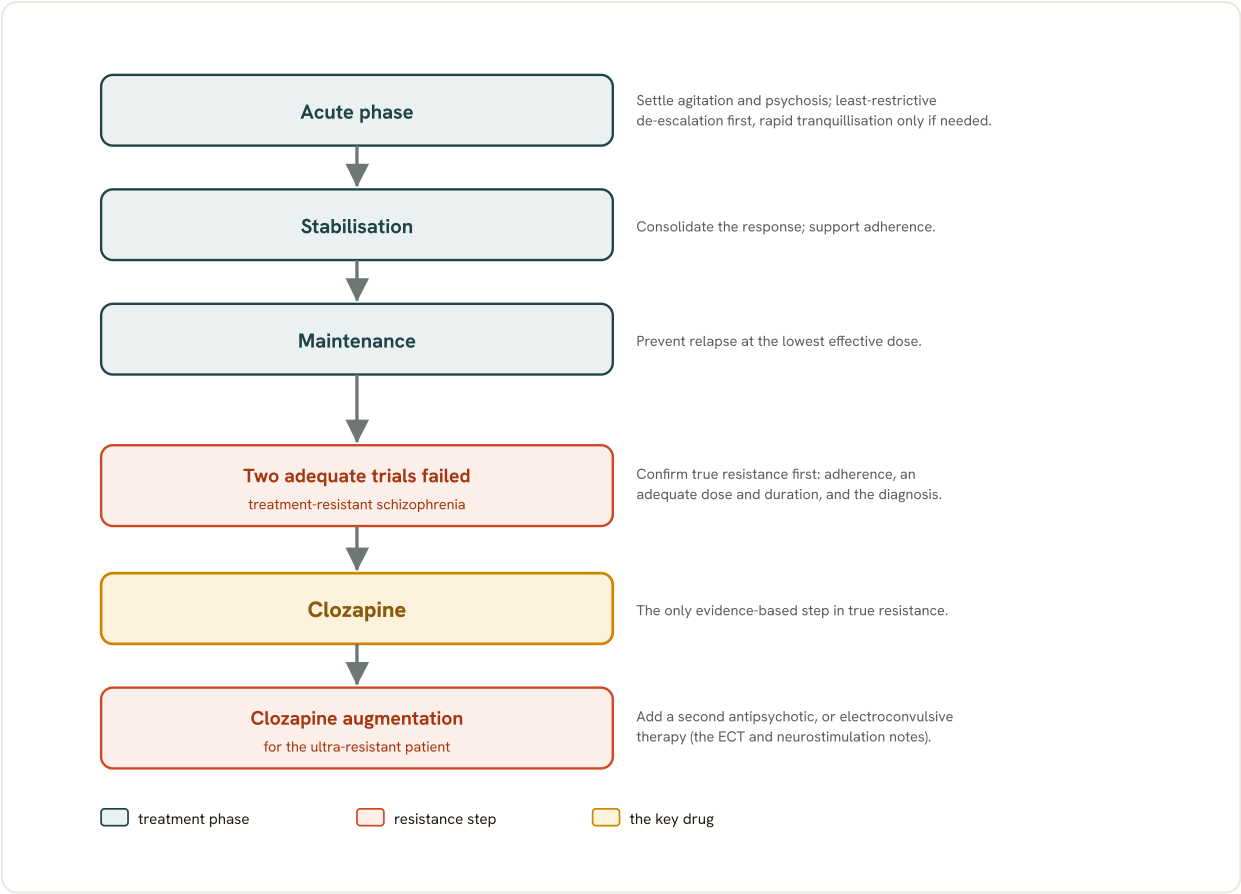


Fig 9.1 The antipsychotic treatment algorithm. Care runs down the phase ladder, acute to stabilisation to maintenance at the lowest effective dose. When two adequate trials have genuinely failed, the illness is treatment-resistant and the evidence-based next step is clozapine, not a third same-class switch; the ultra-resistant patient is then augmented.

1.1 The guidelines-first frame: where the algorithm comes from

Answer from a named guideline, not from memory. Management answers carry more weight when anchored to a source, and three guidelines supply the algorithm used throughout these notes. The Maudsley Prescribing Guidelines (Maudsley 2021) are the practical prescribing backbone: dose ranges, rapid tranquillisation, clozapine initiation and monitoring, and the treatment-resistance pathway. The NICE guideline (NICE CG178/NG, 2014 onward) and the APA Practice Guideline (APA 2020) frame the phase-based structure, the offer of an antipsychotic plus family intervention and CBT, and physical-health monitoring. For the Indian setting the Indian Psychiatric Society (IPS) Clinical Practice Guidelines for schizophrenia, updated in 2025 (IPS 2025, Sahoo et al., Indian J Psychiatry 2026;68:94-121), give the locally calibrated version, including community and resource-aware recommendations. Lead with the guideline the paper names; where unmarked, the phase structure is common to all three, so cite the phase framework and the Maudsley for the numbers.

RULE **Name the source.** Every management recommendation you give should be traceable to the Maudsley, NICE/APA or IPS guidance; a phase-anchored, guideline-cited answer beats an unsourced drug list every time.

1.2 The biopsychosocial management plan: locus, focus, modus

The management spine. A **biopsychosocial management plan** is not a drug prescription with extras bolted on; it is a spine with three limbs that you set for every patient. Hold them as **locus**, **focus** and **modus**. Deciding all three, and revisiting them at each review, is the management task the algorithm then structures.

Locus

Where care is delivered, chosen on the least-restrictive-first principle: outpatient (clinic and community team), day-hospital, inpatient admission, or crisis/community care (home treatment and crisis-resolution teams).

Focus

Which symptoms you are targeting now, set by the **phase of treatment**: agitation and florid psychosis acutely, consolidation and adherence in stabilisation, relapse prevention and function in maintenance.

Modus

Every mode of treatment available: antipsychotics (the pharmacological backbone), psychosocial rehabilitation, family work, and physical-health care, combined rather than chosen between.

Locus, least-restrictive first. The default locus is the least restrictive option that is safe. Most treatment is outpatient. Escalate to day-hospital, then inpatient admission (voluntary where possible, involuntary only where the legal threshold is met), only when risk, non-adherence with deterioration, or the need for supervised initiation demands it. Crisis-resolution and home-treatment teams can hold many acute presentations in the community and are the least-restrictive alternative to admission where they exist.

Focus by phase, modus across all phases. The **focus** is what changes across the phases; the **modus** stays broad throughout. From the first contact the plan runs the antipsychotic alongside psychosocial rehabilitation (social-skills and vocational work), family intervention (psychoeducation and reduction of high expressed emotion), and structured physical-health care (metabolic and cardiovascular monitoring), because the drug alone does not restore function and does not prevent the physical-health mortality gap. The detail of monitoring, family work and rehabilitation is developed in the dedicated topics; the point here is that they are part of the plan from the outset, not an afterthought.

COMMON TRAP

Equating "management" with "which antipsychotic". The drug is one limb of the modus. An answer that names a molecule but never states the locus, the phase-set focus, or the psychosocial and physical-health limbs has missed the biopsychosocial plan the question is testing.

1.3 The treatment algorithm: the orienting schema across the phases

The whole chapter on one decision tree. The **treatment algorithm** is the schema every management topic hangs from. Read it forward as three sequential phases with a resistance branch. In the **acute phase** the target is control of agitation and florid psychosis: secure safety, start (or optimise) a single antipsychotic at an adequate dose, and manage acute agitation by de-escalation, then rapid tranquillisation if needed. In **stabilisation** the target is consolidation: continue the effective drug at the effective dose, allow time for response (an adequate trial is 4 to 6 weeks at optimum dose), treat residual symptoms and adverse effects, and build adherence and the psychosocial plan. In **maintenance** the target is relapse prevention and function: continue the antipsychotic long-term (a long-acting injectable is a key option for adherence), keep physical-health monitoring running, and taper only slowly and with full risk-benefit review. The single most examined branch off this trunk is treatment resistance: where the illness fails to respond to adequate trials of at least two antipsychotics, the pathway turns to clozapine and then to augmentation. That branch, the two-failed-trials definition and the clozapine monitoring detail, is developed in the treatment-resistance and clozapine topics; here it is only the fork in the algorithm.

PHASE	THE ONE TARGET	THE CORE MOVE
Acute phase	Control agitation and psychosis, secure safety	**De-escalate; start/optimise a single antipsychotic; rapid tranquillisation only if needed**
Stabilisation	Consolidate response; adherence; treat residuals	**Continue the effective drug at the effective dose; adequate trial 4 to 6 weeks; add psychosocial limbs**
Maintenance	Prevent relapse; restore function	**Long-term antipsychotic (consider LAI); ongoing monitoring; taper only slowly with review**
Resistance branch	Non-response after two adequate trials	**Turn to clozapine, then augmentation (developed in the treatment-resistance and clozapine topics)**

The treatment algorithm as an orienting schema: three sequential phases, each with a single target, plus the treatment-resistance fork to clozapine. Drawn as Fig 9.1.

TRAP **Switching too early.** Declaring an antipsychotic a failure before an adequate trial (4 to 6 weeks at optimum dose, with adherence confirmed) manufactures pseudo-resistance; much apparent resistance is inadequate dose, duration or covert non-adherence (Maudsley 2021).

1.4 The acute-agitation step: de-escalation, then rapid tranquillisation, then restraint

A staged, least-restrictive escalation. The first move of the acute phase is often managing **acute agitation**, and it is a staged escalation, least-restrictive first. Begin with de-escalation: a calm environment, verbal and non-verbal techniques, addressing needs, and offering oral medication. Only when de-escalation and offered oral treatment fail, and the patient is placing themselves or

others at significant risk, move to rapid tranquillisation with parenteral medication. Physical restraint and seclusion are used only when necessary, for the shortest time, as the least-restrictive means of maintaining safety, and always with monitoring. The drug detail is kept brief here and the wider protocol, including the management of substance-related and undifferentiated agitation, is cross-referenced to the emergency chapter.

The rapid-tranquillisation ladder, in brief. Per the Maudsley (2021), after de-escalation the ladder is: offer *oral* treatment first, for example lorazepam **1 to 2 mg** (with or without promethazine) in a benzodiazepine-naive patient, or an oral antipsychotic such as olanzapine, risperidone or quetiapine; then *intramuscular* treatment if two oral doses fail or sooner if risk is high, with the common IM options being lorazepam **2 mg**, promethazine **50 mg**, or IM olanzapine **10 mg**. Generic names lead in Indian practice; where a brand is needed, haloperidol is marketed as Serenace. Haloperidol IM **5 mg** is the last drug to consider because acute dystonia is common: give it with promethazine, keep procyclidine to hand, and a pretreatment ECG is required. IM olanzapine must not be combined with an IM benzodiazepine, and antipsychotic polypharmacy is avoided in rapid tranquillisation because of the additive QTc risk. After any parenteral dose, monitor level of consciousness, respiratory rate, oxygen saturation, pulse, blood pressure and temperature; keep flumazenil available for benzodiazepine-induced respiratory depression.

1 to 2 mg	10 mg	4 to 6 wk
ORAL LORAZEPAM, RT STEP 2	IM OLANZAPINE, RT STEP 3	ADEQUATE ANTIPSYCHOTIC TRIAL

TRAP **Restraint or rapid tranquillisation before de-escalation.** Reaching for the IM tray or physical restraint before de-escalation and an offered oral dose is both a clinical and a governance error; restraint is a last resort, time-limited and monitored, never the opening move.

INDIA

In Indian practice the antipsychotic backbone is affordable and widely available, and generic prescribing dominates. Where a long-acting injectable is chosen for maintenance adherence, olanzapine pamoate long-acting injection is marketed as Tolaz (Torrent); its binding practical constraint is the post-injection delirium sedation syndrome, which mandates a supervised post-injection observation period after each dose, a service most outpatient setups cannot deliver. Community and resource-aware delivery models sit under the District Mental Health Programme (DMHP) and the IPS guideline; clozapine monitoring in the Indian setting is addressed in the clozapine topic.

1.5 The master mnemonic: chaining the chapter

One hook for the whole management chapter. A single mnemonic chains the management sequence so that one cue unpacks the note. Fix it in reading order and every later topic slots onto its link.

MNEMONIC

"CHOOSE, MAINTAIN, RESIST, REHABILITATE, WATCH THE HARMS"

Unpack it link by link. **Choose** is the acute-phase and stabilisation task: select a single antipsychotic on adverse-effect profile and patient factors, at an adequate dose for an adequate trial. **Maintain** is the maintenance phase: continue long-term for relapse prevention, using a long-acting injectable where adherence is the problem. **Resist** is the treatment-resistance branch: two failed adequate trials turn the algorithm to clozapine and then augmentation. **Rehabilitate** is the psychosocial modus that runs across all phases: family intervention, CBT for psychosis, social-skills and vocational rehabilitation. **Watch the harms** is the safety spine: extrapyramidal side-effects, the metabolic syndrome, QTc and prolactin, and the emergencies of neuroleptic malignant syndrome and clozapine-related neutropenia. One seed, the whole chapter.

WORKED EXAMPLE

A 24-year-old man with a first episode arrives agitated and threatening on the ward. Walk the algorithm. Locus: he needs a safe setting, so admission (least-restrictive that is safe) with the crisis team considered if risk can be held. Focus: this is the acute phase, so the target is agitation and psychosis. Modus, acute step: de-escalate first, offer oral lorazepam 1 to 2 mg or an oral antipsychotic; if he refuses and risk is high, move to IM (olanzapine 10 mg or lorazepam 2 mg), with restraint only if necessary and monitored, and full physical monitoring after any parenteral dose. Then choose a maintenance antipsychotic, run it for an adequate 4 to 6 week trial in stabilisation, add family work and physical-health monitoring, and plan maintenance. If a second adequate trial also fails, the algorithm forks to clozapine. That single case exercises locus, focus, modus and every phase of the algorithm.

HOLD THIS

Schizophrenia is managed, not cured: an antipsychotic backbone across acute, stabilisation and maintenance phases, inside a biopsychosocial plan set by locus, focus and modus, with the algorithm forking to clozapine after two adequate trials fail; acute agitation goes de-escalation, then rapid tranquillisation, then restraint, least-restrictive first.

GOOD TO REMEMBER

- **Antipsychotic (the backbone):** dopamine-D2-blocking agent that is the pharmacological limb across every phase; dose is chosen within the licensed range and titrated (the class and per-drug mechanics belong to the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes); the one caveat to hold is that an adequate trial is 4 to 6 weeks at optimum dose with adherence confirmed before calling it a failure.
- **Lorazepam (rapid tranquillisation):** short-acting benzodiazepine used for acute agitation; oral 1 to 2 mg then IM 2 mg per the Maudsley ladder; the one parameter to hold is respiratory depression, so monitor after parenteral dosing and keep flumazenil available.
- **Olanzapine IM (rapid tranquillisation):** second-generation antipsychotic given IM 10 mg for agitation; the one caveat is that it must never be combined with an IM benzodiazepine, and physical observations are monitored after the dose.
- **Haloperidol (rapid tranquillisation, last-line; brand Serenace):** high-potency first-generation antipsychotic, IM 5 mg; the discriminating caveat is a high rate of acute dystonia and QTc prolongation, so it is the last drug considered, given with promethazine, with procyclidine to hand and a pretreatment ECG.
- **Clozapine (the resistance branch):** the drug for treatment-resistant schizophrenia after two failed adequate trials; the one parameter to hold is mandatory haematological monitoring for neutropenia (developed with the ANC cut-offs in the clozapine topic).
- **Restraint (emergency step):** physical restriction of a dangerously agitated patient; the discriminator from rapid tranquillisation is that it is a last resort after de-escalation fails; the first management principle is least-restrictive, time-limited and continuously monitored, with the wider protocol in the emergency chapter.

Figure. The treatment algorithm, the three-phase decision tree (acute, stabilisation, maintenance) with the acute-agitation ladder and the treatment-resistance fork to clozapine, is drawn as Fig 9.1.

2 · Antipsychotic mechanism and receptor pharmacology

Every antipsychotic earns its place by what it does at the dopamine D2 receptor, and it earns its adverse-effect signature by what else it touches on the way. This topic is the single axis that explains both the benefit and the harm of the whole class, and the examiner rewards a resident who can move from a receptor to a symptom and from a receptor to a side effect without hesitation. The pathway anatomy and the receptor biology themselves are the property of the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; here that biology is applied to predict clinical effect.

Why this is the master key. The **mechanism of action** of every effective agent runs through D2 blockade, and the **receptor pharmacology** of a given drug, its affinities across D2, 5-HT2A, H1, M1 and alpha-1, predicts almost everything a resident is asked in a viva: which symptoms respond, how much extrapyramidal risk there is, whether it sedates, whether it drops blood pressure and whether it raises prolactin (Stahl 2021; Kaplan & Sadock 2024). Learn the receptor profile and the adverse-effect profile falls out of it. The disorder itself, its phenomenology, aetiology and course, belongs to the Schizophrenia: aetiology, phenomenology, classification and course notes and is not re-taught here.

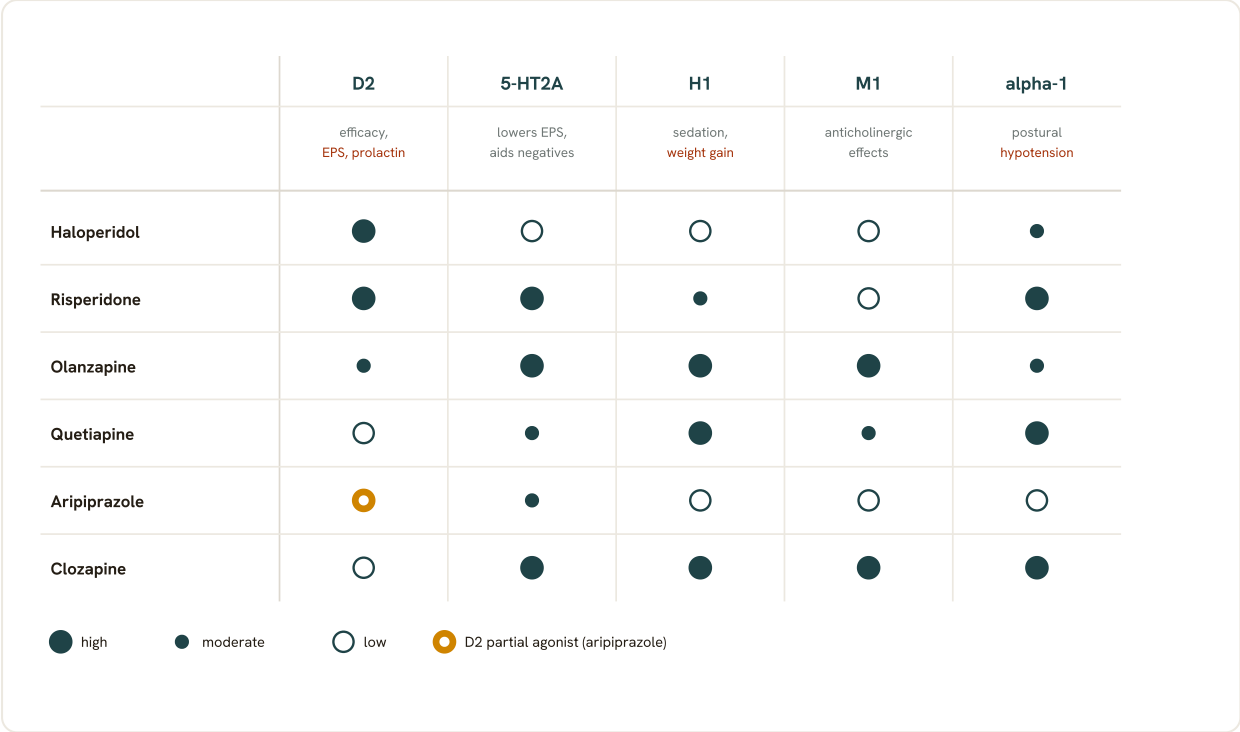


Fig 9.2 The receptor-affinity grid. A drug's receptor profile predicts its adverse-effect signature: D2 blockade buys efficacy but costs extrapyramidal effects and prolactin; 5-HT2A antagonism lowers the extrapyramidal burden; H1 drives sedation and weight gain; M1 the anticholinergic effects; and alpha-1 the postural hypotension. Aripiprazole is a D2 partial agonist, not a full blocker, which is why its profile differs.

2.1 The unifying principle: D2 blockade

One shared action. All clinically effective antipsychotics are antagonists (or partial agonists) at the dopamine D2 receptor, and this d2 blockade is the common final pathway of antipsychotic action (Kaplan & Sadock 2024; Stahl 2021). The classic evidence is that antipsychotic potency across first-generation agents correlates tightly with D2 binding affinity: the tighter a drug binds D2, the lower the milligram dose needed. No agent lacking meaningful D2 activity has proven antipsychotic in schizophrenia, which is why D2 blockade, not any single receptor gimmick, is the definition of the class.

Where the benefit lives. The antipsychotic (antidelusional, antihallucinatory) effect maps onto D2 blockade in the mesolimbic dopamine pathway, where excess dopamine transmission is thought to drive the positive symptoms (Stahl 2021). Blocking D2 here dampens the aberrant signalling behind delusions and hallucinations. The pathway mechanics, the mesolimbic, mesocortical, nigrostriatal and tuberoinfundibular tracts, are owned by the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; this topic uses them only to locate benefit and harm.

RULE **No D2, no antipsychotic.** Every drug that treats schizophrenia blocks or partially agonises D2; potency tracks D2 affinity. The receptor is the definition of the class, not an incidental feature.

2.2 The therapeutic window of striatal D2 occupancy

The occupancy story. Positron-emission-tomography studies define a therapeutic window of striatal D2 occupancy. For at least the first-generation agents, antipsychotic effect requires a striatal D2 receptor occupancy of roughly **65 to 70%**, while occupancy above about **80%**

significantly increases the risk of extrapyramidal side effects (Remington & Kapur 1999; Kapur 2000; Tasman 2024). The practical window a resident holds is therefore roughly **65 to 80%** striatal D2 occupancy: below it the drug underperforms, above about 80 percent the extra occupancy buys extrapyramidal symptoms rather than efficacy. Crucially, response and extrapyramidal risk track occupancy, not dose, and occupancy varies widely between patients on the same dose, which is the pharmacological argument for the lowest effective dose.

65 to 70%	>80%	65 to 80%
STRIATAL D2 FOR ANTIPSYCHOTIC EFFECT	STRIATAL D2 WHERE EPS RISK RISES	THE WORKING THERAPEUTIC WINDOW

An illustration. Olanzapine at its usual clinical dose of 10 to 20 mg/day produces about 71 to 80 percent striatal D2 occupancy, and doses of 30 mg/day and above push occupancy over 80 percent, exactly where extrapyramidal liability climbs (Kapur et al. 1998; Tasman 2024). This is why pushing an antipsychotic ever higher in a non-responder is usually the wrong move: past the window you add extrapyramidal symptoms without adding antipsychotic effect.

TRAP **Assuming more D2 occupancy always means more efficacy.** Above roughly 80 percent striatal occupancy, extra D2 blockade adds extrapyramidal side effects, not response; the non-responder needs a switch or clozapine, not a bigger dose.

2.3 The 5-HT2A/D2 ratio that defines the atypicals

The serotonin-dopamine idea. The second-generation (atypical) antipsychotics are, as a group, characterised by relatively more potent 5-HT2A than D2 receptor antagonism, the high 5-ht2a/d2 ratio (New Oxford Textbook; Stahl 2021). The mechanism is that 5-HT2A antagonism disinhibits dopamine release in selected pathways: serotonin at 5-HT2A normally brakes dopamine neurons, so blocking 5-HT2A lifts that brake and restores dopamine in the nigrostriatal and mesocortical pathways. In the nigrostriatal tract the restored dopamine competes with the drug at D2 and softens extrapyramidal symptoms; in the mesocortical tract the added dopamine is proposed to help the negative and cognitive symptoms, which stem partly from a cortical dopamine deficit. Combined 5-HT2A antagonism with less potent D2 antagonism is the most consistent principle yet found for separating antipsychotic action from motor side effects (New Oxford Textbook).

The instructive exceptions. Aripiprazole works not through the 5-HT2A/D2 ratio but through D2 partial agonism, and amisulpride is a selective D2/D3 antagonist with little 5-HT2A activity, yet both are counted as atypical because they too achieve a low extrapyramidal burden (New Oxford Textbook). The lesson for the exam is that atypicality is a clinical outcome, low extrapyramidal liability, reached by more than one receptor route.

PATHWAY	EFFECT OF 5-HT2A ANTAGONISM	CLINICAL READ-OUT
Nigrostriatal	Disinhibits dopamine, competes with D2 blockade	**Lower extrapyramidal symptoms than a pure D2 blocker**
Mesocortical	Restores dopamine in a dopamine-deficient tract	**Proposed benefit for negative and cognitive symptoms**
Mesolimbic	D2 blockade retained; little dopamine disinhibition where positive symptoms live	**Antipsychotic efficacy preserved**

How a high 5-HT2A/D2 ratio splits antipsychotic action from motor harm: serotonin blockade lifts the dopamine brake selectively in the nigrostriatal and mesocortical tracts while D2 blockade continues to treat mesolimbic positive symptoms.

2.4 The receptor basis of the adverse effects

Read the profile, predict the harm. A drug's off-target receptor affinities generate a predictable adverse-effect signature, and this is the single most examinable idea in antipsychotic pharmacology (Stahl 2021). The D2 receptor produces two of the effects, in the wrong pathways; three other receptors, H1, M1 and alpha-1, produce the rest. Map the receptor to the pathway or organ and the side effect follows.

D2, nigrostriatal

Blockade in the motor pathway produces extrapyramidal side effects: acute dystonia, parkinsonism, akathisia and, with time, tardive dyskinesia.

D2, tuberoinfundibular

Blockade removes dopamine's tonic inhibition of prolactin, producing hyperprolactinaemia (galactorrhoea, amenorrhoea, sexual dysfunction).

H1 (histaminergic)

Blockade causes sedation and, over time, weight gain and increased appetite.

M1 (muscarinic)

Blockade causes the anticholinergic cluster: dry mouth, constipation, blurred vision, urinary retention and cognitive dulling.

Alpha-1 (adrenergic)

Blockade causes postural (orthostatic) hypotension and dizziness, and contributes to sedation.

RECEPTOR BLOCKED	SITE / MECHANISM	ADVERSE EFFECT PREDICTED
D2	Nigrostriatal (motor) pathway	**Extrapyramidal symptoms, tardive dyskinesia**
D2	Tuberoinfundibular pathway (loss of dopamine brake on prolactin)	**Hyperprolactinaemia: galactorrhoea, amenorrhoea, sexual dysfunction**
H1	Histaminergic	**Sedation and weight gain**
M1	Muscarinic (anticholinergic)	**Dry mouth, constipation, blurred vision, urinary retention, cognitive dulling**

RECEPTOR BLOCKED	SITE / MECHANISM	ADVERSE EFFECT PREDICTED
Alpha-1	Adrenergic	**Postural hypotension, dizziness, sedation**

The receptor-to-adverse-effect grid: two effects flow from D2 in the wrong pathways, three from H1, M1 and alpha-1; a drug's receptor-affinity fingerprint predicts which of these it will cause.

RULE **The receptor profile predicts the adverse-effect profile.** Match each receptor a drug blocks to its pathway or organ (D2 motor, D2 prolactin, H1, M1, alpha-1) and its side-effect signature is deducible before you prescribe.

The low-potency phenothiazines (for example chlorpromazine) sit heavily on H1, M1 and alpha-1 and so sedate, dry and drop pressure while causing fewer extrapyramidal symptoms per milligram; the high-potency agents (for example haloperidol, marketed in India as Serenace) are lean on those receptors and so cause prominent extrapyramidal symptoms with little sedation or hypotension. The atypicals redistribute the burden: olanzapine and clozapine load H1 and M1 (sedation, weight gain, metabolic effects), risperidone and amisulpride raise prolactin, and quetiapine and clozapine carry alpha-1 orthostatic effects.

2.5 Partial agonism and the muscarinic mechanism

Partial agonism (dopamine stabilisers). Aripiprazole and its relatives are D2 *partial* agonists rather than full antagonists: they occupy D2 and deliver an intermediate, tuned signal, dampening dopamine where transmission is excessive (mesolimbic) yet providing some tone where it is deficient (Stahl 2021). The consequence is a low extrapyramidal and low prolactin profile, because the receptor is never driven to the near-total blockade that produces those effects. The detailed clinical handling of aripiprazole, cariprazine and brexpiprazole is developed in the atypical-agents topic; here the point is only that partial agonism is a distinct mechanistic route to antipsychotic effect.

The muscarinic mechanism (a newer route). Beyond dopamine and serotonin, direct agonism at central muscarinic M1 and M4 cholinergic receptors is an emerging antipsychotic mechanism that reduces dopaminergic overactivity indirectly, without any D2 blockade, and so without the classical extrapyramidal and prolactin liabilities (Stahl 2021). This muscarinic-agonist strategy is the basis of the newest agents and is developed further in the atypical-agents topic; it is flagged here as the exception that proves the rule that dopamine blockade, while universal among the older drugs, is not the only path to an antipsychotic effect.

INDIA

The olanzapine pamoate long-acting injectable is marketed in India as Tolaz LA (Torrent Pharmaceuticals), the local counterpart of the depot whose pharmacology raises the post-injection syndrome, an inadvertent intravascular release causing sedation and delirium that mandates a supervised observation period after each injection. Verify current strengths, the observation protocol and availability against the product information before prescribing.

HOLD THIS

Antipsychotic effect = D2 blockade in the mesolimbic pathway at roughly 65 to 80 percent striatal D2 occupancy; above about 80 percent you buy extrapyramidal symptoms, not efficacy, and every off-target receptor (D2-motor, D2-prolactin, H1, M1, alpha-1) predicts its own adverse effect.

GOOD TO REMEMBER

- **D2 blockade:** the shared mechanism of action of every effective antipsychotic; potency tracks D2 affinity; the antipsychotic effect maps to mesolimbic D2 occupancy. Hold: striatal D2 occupancy of 65 to 70 percent for effect, above about 80 percent for rising extrapyramidal risk (Remington & Kapur 1999; Kapur 2000).
- **5-HT2A/D2 ratio:** the high 5-HT2A over D2 antagonism that defines most atypicals; 5-HT2A blockade disinhibits dopamine in the nigrostriatal and mesocortical pathways, giving lower extrapyramidal symptoms and a proposed effect on negative symptoms. Caveat: aripiprazole (partial agonism) and amisulpride (selective D2/D3) are atypical by other routes.
- **Extrapyramidal symptoms:** from D2 blockade in the nigrostriatal pathway; discriminator is the motor picture (dystonia, parkinsonism, akathisia, tardive dyskinesia); first step is to reduce dose or switch to a lower-extrapyramidal agent.
- **Hyperprolactinaemia:** from D2 blockade in the tuberoinfundibular pathway; discriminator is galactorrhoea, amenorrhoea, sexual dysfunction; first step is to check prolactin and consider a prolactin-sparing agent.
- **H1 blockade:** sedation and weight gain; the read-out that flags olanzapine and clozapine; first step is to weigh the sedative and metabolic cost against the benefit.
- **M1 (muscarinic) blockade:** the anticholinergic cluster (dry mouth, constipation, blurred vision, urinary retention, cognitive dulling); first step is dose review, especially in the elderly.
- **Alpha-1 blockade:** postural hypotension and dizziness; first step is slow titration and a lying-standing blood pressure check.
- **Partial agonism:** aripiprazole as a D2 partial agonist (dopamine stabiliser); the read-out is low extrapyramidal and low prolactin liability; the muscarinic-agonist route achieves antipsychotic effect with no D2 blockade at all.

3 · Typical (first-generation) antipsychotics

Why this matters. The **typical antipsychotic** agents, the **first-generation** drugs, are the substrate on which all antipsychotic pharmacology is built, and the examiner uses them to test one idea above all others: that a single axis, **potency**, predicts the whole adverse-effect profile. These drugs remain in daily Indian practice because they are effective against positive symptoms, cheap and widely available, so their doses and trade-offs are high-yield rather than historical. This topic teaches the classes, the potency axis, the receptor profile and the practical place today; it does not re-teach the illness (that phenomenology, aetiology, criteria and course belong to the Schizophrenia: aetiology, phenomenology, classification and course notes), nor does it re-derive the dopamine pathways and receptor mechanics (those are owned by the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and are only applied here).

The governing sentence is one line: for a first-generation drug, where it sits on the high-potency to low-potency scale tells you, before you know anything else, whether the patient will suffer more extrapyramidal and prolactin effects or more sedation, anticholinergic and cardiometabolic

effects (Stahl 2021, Kaplan & Sadock 2024). Efficacy against positive symptoms is broadly comparable across the class at adequate dose; what differs is which side effects the patient pays for that efficacy with.

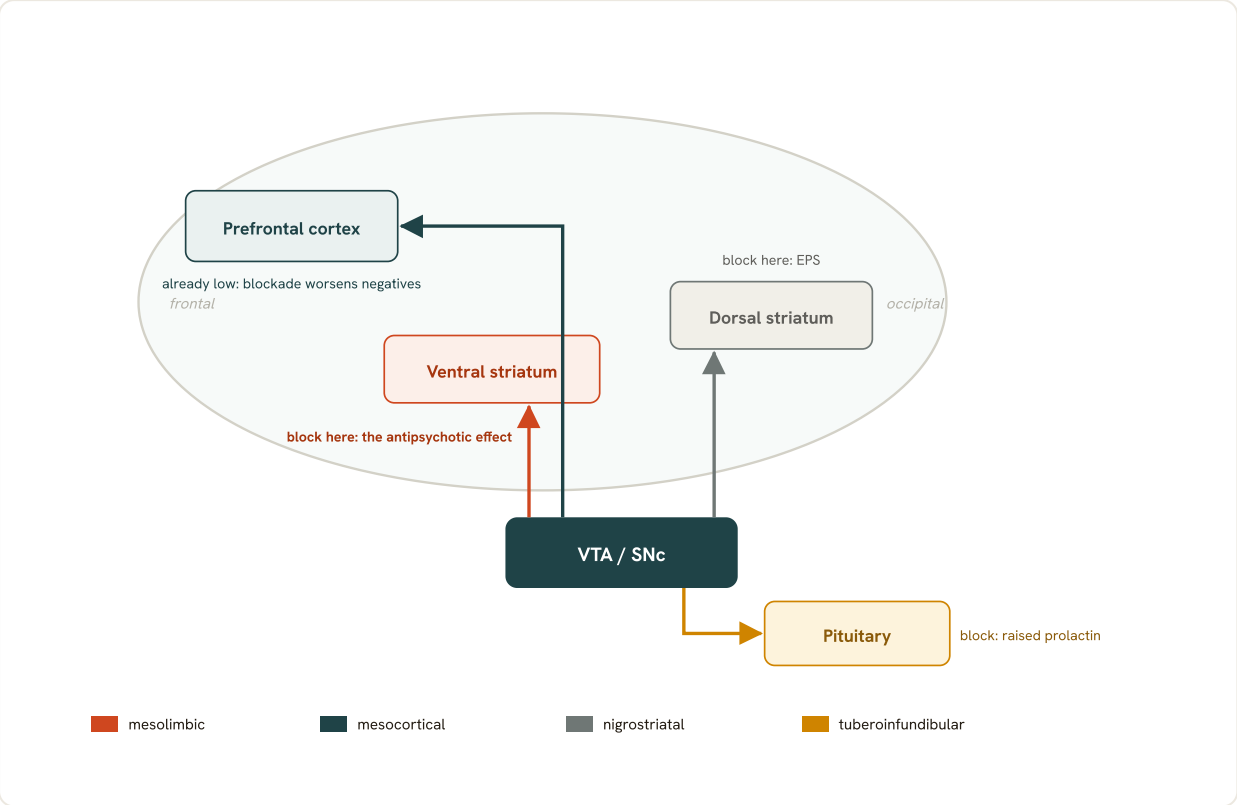


Fig 9.3 What D2 blockade does in each dopamine pathway. Blocking the overactive mesolimbic tract to the ventral striatum produces the antipsychotic effect. The same blockade in the nigrostriatal tract causes extrapyramidal effects, in the tuberoinfundibular tract raises prolactin, and in the already-underactive mesocortical tract can worsen the negative and cognitive symptoms. The pathway mechanics are developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

3.1 What "first-generation" means and how the class is defined

The first-generation antipsychotics, also called typical or conventional antipsychotics or neuroleptics, are the drugs introduced from chlorpromazine (1952) onward whose antipsychotic action rests predominantly on blockade of the dopamine D2 receptor (Stahl 2021). They are grouped chemically into the phenothiazines (chlorpromazine, thioridazine, trifluoperazine, fluphenazine), the butyrophenones (haloperidol), the diphenylbutylpiperidines (pimozide) and the thioxanthenes (flupentixol, zuclopenthixol). For the examination the chemical class matters less than the functional axis that cuts across it, potency, which is what the rest of this topic is built around. The term first-generation and the term first generation are used interchangeably in the literature and refer to the same set of drugs.

RULE **A first-generation antipsychotic is defined by predominant D2 blockade.** The antipsychotic effect tracks D2 occupancy in the mesolimbic pathway; almost everything else about the drug follows from how much of that D2 blockade, and how much off-target receptor blockade, it delivers.

3.2 The potency axis: what "potency" actually measures

In this context potency does not mean efficacy or how "strong" the drug is. It means the milligram dose required to achieve a given degree of D2 blockade, expressed by convention against chlorpromazine as the reference (Kaplan & Sadock 2024). A **high-potency** agent achieves antipsychotic D2 occupancy at a few milligrams (haloperidol); a **low-potency** agent needs hundreds of milligrams (chlorpromazine). Because the high-potency drug is given at a low milligram dose, it carries relatively little of the off-target histamine, muscarinic and alpha-1 blockade, so its D2-driven effects (extrapyramidal symptoms and hyperprolactinaemia) dominate. Because the low-potency drug is given at a high milligram dose, it brings substantial H1, M1 and alpha-1 blockade, so sedation, anticholinergic load and postural hypotension dominate while its relative extrapyramidal burden is lower. This inverse relationship is the single most tested idea in the topic.

> **PEARL**
>
> High potency and low potency describe the milligram dose needed for D2 blockade, not the clinical effectiveness. Haloperidol and chlorpromazine are comparably effective antipsychotics; haloperidol is simply "high-potency" because a few milligrams do what several hundred milligrams of chlorpromazine do.

3.3 Receptor profile: D2 plus the off-target three

Every first-generation antipsychotic blocks the dopamine D2 receptor, and that blockade is responsible for both the therapeutic action (in the mesolimbic pathway) and the signature adverse effects (extrapyramidal symptoms from the nigrostriatal pathway, hyperprolactinaemia from the tuberoinfundibular pathway). The low-potency agents add clinically important blockade of three further receptors: histamine H1 (sedation, weight gain), muscarinic M1 (dry mouth, constipation, blurred vision, urinary retention, cognitive dulling) and alpha-1 adrenergic (postural hypotension, dizziness). The high-potency agents, given at low milligram doses, are relatively "clean" of H1, M1 and alpha-1 activity, which is precisely why they are less sedating and less hypotensive but far more likely to cause extrapyramidal reactions (Stahl 2021). The detailed mechanics of each pathway and receptor sit in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; here we simply read the adverse-effect profile off the receptor list.

D2 (dopamine) blockade

Shared by all; mesolimbic blockade gives the antipsychotic effect, nigrostriatal gives extrapyramidal symptoms, tuberoinfundibular gives raised prolactin.

H1 (histamine) blockade

Prominent in low-potency agents; causes sedation and weight gain.

M1 (muscarinic) blockade

Prominent in low-potency agents; causes dry mouth, constipation, blurred vision, urinary retention and cognitive slowing.

Alpha-1 (adrenergic) blockade

Prominent in low-potency agents; causes postural (orthostatic) hypotension, dizziness and reflex tachycardia.

3.4 High-potency versus low-potency: the comparison

The table sets the two poles side by side. Read every row as the same trade being paid in a different currency: the high-potency end pays in movement disorder and prolactin, the low-potency end pays in sedation, anticholinergic burden, weight and blood pressure. Mid-potency agents (for example trifluoperazine and perphenazine) sit between the poles.

FEATURE	HIGH-POTENCY (HALOPERIDOL, TRIFLUOPERAZINE, FLUPHENAZINE, PIMOZIDE)	LOW-POTENCY (CHLORPROMAZINE, THIORIDAZINE)
Milligram dose for D2 blockade	**Low (few mg)**	High (hundreds of mg)
Extrapyramidal symptoms	**More (prominent)**	Fewer
Hyperprolactinaemia	**More**	Less
Sedation (H1)	Less	**More**
Anticholinergic effects (M1)	Less	**More**
Postural hypotension (alpha-1)	Less	**More**
Weight gain and cardiometabolic load	Less	**More**
Seizure threshold lowering	Less	**More**

The potency axis as an adverse-effect trade-off: extrapyramidal-and-prolactin burden at the high-potency end, sedation-and-metabolic burden at the low-potency end.

RULE **Potency predicts the adverse-effect trade-off.** Extrapyramidal symptoms and prolactin cluster at the high-potency end; sedation, anticholinergic effects, postural hypotension and metabolic load cluster at the low-potency end.

3.5 Indications and the practical place today

First-generation antipsychotics are effective against the positive symptoms of psychosis (delusions, hallucinations, thought disorder) and are used for acute and maintenance treatment of schizophrenia, acute psychotic agitation, mania (as adjuncts) and, for individual agents, for tics (pimozide, haloperidol), nausea and intractable hiccups (chlorpromazine). Their enduring place rests on being cheap and widely available, which matters greatly in resource-limited and public-sector settings; against that stands a higher burden of extrapyramidal symptoms and, over time, tardive dyskinesia compared with the second-generation drugs (Kaplan & Sadock 2024). A key limitation is that they do relatively little for negative and cognitive symptoms, and at high doses the high-potency agents can actually worsen negative and cognitive symptoms through excessive mesocortical D2 blockade (the neuroleptic-induced deficit syndrome) (Stahl 2021). They are not without a place in modern practice, but that place is defined by cost, availability and positive-symptom control, not by breadth of benefit.

INDIA

First-generation antipsychotics remain workhorse drugs in Indian public and private practice on grounds of cost and availability. Verified Indian trade names include haloperidol as Serenace and chlorpromazine, which is marketed generically and under multiple local names; both are on the essential-medicines footing that keeps them in wide use. Where an oral atypical is unaffordable, a low-dose high-potency first-generation agent is a legitimate and guideline-consistent choice for positive symptoms.

3.6 High-potency agents in detail

Haloperidol. The prototype high-potency butyrophenone, near-pure D2 antagonist, still one of the most-used conventional antipsychotics worldwide and effective at low doses; the recurring clinical error is dosing it too high, which buys extrapyramidal symptoms without extra antipsychotic benefit and may worsen negative symptoms (Stahl 2021). **Trifluoperazine and fluphenazine** are high-potency phenothiazines with a similar extrapyramidal-and-prolactin profile; fluphenazine is also available as a long-acting depot. **Pimozide** is a diphenylbutylpiperidine reserved as a second-line agent, notable for dose-dependent QTc prolongation and its use in Tourette's syndrome (Stahl 2021).

GOOD TO REMEMBER

- **Haloperidol:** high-potency butyrophenone, predominant D2 blockade; oral **1 to 40 mg/day** (Stahl), typically effective low, around 2 to 15 mg/day; watch for extrapyramidal symptoms and do not over-dose, as it is frequently dosed too high.
- **Trifluoperazine:** high-potency phenothiazine, D2 blockade; oral psychosis **15 to 20 mg/day** (Stahl); watch for extrapyramidal symptoms.
- **Fluphenazine:** high-potency phenothiazine, D2 blockade; oral **1 to 20 mg/day** maintenance, decanoate depot **12.5 to 100 mg** every 2 weeks (Stahl); watch for extrapyramidal symptoms and raised prolactin.
- **Pimozide:** high-potency diphenylbutylpiperidine, D2 blockade; oral usually **less than 10 mg/day** (maximum 10 mg/day, Stahl); monitor QTc, as prolongation is dose-dependent.

3.7 Low-potency agents in detail

Chlorpromazine is the original low-potency phenothiazine (D2 plus substantial H1, M1 and alpha-1 blockade), broad-spectrum but carrying sedation, anticholinergic load, postural hypotension, photosensitivity and, cumulatively, tardive dyskinesia risk (Stahl 2021). **Thioridazine** is a low-potency phenothiazine now largely restricted because of dose-dependent QTc prolongation with risk of ventricular arrhythmia and sudden death, and pigmentary retinopathy at high doses; it is effectively a last-line agent (Stahl 2021).

GOOD TO REMEMBER

- **Chlorpromazine:** low-potency phenothiazine, D2 plus H1, M1 and alpha-1 blockade; oral **200 to 800 mg/day** (Stahl); watch for sedation, postural hypotension and anticholinergic effects, and counsel on photosensitivity.
- **Thioridazine:** low-potency phenothiazine, D2 plus anticholinergic and alpha-1 blockade; oral **200 to 800 mg/day** in divided doses (Stahl); monitor QTc (dose-dependent prolongation, arrhythmia and sudden-death risk) and beware pigmentary retinopathy at high doses.

3.8 The depot (long-acting injectable) question

Several first-generation agents exist as long-acting depot injections (haloperidol decanoate, fluphenazine decanoate, flupentixol and zuclopenthixol decanoate), given every 2 to 4 weeks to secure adherence in maintenance treatment. A depot changes the route and the pharmacokinetics; it does not change the pharmacology. A first-generation depot is still a predominant D2 blocker, so it treats positive symptoms and covenants the same extrapyramidal-and-prolactin trade-off as its oral form. It does not acquire any new action against negative or cognitive symptoms by being injected. Expecting a depot to lift negative symptoms is a category error about what the molecule does.

TRAP **Expecting a first-generation depot to treat negative symptoms.** A depot only changes the route and dosing interval; the drug is still a D2 blocker that treats positive symptoms and, at high doses, can worsen negative symptoms, not relieve them.

3.9 Chlorpromazine equivalents and dosing across the class

Because the agents differ so widely in milligram potency, doses are compared using the chlorpromazine equivalent, the dose of a drug judged equipotent to a defined amount of chlorpromazine. This lets a clinician convert across agents and gauge total antipsychotic load, and it underpins the maintenance-dose evidence: for first-generation drugs, continuous low-dose maintenance (roughly 50 to 100 mg/day chlorpromazine equivalents) is less effective at preventing relapse than standard dosing (roughly 200 to 500 mg/day chlorpromazine equivalents) (Tasman 2015, Barbui et al. 1996). The practical lesson is to dose adequately for maintenance but no higher than needed, since above the therapeutic window the high-potency agents add extrapyramidal symptoms without added antipsychotic benefit.

1 to 40	200 to 800	200 to 500
HALOPERIDOL ORAL MG/DAY (STAHL)	CHLORPROMAZINE ORAL MG/DAY (STAHL)	STANDARD MAINTENANCE, CPZ-EQUIV MG/DAY

HOLD THIS

For a first-generation antipsychotic, potency predicts the poison: high-potency agents (haloperidol) pay in extrapyramidal symptoms and prolactin, low-potency agents (chlorpromazine) pay in sedation, anticholinergic effects, hypotension and metabolic load, and no first-generation drug, oral or depot, treats negative symptoms.

4 · Atypical, partial-agonist and newer agents, and choosing the antipsychotic

Why this matters. The **atypical antipsychotic** agents, the **second-generation** drugs, are what a psychiatrist reaches for first in most schizophrenia today, and the examiner tests two ideas above all: that they buy a lower extrapyramidal burden at the price of a metabolic one, and that choosing between them is an **adverse-effect** decision, not a search for a large efficacy gap. This topic teaches the atypical mechanism, the individual agents, the dopamine partial agonists, the newer and competitor-delta drugs, and the choice logic. It does not re-teach the illness (phenomenology, aetiology, criteria and course belong to the Schizophrenia: aetiology, phenomenology, classification and course notes), nor does it re-derive the receptor pharmacology and dopamine pathways (owned by the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and only applied here); clozapine and treatment resistance, and the adverse effects, are handled in their own topics.

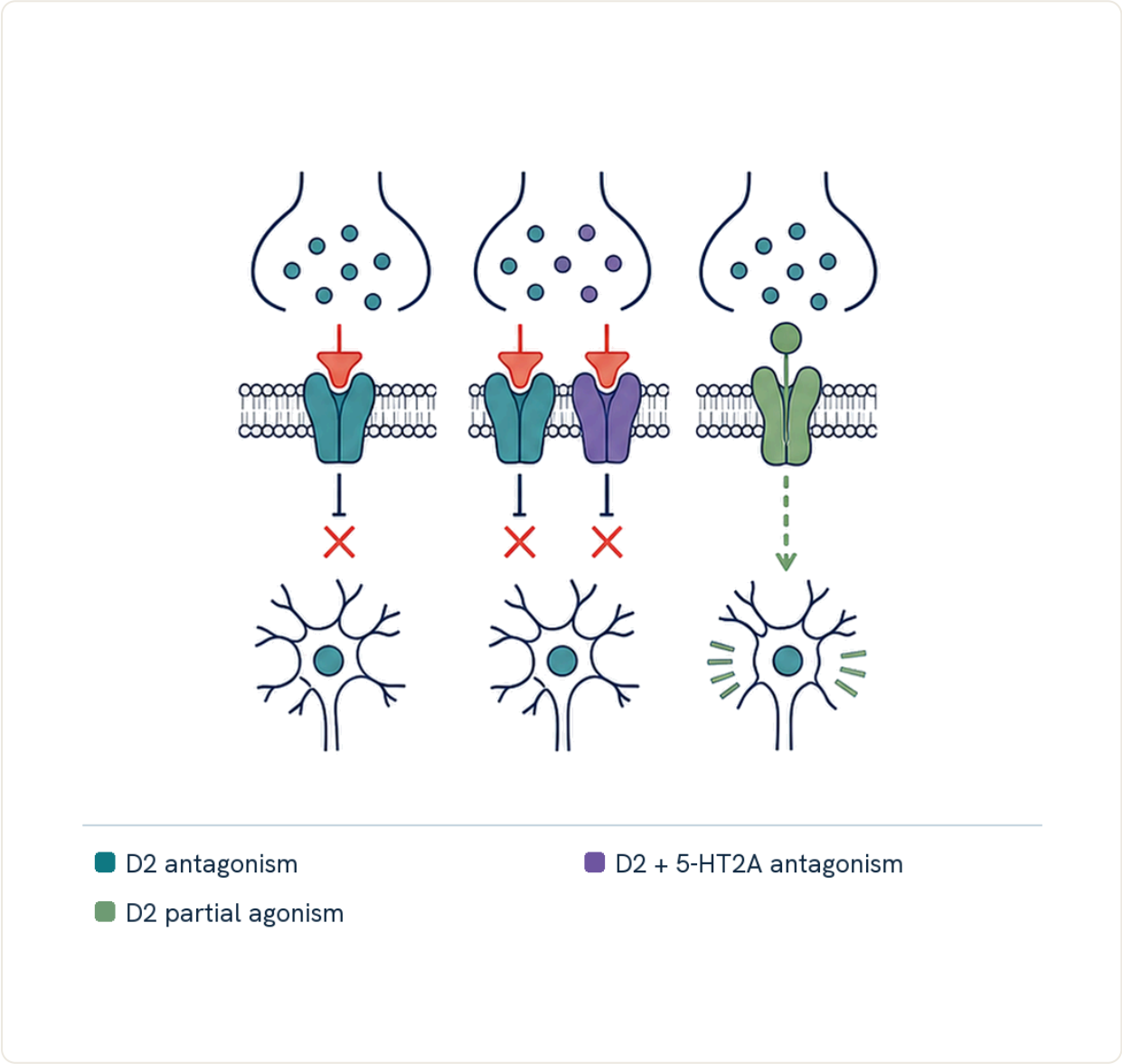


Fig 9.4 Three antipsychotic receptor strategies: dopamine D2 antagonism, combined D2 and 5-HT2A antagonism, and D2 partial agonism that stabilises signalling across different dopamine states.

The governing sentence: apart from clozapine, the landmark effectiveness trials found the second-generation drugs are not dramatically more effective than the first-generation ones, so the drug you pick is decided by which adverse-effect profile fits the patient in front of you (Lieberman 2005, Jones 2006). Second generation does not mean better across the board; it means a different and, for movement disorder, usually gentler trade, and the terms second-generation and second generation are used interchangeably in the literature.

4.1 What "atypical" means: the 5-HT2A/D2 balance

An atypical antipsychotic is defined, at least for the classic agents, by combining dopamine D2 antagonism with potent serotonin 5-HT2A antagonism, the **5-HT2A**/D2 balance (Stahl 2021, Kaplan & Sadock 2024). The "pines" (clozapine, olanzapine, quetiapine, asenapine, zotepine) and the "dones" (risperidone, paliperidone, ziprasidone, lurasidone) bind more potently to the **5-ht2a** receptor than to D2. The functional consequence, worked out mechanistically in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes, is that 5-HT2A blockade disinhibits dopamine release in the nigrostriatal and tuberoinfundibular pathways, which is why these drugs, at therapeutic doses, cause fewer extrapyramidal symptoms and less hyperprolactinaemia than a comparably effective first-generation agent, while retaining mesolimbic D2 blockade for the antipsychotic effect.

Two cautions the examiner likes. First, "atypical" is a loose class: the definition holds well for the 5-HT2A/D2 agents but breaks down for the newer entrants (a dopamine partial agonist, a pure muscarinic agonist), which achieve low extrapyramidal liability by entirely different routes. Second, low extrapyramidal load is not free: most atypicals, and olanzapine and clozapine above all, carry a substantial metabolic burden (weight gain, dyslipidaemia, impaired glucose tolerance).

RULE **The classic atypical trades extrapyramidal burden for metabolic burden.** Potent 5-HT2A antagonism on top of D2 antagonism lowers extrapyramidal and prolactin liability; the price, unevenly across agents, is weight, lipids and glucose.

4.2 The advantages, honestly weighed

Against the first-generation drugs, the atypicals offer three claimed advantages, each real but bounded. **Lower extrapyramidal symptoms and tardive dyskinesia** at therapeutic dose is the most robust, and the reason many guidelines prefer them, though it narrows if a first-generation agent is dosed low (in CATIE, mid-potency perphenazine performed comparably) (Lieberman 2005). **Some negative-symptom benefit** is modest and agent-specific (amisulpride at low dose, cariprazine), not a class property. **Some mood benefit** is genuine for several agents licensed in bipolar disorder (olanzapine, quetiapine, aripiprazole, cariprazine, lurasidone). The honest summary: the advantage is chiefly tolerability of movement, not a leap in antipsychotic efficacy.

4.3 Risperidone

Risperidone is a "done", a potent D2 and 5-HT2A antagonist, effective and widely used and, in India, cheap. Its two signature caveats are both dose-dependent. Extrapyramidal symptoms and, distinctively among atypicals, prolactin elevation rise steeply with dose, so that above roughly 6 mg/day orally it behaves increasingly like a high-potency first-generation drug and the risk of

drug-induced parkinsonism climbs (Stahl 2021, Maudsley 2021). It is metabolically intermediate. Paliperidone, its active metabolite, is treated below.

GOOD TO REMEMBER

- **Risperidone:** atypical (D2 and 5-HT2A antagonist); oral **2 to 8 mg/day** for acute psychosis (Stahl), EMA maximum **16 mg/day** (Maudsley); dose-dependent extrapyramidal symptoms and hyperprolactinaemia, watch prolactin and movement above 6 mg/day. Indian brand Sizodon (also Risdone).

4.4 Olanzapine

Olanzapine is a "pine", a broad multi-receptor antagonist (D2, 5-HT2A, plus H1, M1 and others), highly effective and, after clozapine, one of the drugs to trial before clozapine (Maudsley 2021). Its defining problem is metabolic: alongside clozapine it has the worst metabolic profile of the class, with prominent weight gain, dyslipidaemia and impaired glucose tolerance, so it demands the fullest metabolic monitoring. Its low-EPS, sedating, appetite-driving profile is exactly the trade the CATIE data crystallised: longest time to discontinuation, bought with the heaviest metabolic cost (Lieberman 2005).

GOOD TO REMEMBER

- **Olanzapine:** atypical multi-receptor antagonist (D2, 5-HT2A, H1, M1); oral **10 to 20 mg/day** (Stahl); worst metabolic profile of the class with clozapine, so monitor weight, lipids and glucose closely. Indian brand Oleanz.

4.5 Quetiapine

Quetiapine is a "pine" with relatively weak, transient D2 occupancy and strong H1 antagonism. The clinical signature follows: it is markedly **sedating** (H1) and has the **lowest extrapyramidal liability** of the group, effectively no more than placebo, which makes it the atypical of choice where movement disorder must be avoided (for example in Parkinson's disease psychosis) (Stahl 2021). The costs are sedation, postural hypotension and weight gain; efficacy for schizophrenia sits at the upper end of its range.

GOOD TO REMEMBER

- **Quetiapine:** atypical (D2 and 5-HT2A antagonist, strong H1); schizophrenia **400 to 800 mg/day** in 2 doses (Stahl), EMA maximum **750 mg/day** (800 mg/day modified-release, Maudsley); very sedating, very low EPS, watch sedation and postural drop. Indian brand Qutipin.

4.6 Amisulpride, ziprasidone and paliperidone

Amisulpride is a substituted benzamide that is a fairly selective D2 and D3 antagonist (not a 5-HT2A blocker), with a distinctive dose split: low doses preferentially block presynaptic autoreceptors and help negative symptoms, higher doses block postsynaptic receptors for positive symptoms. It raises prolactin and prolongs QTc dose-dependently, and accumulates in renal impairment (Stahl 2021). **Ziprasidone** is a "done" that is metabolically favourable (little weight gain) but must be **taken with food**, which roughly doubles its bioavailability, and it prolongs QTc; it is often underdosed in practice (Stahl 2021). **Paliperidone** is the active

metabolite of risperidone (9-hydroxyrisperidone), largely renally cleared, prolactin-raising, and available as long-acting palmitate injections.

GOOD TO REMEMBER

- **Amisulpride:** selective D2/D3 antagonist (benzamide); schizophrenia **400 to 800 mg/day**, negative symptoms only **50 to 300 mg/day** (Stahl), EMA maximum 1200 mg/day; dose-dependent QTc and prolactin, accumulates in renal impairment. Indian brand Amazeo (also Soltus).
- **Ziprasidone:** atypical (D2 and 5-HT2A antagonist); schizophrenia **40 to 200 mg/day** in divided doses, best above 120 mg/day (Stahl); metabolically light but must be taken with food (doubles absorption) and prolongs QTc.
- **Paliperidone:** active metabolite of risperidone; oral **3 to 12 mg/day** (usually 6 mg, Stahl), EMA maximum 12 mg/day; raises prolactin, largely renally cleared; palmitate depot available. Indian brand Paliris.

4.7 The partial agonists: aripiprazole, cariprazine, brexpiprazole

The dopamine **partial agonist** class works differently from every drug above. Aripiprazole is a **dopamine partial** agonist, a dopamine D2 **partial agonist** (with 5-HT1A partial agonism and 5-HT2A antagonism). Its **partial agonism** means it stabilises dopamine transmission: where synaptic dopamine is high (mesolimbic, positive symptoms) it acts as a functional antagonist and dampens it, and where dopamine is low it provides modest tone, which gives it a distinct profile, low metabolic burden, low prolactin (it can even lower prolactin), but a propensity to **akathisia** and activation (Stahl 2021). **Cariprazine** is a D3-preferring D2/D3 partial agonist with 5-HT1A partial agonism, marketed with a claim for negative symptoms; it has a long half-life and can cause akathisia. **Brexpiprazole** is a D2 partial agonist closely related to aripiprazole but with a somewhat less activating profile and lower reported akathisia.

RULE **The partial agonists stabilise rather than block dopamine.** Aripiprazole, cariprazine and brexpiprazole buy a low-metabolic, low-prolactin profile at the price of akathisia and activation, not sedation and weight.

GOOD TO REMEMBER

- **Aripiprazole:** dopamine D2 partial agonist (plus 5-HT1A partial agonist, 5-HT2A antagonist); schizophrenia and mania **15 to 30 mg/day** (Stahl), EMA maximum 30 mg/day; low metabolic burden, low or reduced prolactin, watch for akathisia and activation. Indian brand Arip (also Arip MT).
- **Cariprazine:** D3-preferring D2/D3 partial agonist (5-HT1A partial agonist); schizophrenia **1.5 to 6 mg/day** once daily (Stahl); long half-life, negative-symptom claim, watch for akathisia.
- **Brexpiprazole:** dopamine D2 partial agonist (5-HT1A partial agonist, 5-HT2A antagonist); schizophrenia typically **2 to 4 mg/day** (maximum 4 mg/day, Stahl); low-metabolic profile, less activating than aripiprazole.

4.8 The newer agents: asenapine, lurasidone, zotepine

Asenapine is a "pine" atypical distinguished by its route: it is a **sublingual** agent (oral tablets are not absorbed due to very low oral bioavailability), so it must be placed under the tongue with no eating or drinking for 10 minutes after; it causes oral hypoaesthesia and dysgeusia (Stahl 2021).

Lurasidone is a "done" whose selling points are a genuine **metabolic advantage** (weight-, lipid- and glucose-neutral, and one of the few atypicals without a QTc warning) and a pharmacokinetic rule: it must be taken **with food** (a meal of at least 350 calories), because absorption falls by up to 50% on an empty stomach; its common adverse effects are akathisia and somnolence (Stahl 2021). Zotepine is a "pine" atypical of chiefly historical and exam interest, notable for a dose-dependent **seizure risk** (an established dose-related pro-convulsive effect), which limits its use (Maudsley 2021).

GOOD TO REMEMBER

- **Asenapine:** atypical (D2 and 5-HT2A antagonist), sublingual only; **10 to 20 mg/day** in 2 divided doses (Stahl), EMA maximum 20 mg/day sublingual; no food or drink for 10 minutes after dosing, causes oral hypoaesthesia.
- **Lurasidone:** atypical (D2, 5-HT2A, 5-HT7 antagonist, 5-HT1A partial agonist); schizophrenia **40 to 160 mg/day** (Stahl), EMA maximum 148 mg base/day; metabolically friendly with no QTc warning, must be taken with food (350-calorie meal) or absorption drops by half; watch for akathisia.
- **Zotepine:** atypical "pine" (D2 and 5-HT2A antagonist); dose-dependent, established pro-convulsive effect, so seizure risk is the caveat to hold (Maudsley); dose figures not confirmed here, see gaps.

4.9 Xanomeline-trospium (KarXT): a non-D2 route

Xanomeline combined with trospium, marketed as **KarXT** (the combination brand karxt), is the drug that fulfils the forward reference from the illness notes: an antipsychotic that does **not** act by D2 blockade at all. **Xanomeline** is an M1/M4 muscarinic receptor agonist; by stimulating M4 (and M1) receptors it indirectly reduces dopamine release in relevant circuits and increases prefrontal dopamine, producing an antipsychotic effect with essentially no extrapyramidal or prolactin liability because it never blocks the dopamine receptor (Stahl 2021, Maudsley 2021). Because xanomeline alone causes cholinergic side effects (nausea, vomiting, sweating, salivation), it is co-formulated with **trospium**, a peripherally-restricted anticholinergic that does not cross the blood-brain barrier and so blocks the peripheral muscarinic effects while leaving the central antipsychotic action intact (Stahl 2021). It was studied in the EMERGENT phase-3 programme (Kaul 2024). Licensing status is evolving and jurisdiction-dependent (a US approval for schizophrenia was granted for KarXT; not established for India here), so verify the current licence before quoting it, and see gaps.

TRAP **Treating xanomeline-trospium as a D2 blocker.** It is a muscarinic (M1/M4) agonist that indirectly modulates dopamine; trospium is only there to block peripheral cholinergic side effects. There is no D2 antagonism, which is exactly why it has no extrapyramidal or prolactin signature.

GOOD TO REMEMBER

- **Xanomeline-trospium (KarXT):** xanomeline is an M1/M4 muscarinic agonist (not a D2 blocker), co-formulated with trospium, a peripherally-acting anticholinergic that curbs cholinergic side effects; no extrapyramidal or prolactin liability; dose and India licence not confirmed here, see gaps.

4.10 Step 5a: choosing the antipsychotic

With clozapine reserved for treatment resistance (its own topic), the arc's Step 5a is to **choose** the right antipsychotic by weighing **efficacy** against the adverse-effect **trade-off** for the individual patient. The evidence base for this is the pair of landmark effectiveness trials: CATIE (**catie**, Clinical Antipsychotic Trials of Intervention Effectiveness, USA), where olanzapine had the longest time to all-cause discontinuation but at a heavy metabolic cost and the first-generation comparator perphenazine performed broadly comparably to the other second-generation drugs (Lieberman 2005); and CUtLASS (**cutlass**, Cost Utility of the Latest Antipsychotic Drugs in Schizophrenia Study, UK), which found no significant advantage of the second-generation drugs over the first-generation ones in quality of life, symptoms or satisfaction (Jones 2006). The lesson both trials teach is the same: apart from clozapine, no antipsychotic is dramatically more effective than another, so the choice is driven by the adverse-effect fit.

Practically, you read the patient's vulnerabilities and pick the agent whose adverse-effect profile least collides with them, avoiding the agent that would hit hardest. The table below is the working tool.

PATIENT FACTOR	PREFERRED AGENT(S)	WHAT TO AVOID
Metabolic risk (obese, diabetic, dyslipidaemic, young at first episode)	**Aripiprazole, lurasidone, ziprasidone, brexpiprazole**	Olanzapine, clozapine (and quetiapine)
Extrapyramidal vulnerability (elderly, Parkinson's, prior severe EPS)	**Quetiapine, clozapine, aripiprazole**	High-dose risperidone, first-generation high-potency agents
Prolactin-sensitive (young woman, sexual or menstrual concern, fertility)	**Aripiprazole (prolactin-sparing/lowering)**	Risperidone, paliperidone, amisulpride, first-generation high-potency
Prominent insomnia, agitation, need for sedation	**Quetiapine, olanzapine**	Aripiprazole, cariprazine (activating, akathisia)
Cardiac risk or QTc concern	**Aripiprazole, lurasidone (no QTc warning)**	Ziprasidone, amisulpride, high-dose quetiapine, thioridazine, pimozide
Prominent negative symptoms	**Amisulpride (low dose), cariprazine**	Relying on high-dose first-generation agents
Adherence problem	**Long-acting injectable (paliperidone palmitate, aripiprazole, risperidone)**	Sole reliance on unsupervised oral dosing
Seizure history or low threshold	**Higher-threshold agents (e.g. aripiprazole, risperidone)**	Zotepine, clozapine, chlorpromazine (dose-dependent seizure risk)

Step 5a in practice: match the agent to the patient's dominant vulnerability, because apart from clozapine the choice is an adverse-effect decision, not an efficacy one.

2	2 to 8	10 to 20
LANDMARK TRIALS DRIVING THE CHOICE (CATIE, CUTLASS)	RISPERIDONE ORAL MG/DAY (STAHL)	OLANZAPINE ORAL MG/DAY (STAHL)

INDIA

Olanzapine is available as a long-acting injectable, marketed in India as Tolaz (olanzapine pamoate); it carries the drug-specific risk of post-injection syndrome (an inadvertent partial intravascular delivery causing sedation and delirium), so it requires a post-dose observation period. The Indian Psychiatric Society (IPS) schizophrenia guideline supports second-generation agents as reasonable first-line choices while recognising cost and availability, and verified Indian trade names for common atypicals include risperidone as Sizodon (also Risdone), olanzapine as Oleanz, quetiapine as Qutipin, aripiprazole as Arip (also Arip MT), amisulpride as Amazeo (also Soltus) and paliperidone as Paliris; where affordability dominates, a well-chosen atypical or a low-dose high-potency first-generation agent are both defensible.

MNEMONIC

MEPS-C

The five axes to weigh when you choose: **M**etabolic, **E**xtrapyramidal, **P**rolactin, **S**edation, **C**ardiac (QTc). Read the patient against each axis and pick the agent that collides least with the dominant one.

HOLD THIS

Apart from clozapine, CATIE and CUtLASS showed no dramatic efficacy gap between antipsychotics, so you choose by matching the adverse-effect profile (metabolic vs EPS vs prolactin vs sedation vs cardiac) to the individual patient.

5 · First-episode management and early intervention

The **first-episode** is the single most consequential moment in the whole treatment algorithm, and the examiner treats it as a management principle in its own right, not a footnote to acute prescribing. Two ideas carry the topic: the first episode is the *best therapeutic window*, because a drug-naive brain responds at lower doses and the treated trajectory of the illness can still be altered; and the **duration of untreated psychosis** is the one prognostic variable the clinician can actually change. Around these two ideas sits a service model, **early intervention**, built specifically to shorten that untreated interval and to deliver low-dose medication, family work and vocational support during the years when the illness is most malleable (New Oxford 2020, Maudsley 2021).



Fig 9.5 The first-episode pathway: prompt assessment and shared choice lead to cautious antipsychotic initiation, family engagement, coordinated early-intervention care and longitudinal relapse prevention.

How to use this page. Fix the first-episode principle (start a single antipsychotic at the lowest effective dose after a full baseline), then the modifiable predictor (**duration of untreated psychosis**), then the service that operationalises both (**early intervention** services, the **eis**). The disorder itself, its prodrome, at-risk mental state, criteria and course, is not re-taught here; it belongs to the Schizophrenia: aetiology, phenomenology, classification and course notes, and this topic cross-references the prodrome and at-risk state to it. The receptor pharmacology and CYP metabolism behind the drugs belong to the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

5.1 Why the first episode is the best window

The malleable moment. The first episode of psychosis is the point at which the illness is most responsive to treatment and most open to having its course changed. A first-episode patient is antipsychotic-naive, so response occurs at doses well below those needed in multi-episode illness, and the accumulated disability, adverse-effect burden and treatment-resistance of chronic illness have not yet set in. The realistic aim of intervening well here is not merely to abort the acute

episode but to protect the longer trajectory: functional recovery, return to study or work, and prevention of the step-wise decline that follows each subsequent relapse (Maudsley 2021, New Oxford 2020). This is why the management of the first episode is examined as a distinct principle and not simply as "acute treatment in a young patient".

RULE **Start low and go slow in the first episode.** These patients are dose-sensitive: begin a single antipsychotic at the lowest effective dose and titrate against response and tolerability, because they respond at lower doses and are more adverse-effect sensitive than multi-episode patients.

5.2 One drug, lowest effective dose, drug-naive sensitivity

Monotherapy at the minimum effective dose. The prescribing rule for a first episode is a single antipsychotic, chosen on adverse-effect profile and patient preference (there is no clear efficacy winner among non-clozapine agents, with only minor individual advantages for olanzapine and amisulpride), started at the lowest effective dose and titrated slowly (Maudsley 2021). The first-episode minimum effective dose is lower than the multi-episode dose for essentially every agent, and holding a few of these numbers lets you defend a starting dose in a viva. Clozapine has no place at first presentation; it belongs to the treatment-resistance branch after two adequate trials fail, developed in the treatment-resistance and clozapine topics.

ANTIPSYCHOTIC	FIRST-EPISODE MINIMUM EFFECTIVE DOSE (MG/DAY)	MULTI-EPISODE DOSE, MG/DAY (CONTRAST)
Haloperidol (FGA)	2	4
Olanzapine (SGA)	5	7.5
Risperidone (SGA)	2	4
Aripiprazole (SGA)	10	10
Amisulpride (SGA)	300	400 (estimate)

First-episode minimum effective doses run below multi-episode doses, the numeric expression of drug-naive dose sensitivity (Maudsley 2021, Table 1.1). Generic names lead; verify local formulations.

Why lower doses matter beyond tolerability. There is a signal that first-episode patients who receive lower doses have better long-term functional outcomes, and the possibility of dopamine-receptor super-sensitivity on withdrawal reinforces using the lowest possible dose in all patients (Maudsley 2021). Very low or sub-therapeutic doses, however, lose prophylactic efficacy, so "lowest" means lowest *effective*, not homeopathic.

5.3 The full baseline before the first dose

Baseline everything, then start. Before the first antipsychotic dose the first-episode patient needs a full physical and metabolic baseline, both to detect an organic or co-occurring cause and to serve as the reference point for all later monitoring (APA 2020). This baseline is done once, at the front door, and cannot be reconstructed later. The relevant panel is the initial-assessment column of the standard monitoring schedule.

Physical and vitals

History and physical examination, pulse and blood pressure, weight, height and body-mass index.

Metabolic

Fasting blood glucose (or HbA1c) and a fasting lipid panel, with metabolic-syndrome criteria assessed, because the antipsychotic will move all of these.

Cardiac

Baseline ECG where a QTc-prolonging agent is planned or cardiac risk factors are present; full-blood-count, renal, liver and thyroid function and prolactin as clinically indicated.

The detail of the ongoing monitoring intervals (weight, glucose and lipids at defined follow-up points) is developed in the metabolic-monitoring topic; the first-episode point is that the pre-treatment reading is captured before the drug is given.

5.4 Duration of untreated psychosis: the modifiable predictor

The one variable you can change. The duration of untreated psychosis is the interval from the onset of frank psychotic symptoms to the start of adequate treatment. It matters because longer **duration of untreated psychosis** is associated with poorer prognosis: slower and less complete symptomatic response, poorer functional recovery and greater accumulation of secondary harms (substance misuse, self-harm and suicide, interpersonal and family breakdown) (Addington 2004, New Oxford 2020). Unlike age at onset, sex or family history, it is potentially *modifiable*, which is precisely why it is the rational target of early detection and the theoretical engine of the whole early-intervention movement.

The rationale for early detection. If a long untreated interval worsens outcome, then shortening it should improve outcome, so early-intervention services are built to reduce the duration of untreated psychosis by lowering the barriers to help-seeking, running assertive outreach, and providing rapid, low-threshold access to assessment and treatment. The prodrome and at-risk mental state that precede the first frank episode, and the transition risk from those states, are owned by the Schizophrenia: aetiology, phenomenology, classification and course notes; here they matter only as the window during which detection can begin before psychosis is fully manifest.

TRAP **Delaying treatment.** A long duration of untreated psychosis worsens outcome, so do not delay effective treatment; watchful waiting past the point of frank psychosis squanders the modifiable predictor and the best window the illness will offer.

5.5 Early intervention services: the specialist team

What an EIS is. Early intervention services (the **eis**) are specialist, multidisciplinary teams that deliver phase-specific care to first-episode and early-psychosis patients for the first years of illness, rather than folding them into a generic community team. The characteristic package combines low-dose antipsychotic medication, structured family work and psychoeducation, and vocational and educational support, delivered through intensive case management with low caseloads, assertive outreach and easy access to staff (New Oxford 2020, Maudsley 2021). The model targets the "critical period" of the early illness, on the logic that intervening intensively while the illness is malleable buys durable gains.

The three deliverables. Hold the EIS as three limbs delivered together during the early years: *low-dose medication* (a single antipsychotic at first-episode doses, per 5.2); *family work* (psychoeducation and reduction of high expressed emotion, which lowers relapse risk); and *vocational and educational support* (getting the young person back into study or work, the outcome that matters most to them). Individual-placement-and-support style supported employment embedded in early-psychosis services has achieved employment or return-to-study outcomes at rates well above generic vocational rehabilitation (Killackey 2008).

5.6 The evidence: better engagement and outcome

Specialist early care beats treatment as usual. Randomised trials show that specialist early-intervention teams outperform standard community care during the intervention period on engagement, relapse, admission and functional outcomes. The Danish OPUS trial randomised first-episode patients to two years of integrated specialist early treatment versus standard treatment and found benefits on psychotic and negative symptoms and service use during the intervention (Bertelsen 2008). The US RAISE Early Treatment Program showed that coordinated specialty care (the American term for the EIS package) improved quality of life and symptom outcomes over usual community care at two-year follow-up (Kane 2016). The important caveat, also examinable, is durability: the two-year OPUS gains largely eroded once patients stepped down to standard care by five-year follow-up, whereas prolonged early intervention (extending the specialist package by one to three years) produced more sustained benefit (Bertelsen 2008, New Oxford 2020). Integrated early care is also broadly cost-effective, because the added treatment cost is offset by fewer inpatient days.

PEARL

The EIS evidence is a "use it or lose it" story. Specialist early intervention reliably beats standard care *while it runs*; the two-year OPUS advantage faded after step-down, and only prolonged early intervention held the gains. In a viva, name OPUS and RAISE, then add the durability caveat, that is the discriminating detail.

5.7 Response timeline, adherence and shared decision-making

The expected response timeline. Set expectations against the algorithm: an adequate antipsychotic trial in the first episode is an adequate dose for an adequate duration, and much apparent non-response is inadequate dose, inadequate duration or covert non-adherence rather than true resistance (Maudsley 2021). Improvement in agitation and sleep can be early; the fuller antipsychotic response accrues over weeks, and positive symptoms respond better and faster than negative and cognitive symptoms. Do not declare failure and switch before an adequate trial has run with adherence confirmed. After remission of a first episode, current consensus is to continue the antipsychotic for one to two years before considering a very gradual, closely monitored dose reduction, because abrupt discontinuation carries a high relapse rate (Maudsley 2021, APA 2020).

26% vs 61%	1 to 2 yr	55% vs 28%
1ST-EPISODE RELAPSE AT 6 TO 12 MO: MAINTAINED VS PLACEBO	CONTINUE ANTIPSYCHOTIC AFTER 1ST-EPISODE REMISSION	ANY WORK OVER 18 MONTHS, SUPPORTED EMPLOYMENT VS STANDARD (EQOLISE)

Adherence support and shared decision-making. The first episode is where the therapeutic alliance is made or lost, and non-adherence is the commonest driver of relapse. Build adherence deliberately: psychoeducation for patient and family, addressing insight and beliefs about medication, minimising adverse-effect burden (a major reason young people stop), and considering a long-acting injectable early rather than only after a relapse, since guaranteed delivery reduces relapse and rehospitalisation. Frame every choice as **shared decision-making**: present the realistic response timeline, the adverse-effect trade-offs and the maintenance rationale, and decide the drug and route with the patient, because a plan the young person owns is the plan they will actually take.

INDIA

Where a long-acting injectable is chosen to secure early adherence, olanzapine pamoate long-acting injection is marketed in India as Tolaz (Torrent); its binding constraint is the post-injection syndrome (a delirium/excessive-sedation reaction), which mandates a supervised post-injection observation period after every dose, a service most Indian outpatient settings cannot deliver, so it is chosen deliberately, not by default. Community delivery of early psychosis care in India sits under the District Mental Health Programme (DMHP), and the Indian Psychiatric Society (IPS) schizophrenia guideline gives the locally calibrated, resource-aware version of this pathway. Generic prescribing dominates and is affordable; verify the local brand before naming one.

HOLD THIS

The first episode is the best window: one antipsychotic at the lowest effective dose after a full baseline, in a drug-naive dose-sensitive patient, delivered by an early-intervention service that shortens the duration of untreated psychosis (the one modifiable predictor) and combines low-dose medication, family work and vocational support, for one to two years of continued treatment and better engagement and outcome while the specialist team runs.

GOOD TO REMEMBER

- **Antipsychotic in the first episode (the backbone):** a single dopamine-D2-blocking agent (class and per-drug mechanics owned by the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes); first-episode minimum effective doses run low (haloperidol 2 mg/day, olanzapine 5 mg/day, risperidone 2 mg/day, aripiprazole 10 mg/day, amisulpride 300 mg/day); the one caveat is drug-naive dose sensitivity, so start low, go slow, and run an adequate trial before calling it a failure.
- **Duration of untreated psychosis (the modifiable predictor):** the interval from onset of frank psychosis to adequate treatment; the discriminator from fixed predictors (age, sex, family history) is that it is changeable; the first management step is early detection and rapid low-threshold access to treatment, because a longer interval worsens outcome.
- **Early intervention service / EIS (the specialist model):** a multidisciplinary team delivering low-dose medication, family work and vocational support for the first years; the discriminator from a generic community team is intensive low-caseload case management and assertive outreach; the first step is early engagement, with the durability caveat that gains fade after step-down unless intervention is prolonged.
- **Baseline panel (before the first dose):** physical examination and vitals, weight/height/BMI, fasting glucose and lipids, ECG where indicated; the discriminator is that it is captured once, pre-treatment, as the reference for later monitoring; the first step is to complete it before giving the antipsychotic (APA 2020).

Figure. The first-episode pathway, early detection reducing the duration of untreated psychosis, then EIS delivery of low-dose medication plus family and vocational work across the critical early years, is flagged for a concept figure.

6 · Maintenance treatment, relapse prevention and discontinuation

Why this matters. Acute treatment gets the patient well; **maintenance treatment** keeps them well, and it is the single most consequential decision in the long-term care of schizophrenia. The examiner tests one idea above all: that continuing an antipsychotic after remission is not optional polish but the core intervention that prevents relapse. Off medication, the natural history of the illness reasserts itself and most patients relapse within one to two years; on medication, that risk falls sharply. Maintenance treatment is therefore **relapse prevention** by another name, and the practical questions the examiner asks are three: at what dose, for how long, and how to stop if stopping at all.

The illness itself, its phenomenology, aetiology, criteria and course, is owned by the Schizophrenia: aetiology, phenomenology, classification and course notes and is not re-taught here; the receptor pharmacology and dopamine-pathway mechanics behind why continued blockade prevents relapse belong to the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and are applied, not re-derived. What this topic teaches is the maintenance decision: the evidence that maintenance prevents relapse (Leucht et al. 2012, Maudsley 2021), the duration of treatment guidelines recommend, the maintenance dose that works, and the safe conduct of discontinuation when it is attempted.

6.1 The rationale: continued treatment markedly reduces relapse

The evidence for maintenance treatment is among the most robust in psychiatry. A landmark systematic review and meta-analysis of antipsychotic drug versus placebo for relapse prevention pooled 65 trials and found that continuing an antipsychotic roughly halved the relapse rate against placebo (Leucht et al. 2012). In that analysis relapse at seven to twelve months occurred in **27 percent** of patients on an antipsychotic versus **64 percent** on placebo, a number needed to treat of **3**, and re-admission fell from 26 percent to 10 percent, a number needed to treat of **5** (Leucht et al. 2012, tabulated in Maudsley 2021). Read against off-medication figures that commonly reach 60 to 80 percent relapse over one to two years, this is a large, reproducible effect. Continued antipsychotic treatment does not cure the illness, but it substantially and reliably reduces the probability that positive symptoms return.

The corollary is that **relapse prevention** is the explicit goal of maintenance, and relapse is costly: each episode risks hospitalisation, carries a suicide and aggression risk, erodes the baseline level of functioning, and the majority of that functional decline occurs in the first decade of illness (Maudsley 2021). Preventing relapse is therefore not merely symptom-suppression, it is protection of the patient's long-term trajectory.

RULE **Maintenance treatment is relapse prevention.** Continuing an antipsychotic after remission roughly halves the relapse rate versus stopping (27 versus 64 percent at 7 to 12 months, NNT 3), and each prevented relapse protects hospitalisation-free functioning.

PEARL

The Leucht et al. 2012 figures (relapse 27 versus 64 percent, NNT 3; re-admission 10 versus 26 percent, NNT 5) are the single most quotable relapse-prevention numbers in the antipsychotic literature. If you memorise one maintenance statistic, memorise the NNT of 3 for relapse.

6.2 The natural history off medication: why relapse is the default

Discontinuation studies make the argument for maintenance from the other direction. When antipsychotics are withdrawn after remission, relapse becomes the expected outcome rather than the exception. A meta-analysis of placebo-controlled first-episode trials found that 26 percent of patients on maintenance antipsychotic relapsed at six to twelve months compared with 61 percent on placebo (Leucht et al. 2012, cited in Maudsley 2021). Longer follow-up is starker: one study of withdrawal after a first episode reported a relapse rate of almost **80 percent** after one year medication-free and **98 percent** after two years (Maudsley 2021), and only a small minority of patients who discontinue remain well one to two years later. A more optimistic 2018 meta-analysis still found relapse rates averaging 35 percent (treated) versus 61 percent (discontinued) at eighteen to twenty-four months (Maudsley 2021). Across every dataset the direction is the same: off medication, the illness returns for most patients within one to two years.

WORKED EXAMPLE

A young man has fully remitted six months after a first episode and asks to stop his olanzapine. The honest framing is not "you are cured" but "the medication is why you are well; stopping in the first year or two carries a relapse risk that studies put anywhere from around 60 percent up to 80 percent, against roughly a quarter if you continue." That risk-benefit framing, not a bare yes or no, is what the guidelines ask you to deliver (Maudsley 2021).

6.3 Duration of treatment: how long guidelines advise continuing

The **duration of treatment** is titrated to the illness stage and prior course. The current consensus, and the figure to hold, is that antipsychotics should be continued for at least **1 to 2 years** after a first episode of schizophrenia before any attempt at withdrawal is considered (Maudsley 2021). After a relapse, and after each subsequent episode, a longer duration is advised because the relapse risk on withdrawal is higher and the functional cost of a further episode is greater. For patients with a history of serious aggression or serious suicide attempts, and those with residual psychotic symptoms, guidelines advise considering **life-long (indefinite) treatment** (Maudsley 2021). The New Oxford Textbook and APA positions are concordant: duration scales with the number of episodes and the severity and dangerousness of the illness.

The reason duration is not simply "forever for everyone" is the trade-off against long-term adverse effects. Continued antipsychotic exposure carries cumulative risks, tardive dyskinesia, metabolic burden and weight gain, hyperprolactinaemia, that must be weighed against the relapse risk of stopping. The individual adverse-effect syndromes are taught in the adverse-effect topics; here the point is that the duration decision is an explicit risk-benefit calculation, revisited over time, not a fixed rule.

CLINICAL SITUATION	GUIDELINE DURATION OF TREATMENT
After a first episode, fully remitted	**At least 1 to 2 years before considering withdrawal**
After a relapse / multi-episode illness	Longer maintenance (several years, individualised)
Severe illness, residual symptoms	Longer, often indefinite
History of serious aggression or serious suicide attempts	**Consider life-long (indefinite) treatment**

Duration of treatment scales with episode number and the danger the illness poses; withdrawal is only considered after the minimum first-episode period of 1 to 2 years (Maudsley 2021).

RULE **Continue at least 1 to 2 years after a first episode, longer after relapses.** Indefinite treatment is advised where the illness is severe, symptoms are residual, or there is a history of serious aggression or serious suicide attempts.

6.4 The maintenance dose: the lowest effective dose that prevents relapse

The governing principle of the **maintenance dose** is the lowest dose that reliably prevents relapse, no lower. The evidence sets a floor. In a meta-analysis of randomised trials, continuous low-dose treatment with first-generation drugs (defined as 50 to 100 mg/day chlorpromazine

equivalents) was less effective than standard dosage (200 to 500 mg/day chlorpromazine equivalents) at preventing relapse (Barbui et al. 1996, in Tasman 2015). Older dose-response work found that lowering the acute dose by about 80 percent may be relatively safe in the maintenance phase, but that relapse rates become excessively high when the dose is reduced further (Kane et al. 1983, Marder et al. 1987, in Tasman 2015). Guideline-level dosing for first-generation maintenance is commonly cited as **300 to 600 mg/day** chlorpromazine equivalents (Buchanan et al. 2010 PORT, in Tasman 2015), with no good evidence that doses above 600 mg/day chlorpromazine equivalents add benefit. For the newer drugs there are no data to support routinely using lower-than-standard doses as prophylaxis; the dose that was acutely effective is generally continued, the one supportable exception being very careful dose reduction after a first episode (Maudsley 2021).

The practical rule that emerges is directional: dose adequately for maintenance but no higher than needed. High maintenance doses buy adverse effects, extrapyramidal symptoms and metabolic load, without added antipsychotic benefit once the efficacy threshold is passed, while **very low doses raise relapse risk**. Where dose reduction is undertaken, an international consensus recommended a gradual reduction of about 20 percent every six months until a minimum maintenance dose is reached (Kissling 1991, in Tasman 2015).

27 vs 64	3	10 vs 26
RELAPSE % DRUG VS PLACEBO, 7 TO 12 MO (LEUCHT 2012)	NNT FOR RELAPSE PREVENTION (LEUCHT 2012)	RE-ADMISSION % DRUG VS PLACEBO (LEUCHT 2012)

TRAP **Pushing the maintenance dose too low to spare side effects.** Very-low-dose maintenance (roughly 50 to 100 mg/day chlorpromazine equivalents for the older drugs) raises relapse; the target is the lowest dose that still prevents relapse, not the lowest tolerated dose.

6.5 Intermittent and targeted dosing: why they are not recommended

An intuitively attractive strategy is to stop the antipsychotic once the patient is well and restart it only when prodromal symptoms of relapse appear, so-called intermittent dosing or **targeted** (prodrome-based) dosing, sparing the patient continuous exposure. The evidence is clear and negative. Targeted or intermittent pharmacotherapy is associated with increased risks of symptom exacerbation, relapse and rehospitalisation, and guideline reviews conclude that intermittent strategies should be avoided (Hasan et al. 2013, in Tasman 2015). The Maudsley states the same point directly: targeted relapse treatment is much less effective than continuous prophylaxis (Maudsley 2021). The strategy fails because the prodrome is an unreliable early-warning system; by the time symptoms are detectable, relapse is often already under way, and reinstating the drug does not fully reverse it. Continuous maintenance at the lowest effective dose, not intermittent treatment, is the recommended approach.

TRAP **Intermittent or targeted (prodrome-based) dosing to spare exposure.** It raises relapse, exacerbation and rehospitalisation and is not recommended; continuous maintenance at the lowest effective dose is the standard of care.

6.6 Discontinuation: taper slowly and monitor for early relapse

When **discontinuation** is agreed after a full risk-benefit discussion, how it is done matters as much as whether it is done. Withdrawal of antipsychotic drugs after long-term treatment should be gradual and closely monitored (Maudsley 2021). Abrupt discontinuation carries a distinctly higher relapse risk: the relapse rate in the first six months after abrupt withdrawal is roughly **double** that seen after gradual withdrawal, with gradual defined as a slow taper over at least **3 weeks** for oral antipsychotics (Maudsley 2021). Abrupt cessation of oral treatment may also provoke discontinuation symptoms such as headache, nausea and insomnia. Part of the excess relapse on abrupt withdrawal is thought to reflect a dopamine supersensitivity rebound rather than pure re-emergence of the underlying illness, which is a further argument for tapering slowly (Maudsley 2021).

Throughout discontinuation the patient, carers and key workers must be educated in the early signs of relapse (sleep disturbance, return of suspiciousness, social withdrawal, subtle thought changes) and how to access help quickly, so that treatment can be reinstated at the first sign of deterioration. The factors to weigh before stopping include how long the patient has been symptom-free, the severity of adverse effects driving the wish to stop, the previous pattern and dangerousness of illness, the outcome of any prior dose-reduction attempts, current social stability and the social cost of relapse (Maudsley 2021). Where the concern is adherence rather than the decision to treat, a long-acting injectable secures guaranteed drug delivery and is associated with a reduced risk of relapse and rehospitalisation, discussed in the depot topic on long-acting injectable antipsychotics.

RULE **If stopping, taper slowly and monitor for early relapse.** Abrupt withdrawal roughly doubles the six-month relapse rate versus a gradual taper (at least 3 weeks for an oral antipsychotic); educate the patient and carers on early relapse signs before you start.

INDIA

Where medication adherence is the limiting factor, long-acting injectables that support maintenance in Indian practice include haloperidol decanoate, fluphenazine decanoate and the second-generation injectables; among the latter is the olanzapine long-acting injectable marketed in India as Tolaz, which carries the specific caveat of post-injection delirium/sedation syndrome and mandates a post-dose observation period. Detailed handling of the injectables sits in the depot topic on long-acting injectable antipsychotics; the maintenance point is that a depot converts a maintenance-dose decision into a guaranteed-delivery one and lowers relapse risk in poorly adherent patients (Maudsley 2021).

6.7 Non-adherence: the commonest driver of avoidable relapse

Non-adherence undermines maintenance more than any pharmacological subtlety. Among people with schizophrenia, non-adherence is high and rises steeply: up to 25 percent are partially or non-adherent by just ten days after discharge, rising to about 50 percent at one year and 75 percent at two years (Maudsley 2021). Non-adherence not only increases the risk of relapse, it may increase the severity of relapse and the duration of hospitalisation, and is associated with a

roughly four-fold increase in suicide attempts (Maudsley 2021). This is why a maintenance plan that looks adequate on paper can fail in practice, and why identifying covert non-adherence, and offering a long-acting injectable where appropriate, is part of relapse prevention rather than separate from it. The depot topic on long-acting injectable antipsychotics develops the adherence solution.

GOOD TO REMEMBER

- **Maintenance treatment (the intervention):** continued antipsychotic after remission; roughly halves relapse (27 versus 64 percent at 7 to 12 months, NNT 3; re-admission 10 versus 26 percent, NNT 5, Leucht et al. 2012); the one thing to hold is that maintenance equals relapse prevention.
- **Duration of treatment:** at least **1 to 2 years** after a first episode, longer after relapses, indefinite if severe, residual symptoms, or serious aggression or suicide-attempt history; the caveat is the trade-off against cumulative long-term adverse effects (Maudsley 2021).
- **Maintenance dose:** the lowest effective dose that prevents relapse (first-generation guideline dosing about **300 to 600 mg/day** chlorpromazine equivalents, Buchanan et al. 2010); the caveat is that very-low-dose maintenance raises relapse and high doses add only side effects.
- **Intermittent / targeted dosing:** stopping and restarting on prodrome; the discriminator is that it raises relapse, exacerbation and rehospitalisation; the first step is not to use it, prefer continuous maintenance (Hasan et al. 2013).
- **Discontinuation:** gradual, monitored withdrawal; the discriminator is that abrupt stopping roughly doubles the six-month relapse rate; the first step is a slow taper (at least 3 weeks oral) with patient and carer education on early relapse signs (Maudsley 2021).
- **Non-adherence:** commonest cause of avoidable relapse; the discriminator is the steep rise (25 percent by 10 days, 50 percent at 1 year, 75 percent at 2 years); the first step is to detect it and offer a long-acting injectable (Maudsley 2021).

HOLD THIS

Maintenance treatment is relapse prevention: continue at least 1 to 2 years after a first episode (longer, up to indefinitely, after relapses or severe illness) at the lowest dose that still prevents relapse, never use intermittent or targeted dosing, and if you ever stop, taper slowly over weeks with monitoring for early relapse because abrupt withdrawal roughly doubles the relapse rate.

7 · Depot and long-acting injectable antipsychotics

A **depot** or long-acting injectable antipsychotic delivers a slow-release intramuscular formulation every few weeks, so the patient does not have to take a tablet every day. The old image of the depot as a punishment for the non-adherent is wrong: an **lai** gives assured medication delivery, steadier plasma levels and fewer relapses, and it is worth offering early to any patient for whom continuous cover matters, not only after adherence has failed (Maudsley 2021).

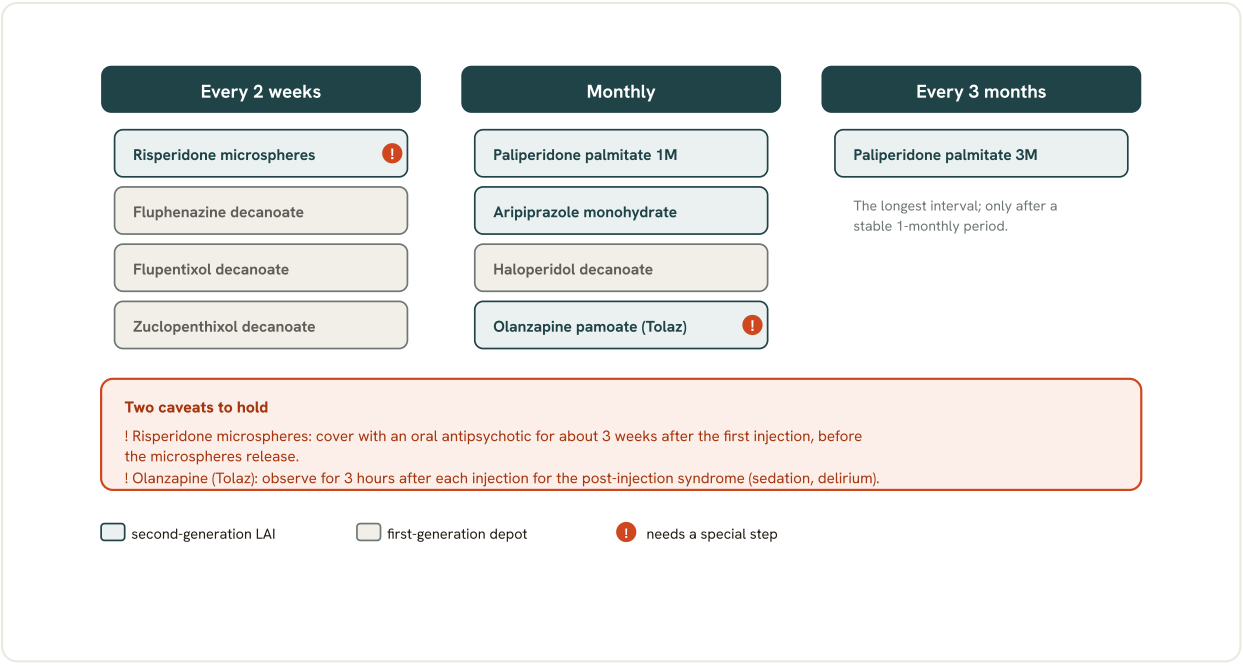


Fig 9.6 Depot and long-acting injectable antipsychotics, grouped by dosing interval. An assured-adherence tool that cuts relapse, worth considering early rather than only after failure. Two caveats matter: risperidone microspheres need oral cover for about three weeks after the first dose, and the olanzapine injectable (marketed in India as Tolaz) needs a three-hour observation for the post-injection syndrome.

7.1 Why use a long-acting injectable

Assured adherence and fewer relapses. Covert non-adherence is common and is a leading cause of relapse, and it is invisible with oral drugs. A depot removes that uncertainty: the clinician knows exactly what has been given. In comparison with oral antipsychotics there is strong evidence that depots reduce relapse and rehospitalisation (Leucht 2012; Tiihonen 2017), and a nationwide cohort found the risk of rehospitalisation roughly **20 to 30 percent** lower on a long-acting injectable than on the same drug by mouth (Tiihonen 2017).

Steadier levels, a clearer dose. The **lai** avoids first-pass metabolism and the peaks and troughs of daily dosing, and because the therapeutic dose range of most injectables is well defined the optimal dose is more likely to be prescribed. Consider it early, and offer it as a positive choice rather than a last resort.

RULE **Offer a long-acting injectable early.** It guarantees delivery and cuts relapse; it is not only for the patient who has already defaulted.

7.2 The first-generation depots

The first-generation depot agents are esterified in an oil vehicle and given every two to four weeks.

Haloperidol decanoate

a high-potency butyrophenone, given every 4 weeks; the most widely used first-generation depot.

Fluphenazine decanoate

a high-potency phenothiazine, every 2 to 4 weeks; a small test dose is given first because of the risk of early extrapyramidal effects.

Zuclopenthixol decanoate

every 2 to 4 weeks; the separate short-acting acetate (acuphase) is for acute disturbance and must not be confused with the depot.

Flupentixol decanoate

every 2 to 4 weeks; the optimal dose is around 40 mg every 2 weeks, only a small fraction of the licensed maximum.

Their trade-off is the first-generation profile: effective against positive symptoms and inexpensive, but with more extrapyramidal effects and prolactin elevation and no advantage against negative symptoms.

TRAP **Zuclopenthixol acetate is not the depot.** The acetate (acuphase) is a short-acting agent for acute disturbance; the decanoate is the long-acting maintenance depot.

7.3 The second-generation long-acting injectables

The second-generation long-acting injectable agents carry the lower extrapyramidal burden of the atypicals into an injectable form.

Risperidone microspheres

given every 2 weeks; because the microspheres do not release drug for about three weeks, oral cover is needed after the first injection.

Paliperidone palmitate

the active metabolite of risperidone, as a 1-monthly and a 3-monthly injection (and now a 6-monthly), which can be initiated without oral supplementation using a loading regimen.

Aripiprazole monohydrate

a monthly injection; overlap with oral aripiprazole for 14 days after the first dose while levels build.

Olanzapine pamoate

every 2 or 4 weeks; carries the post-injection syndrome (see below).

7.4 Olanzapine long-acting injectable and the post-injection syndrome

The olanzapine long-acting injectable, marketed in India as **Tolaz** (olanzapine pamoate), carries a distinctive hazard. Inadvertent entry of the depot into a blood vessel produces the post-injection syndrome: a delirium and excessive sedation, sometimes with dysarthria, ataxia and agitation, coming on within minutes to a few hours of the injection as a bolus of olanzapine reaches the circulation. Because of this the patient must be observed for **3 hours** after every injection in a facility with resuscitation access, and must not drive home the same day.

INDIA

The olanzapine long-acting injectable is available in India as Tolaz. The mandatory 3-hour post-injection observation applies to every dose, which shapes how and where it can be given.

3 hours	2 or 4 weeks	~3 weeks
POST-INJECTION OBSERVATION	OLANZAPINE LAI INTERVAL	ORAL COVER AFTER RISPERIDONE LAI

7.5 Initiation and oral-to-depot conversion

Establish the oral drug first. The safest conversion is to establish efficacy and tolerability on the oral form of the same drug, then give the equivalent dose as the long-acting injectable, using the manufacturer's conversion table. A small test dose is prudent for the first-generation depots to check for a hypersensitivity or early extrapyramidal reaction.

Do not judge the dose too early. With regular injections the plasma level continues to rise for at least **6 to 12 weeks** after starting, even with no change in dose, so a dose increase during this window is difficult to evaluate and often unnecessary. Continue the oral overlap that each agent requires while the depot level builds.

AGENT	INTERVAL	THE ONE CAVEAT
Haloperidol decanoate	every 4 weeks	first-generation extrapyramidal and prolactin burden
Fluphenazine or flupentixol decanoate	every 2 to 4 weeks	give a test dose first
Risperidone microspheres	every 2 weeks	**oral cover for about 3 weeks after the first dose**
Paliperidone palmitate	1-monthly or 3-monthly	loading regimen, no oral cover needed
Aripiprazole monohydrate	monthly	14-day oral overlap
Olanzapine pamoate (Tolaz)	every 2 or 4 weeks	**3-hour post-injection observation**

The long-acting injectable agents, their dosing interval and the single practical caveat for each.

HOLD THIS

A long-acting injectable guarantees delivery and cuts relapse; the two things to remember are that risperidone microspheres need about three weeks of oral cover and the olanzapine injectable (Tolaz) needs a three-hour post-injection observation.

GOOD TO REMEMBER

- **Long-acting injectable:** assured-adherence maintenance treatment; reduces relapse and rehospitalisation by roughly 20 to 30 percent versus the same oral drug; offer early.
- **Risperidone microspheres:** every 2 weeks; needs oral antipsychotic cover for about 3 weeks after the first injection because the microspheres release late.
- **Paliperidone palmitate:** 1-monthly and 3-monthly; a loading regimen means no oral cover is needed.
- **Aripiprazole monohydrate:** monthly; overlap with oral aripiprazole for 14 days.
- **Olanzapine pamoate (Tolaz):** every 2 or 4 weeks; observe 3 hours after each injection for the post-injection syndrome (delirium and sedation from inadvertent vascular uptake).

8 · Treatment-resistant schizophrenia

Treatment-resistant schizophrenia, the **trs**, is a defined clinical endpoint, not a vague impression that a patient is "difficult". It is one of the highest-yield management topics because it

hangs on a single operational definition and a single correct next step: once a patient truly meets criteria for treatment resistance, the evidence-based move is **clozapine**, and everything before that point is about proving that the resistance is real. Around 20 to 30% of patients with schizophrenia fail to respond adequately to non-clozapine antipsychotics and fall into this group (Stahl Clozapine Handbook 2019, Kane 2016), yet clozapine remains badly underused, with mean delays to initiation measured in years after criteria are met.



Fig 9.7 Treatment-resistant schizophrenia is established after two adequate antipsychotic trials have failed; the subsequent clozapine pathway requires structured haematological and clinical monitoring.

How to use this page. Learn the definition first (the **failed trials** criterion, two adequate antipsychotic trials), then learn to exclude pseudo-resistance before you accept it, then hold the management algorithm that ends in clozapine, not a third same-class switch. The illness itself, its phenomenology, aetiology, criteria and course, is not re-taught here; it belongs to the Schizophrenia: aetiology, phenomenology, classification and course notes. The receptor pharmacology and CYP metabolism behind the drugs belong to the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes. Clozapine's own dosing, titration, ANC monitoring and adverse effects are developed in the clozapine topic; here

it is only the destination of the algorithm. Electroconvulsive therapy for augmentation of clozapine and for resistant illness points to the ECT and neurostimulation notes.

8.1 The definition: two failed adequate trials

The operational definition. Treatment resistance is a failure to respond to **two adequate** antipsychotic trials, each of adequate dose and duration, in a patient with confirmed adherence. In the consensus wording, roughly 20 to 30% of patients "fail to adequately respond to two or more documented antipsychotic trials of sufficient dosage and duration" (Stahl Clozapine Handbook 2019). The APA states the same clinical threshold: persistent symptoms of at least moderate severity despite two adequate antipsychotic trials, and where a trial has not produced more than a 20% reduction in symptoms this provides additional evidence of treatment resistance (APA 2020). The two elements a resident must be able to defend are the **failed trials** count (two, not one, since single-trial non-response is far too common to qualify) and the word *adequate*, which is where most of the exam marks and most of the clinical errors live.

Adequate dose

A therapeutic dose, conventionally equivalent to at least **600 mg** chlorpromazine per day, sustained long enough to act (Stahl Clozapine Handbook 2019, TRRIP 2017).

Adequate duration

At least **6 weeks** at that therapeutic dose for each trial (TRRIP 2017); a shorter exposure is an inadequate trial, not a failed one.

Adequate number

At least two past adequate treatment episodes with two different antipsychotics; commonly at least one is a second-generation agent (TRRIP 2017, Maudsley 2021).

Confirmed adherence

At least 80% of prescribed doses taken, established by more than one method (pill counts or dispensing review, patient and carer report, and at least one antipsychotic plasma level) (TRRIP 2017).

RULE **True treatment-resistant schizophrenia is two failed adequate trials, and the answer is clozapine.** Not a third me-too switch to another non-clozapine antipsychotic of the same class.

8.2 The TRRIP consensus criteria for an adequate trial

Why the criteria were formalised. The Treatment Response and Resistance in Psychosis working group published consensus criteria in 2017 to let clinicians decide reliably when a patient is treatment resistant, and recommended that the older term "refractory" be dropped (Stahl Clozapine Handbook 2019). The value of the criteria for the exam is that they turn the loose phrase "didn't respond to a couple of drugs" into four checkable minimum requirements, so a trial that fails any one of them is inadequate rather than failed.

DOMAIN	MINIMUM REQUIREMENT (ADEQUATE TRIAL)	THE DISCRIMINATOR
Duration	At least **6 weeks** at a therapeutic dose, per treatment episode	**Under 6 weeks = inadequate trial, not failure**
Dosage	Equivalent to at least **600 mg** chlorpromazine per day	**Sub-therapeutic dose = pseudo-resistance**
Number of antipsychotics	At least two past adequate episodes with two *different* antipsychotics	**Two of the same, or only one, does not count**
Current adherence	At least **80%** of prescribed doses taken, verified by two or more sources plus one plasma level	**Covert non-adherence is the commonest cause of false resistance**

TRRIP consensus criteria for an adequate antipsychotic trial: all four domains must be met before the trial counts as a genuine failure (TRRIP 2017, as tabulated in Stahl Clozapine Handbook 2019).

The optimum (research-grade) criteria. The optimum version tightens two domains: at least one of the two adequate episodes should use a long-acting injectable for at least 4 months (to guarantee exposure), and trough antipsychotic serum levels should be measured on at least two occasions at least 2 weeks apart, without prior warning to the patient (TRRIP 2017). These are the belt-and-braces version of "we are certain the drug was actually in the patient".

8.3 Staging: exclude pseudo-resistance first

Pseudo-resistance versus true resistance. The **staging** logic of resistance is that apparent non-response must be triaged into pseudo-resistance and true resistance before the label is applied, because the two demand opposite actions. Pseudo-resistance is apparent non-response driven by a fixable reason, and "apparent treatment resistance may simply be a result of inadequate treatment" (Maudsley 2021). True resistance is non-response that persists after every fixable reason has been excluded and two genuinely adequate trials have failed. The examiner wants you to name the four classic drivers of pseudo-resistance and check them before ever writing "resistant".

GOOD TO REMEMBER

- **Non-adherence:** the single commonest cause of false resistance; most non-adherence is undetected in practice (Maudsley 2021). Discriminator: a plasma level below the expected range, or missed refills. First step: confirm exposure with a long-acting injectable or plasma-level monitoring before relabelling.
- **Inadequate dose or duration:** a sub-therapeutic dose or a trial shorter than 6 weeks. Discriminator: the trial fails a TRRIP domain. First step: optimise to a therapeutic dose for an adequate period, then reassess.
- **Substance use:** ongoing cannabis, stimulants or alcohol sustaining symptoms. Discriminator: history and urine drug screen. First step: address the substance use as a treatment target in its own right.
- **Wrong diagnosis:** an organic, mood or other psychotic disorder mislabelled as schizophrenia. Discriminator: atypical course, features or investigations. First step: re-examine the diagnosis before escalating pharmacology.

TRAP **Calling covert non-adherence or an inadequate trial "resistance".** An unswallowed or under-dosed drug has not failed; verify adherence, dose and duration before you ever write "treatment-resistant".

8.4 The TRS work-up before you commit

The confirm-resistance checklist. Before the label is committed and clozapine is offered, the patient is worked up against a fixed set of questions that operationalise the exclusion of pseudo-resistance. This is the checklist a viva expects you to run through out loud.

WORK-UP STEP	WHAT TO CONFIRM	IF IT FAILS, THIS IS PSEUDO-RESISTANCE
Adherence	At least 80% of doses actually taken, verified by two sources and a plasma level; consider a long-acting injectable to guarantee exposure	**Covert non-adherence, not resistance**
Dose	Each of the two trials reached a therapeutic dose (about **600 mg** chlorpromazine equivalent per day)	**Under-dosing, not resistance**
Duration	Each trial ran at least **6 weeks** at that dose	**Inadequate trial, not resistance**
Comorbidity	No active substance use, and no untreated depression, anxiety or physical illness sustaining symptoms; diagnosis re-checked	**Comorbid or misdiagnosed, not resistance**

The TRS work-up: confirm adherence, dose, duration and comorbidity before accepting true resistance and moving to clozapine (Maudsley 2021, TRRIP 2017).

8.5 The management algorithm: confirm, then clozapine

Where the algorithm goes. The **management algorithm** is short and its endpoint is not negotiable. Step one: try two different antipsychotics in sequence, each at an adequate dose for an adequate duration, at least one commonly a second-generation agent. Step two: if response is inadequate, run the work-up above and confirm the resistance is true, not pseudo-resistance. Step three: once resistance is confirmed, move to clozapine. The Maudsley states it flatly: "where there is confirmed treatment resistance (failure to respond to adequate trials of at least two antipsychotic medications), evidence supporting the use of clozapine (and only clozapine) is overwhelming" (Maudsley 2021). Clozapine is the only antipsychotic with proven superiority in this population, established by the landmark double-blind comparison against chlorpromazine in resistant patients (Kane 1988).

What the algorithm is not. The wrong branch, and the classic exam distractor, is a third switch to yet another non-clozapine antipsychotic of the same broad class. Switching among non-clozapine agents in a confirmed-resistant patient yields little: increasing the dose of olanzapine or risperidone in non-responders gave only about a 4% absolute gain in response, whereas switching to clozapine was considerably more successful (Maudsley 2021). Neither high-dose monotherapy

nor antipsychotic polypharmacy is a substitute for clozapine in true resistance; delaying clozapine to try them wastes the window, and longer delay independently predicts poorer clozapine response (Stahl Clozapine Handbook 2019). ECT is an augmentation option in clozapine-resistant illness rather than a replacement for clozapine, and its technique belongs to the ECT and neurostimulation notes.

20 to 30%	2	6 weeks	600 mg
OF PATIENTS MEET TRS CRITERIA	ADEQUATE FAILED TRIALS TO DEFINE TRS	MINIMUM ADEQUATE TRIAL DURATION	CPZ-EQUIVALENT ADEQUATE DAILY DOSE

COMMON TRAP

Reaching for a third non-clozapine antipsychotic, high-dose monotherapy or polypharmacy in a confirmed-resistant patient. Increasing the dose of a non-clozapine agent in non-responders gave roughly a 4% absolute response gain; switching to clozapine was far more effective (Maudsley 2021). Every month of me-too switching is a month clozapine is withheld, and delay independently lowers the odds of clozapine response.

8.6 Clozapine as the evidence-based next step

Why clozapine and only clozapine. Clozapine is the single agent with robust, replicated superiority in treatment-resistant schizophrenia, first shown in Kane's double-blind trial against chlorpromazine (Kane 1988) and confirmed in network meta-analysis, which ranks clozapine best for both negative symptoms and overall symptom improvement (Maudsley 2021, Samara 2016). Real-world cohort studies of tens of thousands of patients show clozapine outperforming other antipsychotics for the resistant population and lowering all-cause mortality while the patient stays on it (Stahl Clozapine Handbook 2019). This is why the algorithm converges on clozapine the moment resistance is confirmed, and why unnecessary delay is treated as a quality failure.

GOOD TO REMEMBER

- **Clozapine (dibenzodiazepine second-generation antipsychotic; weak, transient D2 plus 5-HT2A and multi-receptor action):** the only agent proven superior in true TRS. Indian brand: Sizopin (also Lozapin). Dose range and full ANC monitoring are developed in the clozapine topic; the one caveat to hold here is that it is reserved for confirmed resistance and started promptly once criteria are met, because delay lowers response (Kane 1988, Stahl Clozapine Handbook 2019).

INDIA

The Indian Psychiatric Society schizophrenia guideline endorses the same core pathway: confirm resistance across two adequate antipsychotic trials, then move to clozapine as the treatment of choice, with adherence and comorbidity excluded first (IPS CPG). Clozapine is widely available in India as Sizopin (and Lozapin), and its use is governed by the same blood-count monitoring discipline; the practical Indian barrier is the monitoring logistics rather than drug cost. Verify the exact IPS monitoring schedule against the current guideline before quoting frequencies.

MNEMONIC

ADAM: Adherence, Dose, Adequate duration, Misdiagnosis or comorbidity

Run ADAM before you ever write "resistant": confirm *Adherence* (was the drug taken), an adequate *Dose* (about 600 mg CPZ-equivalent), an *Adequate duration* (at least 6 weeks each), and exclude *Misdiagnosis or comorbidity* (substance use, wrong diagnosis). Only when ADAM is clean and two adequate trials have failed is it true TRS, and the answer is clozapine.

HOLD THIS

Treatment-resistant schizophrenia is failure of two adequate antipsychotic trials (each at least 6 weeks at about 600 mg chlorpromazine-equivalent per day, adherence confirmed at 80% or more), and once that is proven the answer is clozapine, never a third same-class switch.

9 · Clozapine: indications, monitoring and the haematological emergencies

Clozapine is the single most effective antipsychotic and the only one with proven superiority in treatment-resistant schizophrenia, yet it is reserved because of a small risk of a fatal blood dyscrasia. The whole of its use is a trade of that superior efficacy against a monitoring discipline: no drug in psychiatry rewards knowing the numbers more, and none punishes guessing them more. Every threshold below is worth committing to memory and confirming against the local monitoring service.

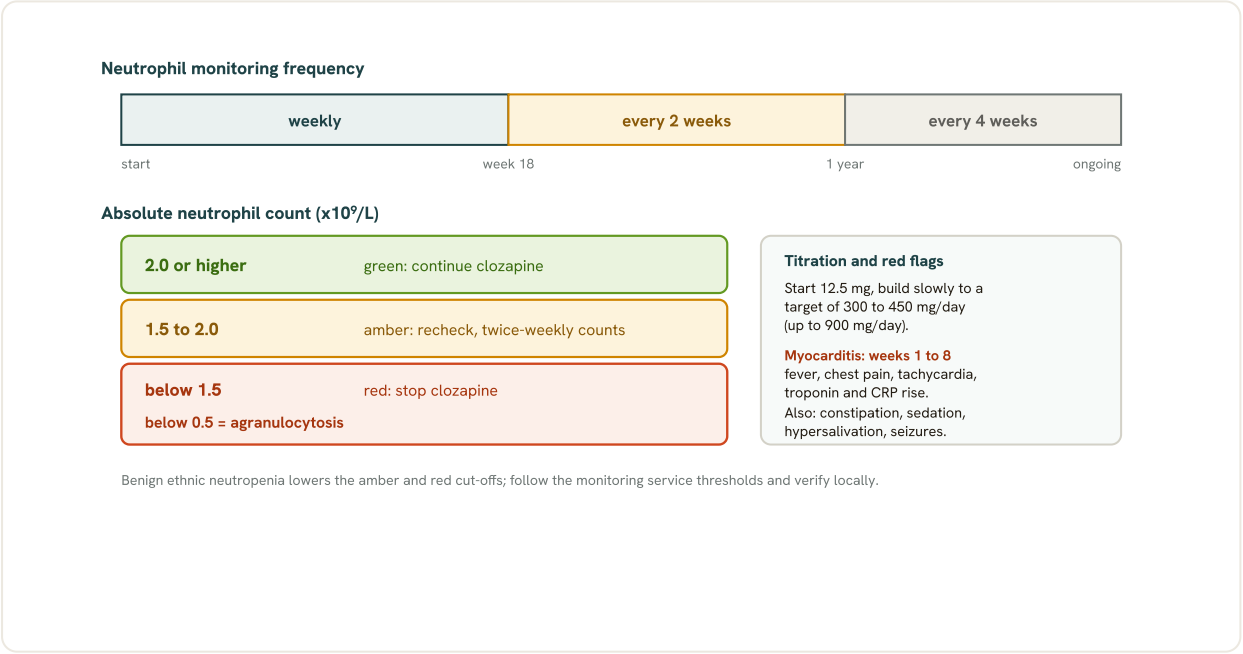


Fig 9.8 Clozapine titration and neutrophil monitoring. Counts run weekly for the first 18 weeks, then every 2 weeks to a year, then every 4 weeks. The traffic-light rule on the absolute neutrophil count decides continuation: green at 2.0 or above, amber at 1.5 to 2.0, red below 1.5 (stop), with agranulocytosis below 0.5. Myocarditis is the other early emergency, in the first one to eight weeks. Verify every threshold against the local monitoring service.

9.1 Indications

Treatment resistance is the main indication. The evidence for clozapine in treatment-resistant schizophrenia is unmatched: the landmark trial found **30 percent** of resistant patients responded to clozapine against **4 percent** to chlorpromazine (Kane 1988), and meta-analysis

confirms its superiority over other agents in true resistance with a number needed to treat of about **9** (Siskind 2016). It is the right next step once two adequate trials have failed, not a third me-too switch.

Two further indications. Persistent suicidality in schizophrenia (clozapine reduced suicidal behaviour more than olanzapine in the International Suicide Prevention Trial, Meltzer 2003), and persistent aggression or hostility that has not responded to other antipsychotics.

RULE **Clozapine is the answer to true resistance.** Do not delay it, and do not reach for a third ordinary antipsychotic in its place.

9.2 Initiation and titration

Start low, build slowly. Titration begins at **12.5 mg** on day one, and each dose is roughly doubled if the previous one was tolerated (12.5, then 25, then 50, and so on), so that a target of **300 to 450 mg/day** is reached over about two to three weeks, up to a maximum of **900 mg/day** (Maudsley 2021). Slower titration is used in the community, in the elderly and where cardiac risk is a concern, because it lowers the risk of myocarditis, seizures, hypotension and tachycardia.

Gaps reset the clock. If more than 48 hours of clozapine have been missed, the dose must be re-titrated from a low start; if more than a week has been missed, restart as if it were a first initiation, because tolerance to the cardiovascular and sedative effects is lost within days.

Plasma levels guide the dose in non-response. Where response is inadequate, a trough plasma level (a target around **350 to 600 micrograms/L**) confirms whether the trial is truly adequate before the illness is called clozapine-resistant.

12.5 mg	300 to 450	900 mg
STARTING DOSE	TARGET DOSE (MG/DAY)	DAILY MAXIMUM

9.3 The neutrophil monitoring schedule

Every patient must be registered with a monitoring service before the first dose: no valid blood count, no clozapine. The absolute neutrophil count is the number that decides continuation. The full blood count is taken weekly for the first **18 weeks**, then every 2 weeks to one year, then every 4 weeks thereafter (Maudsley 2021), because the agranulocytosis risk is concentrated in the first months and falls to a low level after the first year.

The result is read as a traffic light on the absolute neutrophil count, in units of 10^9/L:

ABSOLUTE NEUTROPHIL COUNT	SIGNAL	ACTION
2.0 or higher	green	continue clozapine
1.5 to 2.0	amber	**continue but recheck, twice-weekly counts**
below 1.5	red	**stop clozapine, daily counts, haematology**
below 0.5	agranulocytosis	**stop, reverse-barrier nurse, treat as a medical emergency**

The absolute neutrophil count traffic light. Benign ethnic neutropenia, common in patients of African and Middle Eastern descent, lowers these cut-offs, so a low baseline count is worked up before it is called a red result.

9.4 Agranulocytosis and neutropenia

The feared complication. Agranulocytosis (an absolute neutrophil count below 0.5) occurs in roughly **0.8 percent** of patients, with the risk highest in the first 18 weeks and receding after the first year. Managed by the monitoring system the death rate is now low, but an untreated agranulocytosis carries a serious risk of fatal sepsis, which is why the monitoring is mandatory and non-negotiable.

Neutropenia short of agranulocytosis. A fall to the amber or red range without reaching agranulocytosis (neutropenia) prompts more frequent counts or stopping; a transient benign neutropenia, or one due to benign ethnic neutropenia or a concurrent infection, is distinguished from a true clozapine effect before the drug is abandoned.

TRAP **Do not stop clozapine for a benign transient neutropenia.** A dip in the amber range from an infection or benign ethnic neutropenia is not an agranulocytosis; work it up before throwing away the one drug that works.

9.5 Myocarditis and the cardiac risks

The early cardiac emergency. Myocarditis is the other serious early complication, typically in the first month of treatment. It presents with persistent tachycardia, chest pain, fever, breathlessness and unexplained features of heart failure, with a rise in troponin, C-reactive protein and eosinophils. Many centres monitor **CRP, troponin and creatine kinase weekly for the first four weeks**; a rise prompts an echocardiogram and B-natriuretic peptide to confirm, and confirmed myocarditis means stopping clozapine.

Fever is common and usually benign. Clozapine induces an inflammatory response (raised CRP, interleukin-6 and eosinophils) that produces a benign fever in the first weeks, but a fever always prompts a check for myocarditis, neuroleptic malignant syndrome, pneumonia and neutropenia before it is dismissed.

9.6 The other adverse effects

Constipation can kill. Clozapine causes a gastrointestinal hypomotility whose risk is highest in the first four months and which persists; severe cases progress to ileus, obstruction and death. It is prevented and treated actively with stimulant laxatives (senna or bisacodyl) first-line and

osmotics, while bulk-forming laxatives and systemic anticholinergics are avoided because they worsen it.

The rest of the burden. Hypersalivation (troublesome at night), sedation and postural hypotension early in treatment; dose-related seizures, more likely above **600 mg/day**, where prophylactic valproate is added; and substantial weight gain and metabolic disturbance, so metabolic monitoring runs alongside the blood count.

INDIA

Clozapine is available in India as Sizopin and Lozapin. Registration with a clozapine monitoring service and the same absolute-neutrophil-count discipline apply; point-of-care neutrophil testing is increasingly used to make weekly monitoring feasible.

9.7 Rechallenge after a blood dyscrasia

After agranulocytosis, generally do not rechallenge. A clozapine-induced agranulocytosis is a strong contraindication to rechallenge: on re-exposure the dyscrasia tends to recur sooner and more severely. Relisting a patient for a clozapine rechallenge after agranulocytosis is done only exceptionally, under specialist haematology supervision, when no alternative exists and the benefit is judged to outweigh a potentially fatal recurrence.

After a lesser or non-clozapine neutropenia, rechallenge may be possible. Where the neutropenia was benign, due to benign ethnic neutropenia, or clearly caused by another drug or an infection rather than by clozapine, a specialist-supervised rechallenge with close monitoring can be considered, because the clozapine-induced blood picture was never established.

HOLD THIS

Clozapine is the only evidence-based drug for true resistance; its price is mandatory neutrophil monitoring (green at 2.0 and above, amber 1.5 to 2.0, red below 1.5, agranulocytosis below 0.5) and vigilance for myocarditis in the first month and for a constipation that can be fatal.

GOOD TO REMEMBER

- **Clozapine:** a dibenzodiazepine, the only agent proven superior in treatment-resistant schizophrenia (Kane 1988); start 12.5 mg, target 300 to 450 mg/day (up to 900); the one parameter is the absolute neutrophil count.
- **Neutrophil monitoring:** weekly for 18 weeks, then fortnightly to a year, then 4-weekly; continue at 2.0 or above, recheck at 1.5 to 2.0, stop below 1.5, agranulocytosis below 0.5 ($x10^9$/L).
- **Agranulocytosis:** about 0.8 percent, highest in the first 18 weeks; the reason for the monitoring; do not rechallenge after it.
- **Myocarditis:** first month; persistent tachycardia, chest pain, fever; monitor CRP, troponin and creatine kinase weekly for four weeks; confirmed myocarditis means stopping.
- **Constipation (gastrointestinal hypomotility):** can be fatal; prevent and treat with stimulant laxatives, never bulk-forming or anticholinergic agents.

10 · Clozapine augmentation and rational polypharmacy

Some patients remain symptomatic even on an adequate trial of clozapine, and this **ultra-resistant** group forces the two hardest management decisions in schizophrenia pharmacology: what, if anything, to add on top of clozapine, and when a second antipsychotic is ever defensible outside that setting. Both questions are examined heavily because both are dominated by a weak evidence base and a strong temptation to reach for more drugs. The examiner wants two disciplines from you: optimise the clozapine trial before you augment it, and never let a second antipsychotic become a permanent fixture without a defined target and a plan to stop.

How to use this page. Learn **clozapine augmentation** as the strategy for the patient who has not fully responded to a genuinely optimised clozapine trial, then learn **antipsychotic polypharmacy** as the broader, less defensible practice of combining two antipsychotics outside clozapine augmentation, and hold the single principle that reconciles them: **rational polypharmacy**, meaning a defined target, a defined trial, and a plan to stop if there is no benefit. The illness itself, its phenomenology, aetiology, criteria and course, is owned by the Schizophrenia: aetiology, phenomenology, classification and course notes. Receptor pharmacology, dopamine pathways and CYP metabolism belong to the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; here the pharmacology is applied, not derived. Clozapine's own dosing, titration and adverse-effect monitoring are developed in the clozapine topic and only referenced here. Electroconvulsive therapy for clozapine augmentation is owned by the ECT and neurostimulation notes and cross-referenced, not taught.

10.1 Optimise the clozapine trial before you augment

Augmentation is the last resort, not the reflex. Inadequate response to clozapine monotherapy is a frequent clinical event, and augmenting is common practice, but the first move in the partial responder is not to add a drug: it is to prove the clozapine trial was truly optimised. That means confirming the **dose**, the **duration**, and the **plasma level** were all adequate before accepting non-response (Maudsley 2021). Response to clozapine is usually seen across a wide dose range and the average maintenance dose is around **450 mg/day**, but dose alone is a poor guide; the more reliable target is a trough clozapine plasma concentration, with most studies placing the threshold for response in the range **350 to 420 mcg/L** (Maudsley 2021). A patient labelled a clozapine non-responder at a plasma level below that threshold has not failed clozapine at all, and augmenting them is treating the wrong problem. The full plasma-level and dose-optimisation logic belongs to the clozapine topic; here it is the mandatory precondition for the word *augmentation*.

RULE **Optimise the clozapine trial (dose, duration, plasma level) before you augment.** A subtherapeutic plasma level is under-treatment, not treatment resistance; fix the trial before adding a second drug.

HOLD THIS
Before augmenting clozapine, confirm the trial was optimised on all three of dose, duration and plasma level (threshold for response about 350 to 420 mcg/L); the evidence for every augmentation strategy is modest at best, so give an adequate trial and stop what does not clearly work.

10.2 The ultra-resistant patient: what clozapine augmentation is

Defining the group. A minority of patients are **ultra-resistant**, meaning they remain significantly symptomatic despite an adequate, optimised trial of clozapine, the single most effective agent in treatment-resistant illness. Clozapine augmentation is the addition of a second agent to clozapine in this group to try to capture the residual symptoms that clozapine alone has not touched. It has become common practice precisely because inadequate response to clozapine on its own is frequent (Maudsley 2021). The critical framing for the exam is that clozapine augmentation is a distinct, partially defensible exception to the general rule against combining antipsychotics, and it is the one polypharmacy scenario that guidelines explicitly permit (Maudsley 2021).

TRAP **Augmenting a clozapine "non-responder" who was never optimised.** Check the plasma level first; a level below about 350 mcg/L means the clozapine trial itself was inadequate, not that the patient needs a second drug.

10.3 The augmentation strategies and how strong the evidence is

The menu, and the honest verdict on it. The augmentation strategies fall into four groups: a second antipsychotic (clozapine plus amisulpride or clozapine plus aripiprazole being the most commonly cited), a mood stabiliser (lamotrigine), an antidepressant for residual negative or depressive symptoms, and electroconvulsive therapy. Despite more than fifty reviews and meta-analyses, the evidence remains insufficient to support any single algorithm, the result of augmentation is often disappointing, and the effect size is small at best (Maudsley 2021). Meta-analyses restricted to large, high-quality studies mostly report no benefit from pharmacological augmentation of clozapine (Maudsley 2021). The practical rule that follows is to pick one strategy, give it an adequate trial, and abandon it after **3 to 6 months** if there is no clear benefit (Maudsley 2021).

AUGMENTATION STRATEGY	TYPICAL ADD-ON DOSE	EVIDENCE AND THE POINT TO HOLD
Clozapine plus amisulpride (second antipsychotic)	**400 to 800 mg/day**	**Some RCT and clinical support; may allow clozapine dose reduction, but watch additive cardiac adverse effects (Maudsley 2021)**
Clozapine plus aripiprazole (second antipsychotic)	**15 to 30 mg/day**	**Very limited efficacy evidence; its real value is reducing weight and LDL cholesterol on clozapine (Maudsley 2021)**
Clozapine plus lamotrigine (mood stabiliser)	**25 to 300 mg/day**	**May help partial or non-responders; several equivocal reports, meta-analytic signal driven by outlying studies (Maudsley 2021)**
Clozapine plus an antidepressant	Agent-specific	**For residual negative or depressive symptoms; weak signal, mirtazapine has the largest (still weak) effect (Maudsley 2021)**
Clozapine plus electroconvulsive therapy	Course-based	**An option in clozapine-resistant illness; technique and evidence owned by the ECT and neurostimulation notes**

Suggested options for augmenting clozapine after 3 to 6 months of optimised clozapine alone has given unsatisfactory benefit; the overall evidence base is modest and no algorithm is established (Maudsley 2021).

GOOD TO REMEMBER

- **Amisulpride:** a benzamide second-generation antipsychotic, predominantly D2/D3 antagonist. Add-on dose **400 to 800 mg/day** in clozapine augmentation (Maudsley 2021). Hold: watch additive cardiac and QTc effects, and it may permit a clozapine dose reduction. Lead Indian brand where a trade name is needed: Amazeo.
- **Aripiprazole:** a dopamine D2 partial agonist. Add-on dose **15 to 30 mg/day** (Maudsley 2021). Hold: efficacy signal is very limited, but it reliably reduces clozapine-associated weight and LDL cholesterol, which is its main rationale. Lead Indian brand: Arip.
- **Lamotrigine:** an anticonvulsant mood stabiliser (sodium-channel blocker). Add-on dose **25 to 300 mg/day** (Maudsley 2021). Hold: titrate slowly and hold the risk of serious rash (Stevens-Johnson syndrome); evidence in clozapine augmentation is equivocal.
- **Electroconvulsive therapy:** a neurostimulation treatment, an augmentation option in clozapine-resistant illness. Discriminator: it is added to, not a substitute for, an optimised clozapine trial. First step and technique: owned by the ECT and neurostimulation notes.

10.4 Rational antipsychotic polypharmacy outside clozapine augmentation

The general rule against combining antipsychotics. Apart from exceptional circumstances such as clozapine augmentation, antipsychotic polypharmacy should generally be avoided because of the increased adverse-effect burden and the risks of QT prolongation and sudden cardiac death (Maudsley 2021). The efficacy evidence for combining two antipsychotics outside clozapine

augmentation is weak: a meta-analysis of RCTs comparing augmentation with a second antipsychotic against continued monotherapy found the combination lacked high-quality evidence for overall efficacy (Maudsley 2021). The general consensus across guidelines is that combined antipsychotics for refractory illness should be considered only after evidence-based options such as clozapine have been exhausted (Maudsley 2021).

Why the harm evidence is more convincing than the benefit. The case against antipsychotic polypharmacy is not just absent benefit, it is present harm. Combined antipsychotic regimens carry additive adverse effects, are commonly a high-dose prescription, and are associated with increased extrapyramidal symptoms, metabolic effects and diabetes, sexual dysfunction, hip fracture, paralytic ileus, seizures, prolonged QTc and arrhythmias (Maudsley 2021). They also worsen adherence, because a more complex regimen is harder to take, and they make it difficult to attribute any response to a single drug, which muddies every subsequent decision (Maudsley 2021). Some strategies buy tolerability rather than efficacy: adding aripiprazole to reduce weight on clozapine, or to normalise prolactin on haloperidol or risperidone, has a valid rationale, but in many such cases using aripiprazole alone would be the more logical choice (Maudsley 2021).

3 to 6	350 to 420	450
MONTHS, THEN ABANDON AUGMENTATION IF NO BENEFIT	CLOZAPINE PLASMA THRESHOLD FOR RESPONSE (MCG/L)	AVERAGE CLOZAPINE DOSE (MG/DAY)

10.5 The principle of rational polypharmacy

Three conditions make polypharmacy rational. If a second antipsychotic is ever used, it must be used rationally, and rational polypharmacy has three defining conditions. First, a defined target: a specific symptom or symptom cluster the combination is meant to address, not a vague sense that the patient is unwell. Second, a defined trial: an adequate dose for an adequate period against that target, so the question can actually be answered. Third, a plan to stop: an explicit commitment to withdraw the second antipsychotic if the target does not improve, rather than letting the combination drift into a permanent, undocumented regimen. Because combined antipsychotics carry a greater adverse-effect burden, the rationale, benefits and adverse effects of the trial should be documented in the records (Maudsley 2021). Where polypharmacy continues, the minimum requirement is systematic monitoring for adverse effects, including an ECG, with any benefit carefully recorded (Maudsley 2021).

TRAP **Long-term two-antipsychotic polypharmacy without a defined target or a stop plan.** A combination started for a crisis or a cross-taper that is never reviewed becomes a permanent high-dose regimen delivering additive harm and no measurable benefit.

COMMON TRAP

Confusing rational clozapine augmentation with routine antipsychotic polypharmacy. Clozapine augmentation is a defined exception in an ultra-resistant patient after clozapine has been optimised; combining two non-clozapine antipsychotics as a first response to poor monotherapy response is the practice guidelines warn against, because the harm evidence is more convincing than any efficacy signal (Maudsley 2021).

INDIA

Where a second antipsychotic or a long-acting injectable is added rationally in Indian practice, lead with the Indian trade name where one is needed: olanzapine long-acting injectable is marketed as Tolaz, and it carries a recognised post-injection delirium/sedation syndrome that mandates a supervised post-dose observation period. Aripiprazole (Arip) and amisulpride (Amazeo) are the augmentation agents most often reached for. The IPS schizophrenia guideline and the community-based DMHP model both frame clozapine, when used, as monotherapy to be optimised first, consistent with the rule above.

MNEMONIC

TARGET, TRIAL, STOP

The three conditions for rational polypharmacy: a defined TARGET (which symptom), a defined TRIAL (adequate dose and duration to answer the question), and a STOP plan (withdraw if the target does not improve). If any one is missing, the combination is not rational.

WORKED EXAMPLE

A man on clozapine 450 mg/day for eight months has persistent delusions; his trough clozapine level is 220 mcg/L. The correct next step is not augmentation but optimisation: his level is below the 350 to 420 mcg/L response threshold, so his clozapine trial was never adequate. You raise the dose (or add a CYP inhibitor with caution) to reach a therapeutic plasma level and reassess. Only if he remains symptomatic on an optimised, plasma-level-confirmed clozapine trial does clozapine augmentation, for example clozapine plus amisulpride 400 to 800 mg/day with a 3 to 6 month trial and a stop plan, become the rational next move (Maudsley 2021).

11 · Management of the negative symptoms

The **negative symptoms** are the diminution or absence of normal function, the expressive deficits (blunted affect, alogia, poor eye contact, decreased spontaneous movement) and the avolition or amotivation cluster (reduced interests, desires, goals and self-initiated activity). They are the domain that responds least to D2 blockade, they carry much of the long-term morbidity and poor functional outcome, and they are the reason a patient whose voices have stopped may still not work, socialise or self-care (Maudsley 2021, Kaplan & Sadock 2024). For the exam this is a high-yield topic precisely because the correct first move is not a drug at all: it is to decide whether the negative symptoms are *secondary* and reversible or *primary* and enduring, because the two demand opposite actions.

How to use this page. Learn the primary-versus-secondary split first, because it drives everything downstream. Then hold the short list of pharmacological options for the primary deficit (modest at best, no drug reliably treats it) and the non-pharmacological mainstay (cognitive remediation and psychosocial rehabilitation) for the functional deficit. The illness itself, its phenomenology, aetiology, criteria and course, is not re-taught here; it belongs to the Schizophrenia: aetiology, phenomenology, classification and course notes. The receptor

pharmacology and dopamine pathways behind these agents belong to the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes. The rehabilitation interventions named here are developed as clinical programmes in the rehabilitation and psychosocial topics; here they are applied to the negative-symptom problem.

11.1 First separate secondary from primary negative symptoms

The clinical distinction that drives management. Before any treatment is chosen, the negative symptoms must be triaged into two categories, because the treatable causes differ. **Primary negative** symptoms comprise an enduring deficit state, are stable over time and predict a poor prognosis. **Secondary negative** symptoms are consequent upon another, potentially reversible, cause: active positive symptoms, depression or demoralisation, medication side effects such as bradykinesia as part of drug-induced parkinsonism, or understimulation, social deprivation and hospitalisation, and chronic substance or alcohol use (Maudsley 2021, Barnes 1995). "It is important to determine the most likely cause in any individual case before embarking on a treatment regimen" (Maudsley 2021). The whole management strategy pivots on this: a secondary cause is treated at its source, and only what remains after every reversible driver is removed is called primary.

Why it matters for numbers. Negative symptoms are seen to a varying degree in up to three-quarters of people with established schizophrenia, but only around **20%** have persistent primary negative symptoms (Maudsley 2021). In other words most negative symptoms you meet have a reversible component to hunt for first.

RULE **Always look for and treat a secondary cause before calling negative symptoms primary.** Reduce the high-EPS antipsychotic, treat the depression, add stimulation, address the substance use, then reassess what is left.

11.2 The reversible causes of secondary negative symptoms

What to exclude, and the action each demands. The value of the secondary category is that each cause has a specific and often reversible treatment. This is the checklist a viva expects you to run before you accept a deficit as primary.

SECONDARY CAUSE	HOW IT MASQUERADES AS NEGATIVE SYMPTOMS	THE TREATING ACTION
Drug-induced parkinsonism	Bradykinesia, masked facies and reduced movement overlap phenomenologically with expressive deficits	**Reduce dose or switch off a high-EPS antipsychotic; add an anticholinergic if needed**
Depression or demoralisation	Anergia, anhedonia and withdrawal mimic avolition and blunted affect	**Detect and treat the depressive episode; add an antidepressant**
Active positive symptoms	Withdrawal driven by paranoia or preoccupation with hallucinations	**Optimise antipsychotic control of the positive symptoms first**
Understimulation and institutionalisation	Apathy and inactivity from an impoverished, low-demand environment	**Increase stimulation and structured activity; psychosocial rehabilitation**
Chronic substance or alcohol use	Amotivation and social withdrawal sustained by ongoing use	**Address the substance use as a treatment target in its own right**

The reversible drivers of secondary negative symptoms and the specific action each demands: treat the secondary cause first (Maudsley 2021, Barnes 1995).

TRAP **Mislabelling drug-induced parkinsonism or a depressive episode as primary negative symptoms.** Bradykinesia and anergia are treatable secondary causes; do not write "primary deficit" until you have reduced the EPS burden and treated the depression.

11.3 The first move for secondary negative symptoms: treat the cause

The management principle. For secondary negative symptoms the treatment is the treatment of the underlying cause, not a new agent aimed at the negative symptoms themselves. Where drug-induced parkinsonism is the driver, the correct move is to *reduce* the offending high-EPS antipsychotic or switch to a lower-EPS agent, because there is some evidence that reducing antipsychotic dose from very high to high levels improves cognition and negative symptoms (Maudsley 2021). Where a depressive component contributes, treat the depression. Where the environment is impoverished, add stimulation and structured psychosocial input. Antipsychotic medication does improve negative symptoms, but this benefit "seems to be limited to secondary negative symptoms in acute psychotic episodes" (Maudsley 2021): it works on the reversible fraction, not the enduring deficit.

WORKED EXAMPLE

A man on high-dose haloperidol is flat, slow and barely speaks, and the team is discussing "burnt-out" primary negative symptoms. Before accepting that label: he has cogwheel rigidity and a masked face, so the flatness is at least partly neuroleptic-induced. The correct first step is to reduce the haloperidol or switch to a lower-EPS antipsychotic and reassess, not to add a second drug for the negative symptoms. Reducing a high antipsychotic dose can itself improve negative symptoms and cognition (Maudsley 2021).

11.4 Pharmacological options for primary negative symptoms

The honest state of the evidence. The pharmacological management of negative symptoms that are genuinely primary and persistent is nearly bare. The literature is mostly sub-analyses of acute efficacy studies rather than trials recruiting persistent negative symptoms, and "there is no robust evidence for an effective treatment for persistent primary negative symptoms" (Maudsley 2021). There is no consistent evidence for the superiority of second-generation over first-generation agents as a class, and a meta-analysis of second-generation agents found a statistically significant but sub-clinical reduction that did not reach a threshold for minimally detectable clinical improvement (Maudsley 2021, Fusar-Poli 2015). Two management moves nonetheless have some signal and are examinable: switch to an agent with a better negative-symptom signal, or add an antidepressant where a depressive component contributes.

Switch to an agent with a better negative-symptom signal. Certain treatment strategies show more robust superiority for negative symptoms, notably amisulpride and cariprazine, with olanzapine and quetiapine possibly better than risperidone and aripiprazole augmentation possibly effective (Maudsley 2021, Krause 2018). The single strongest piece of evidence is the head-to-head cariprazine-versus-risperidone trial in patients with predominant negative symptoms, which favoured cariprazine (Nemeth 2017). Amisulpride is the classic exam answer here, and the dosing is a discriminator: efficacy for negative symptoms is achieved at *low* doses, while positive symptoms need higher doses (Stahl 2021, Danion 1999). The newer muscarinic agonist agents and the dopamine partial agonists are the emerging additions to this list, but the effect sizes remain modest.

Add an antidepressant where a depressive component contributes. A Cochrane review concluded antidepressant augmentation might reduce affective flattening, alogia and avolition, though randomised evidence is inconsistent and modest, and one meta-analysis found benefit only with augmentation of first-generation agents (Maudsley 2021). The pragmatic reading is that an antidepressant trial is reasonable where a depressive component is plausible, choosing an agent that will not compound side effects, but not as a reliable treatment for the pure deficit.

50 to 300 mg/day	1.5 to 6 mg/day	~20%
AMISULPRIDE, NEGATIVE SYMPTOMS ONLY	CARIPRAZINE, SCHIZOPHRENIA	HAVE PERSISTENT PRIMARY NEGATIVE SYMPTOMS

RULE **No drug reliably treats primary negative symptoms.** The best you can offer is a switch to a better-signal agent (amisulpride, cariprazine) or an antidepressant where depression contributes, and the evidence for both is modest.

GOOD TO REMEMBER

- **Amisulpride (substituted benzamide, second-generation antipsychotic; preferential blockade of presynaptic D2/D3 at low dose, postsynaptic at high dose):** the classic negative-symptom agent. Dose: schizophrenia **400 to 800 mg/day**, but negative symptoms only **50 to 300 mg/day** (Stahl 2021). One caveat to hold: dose-dependent QTc prolongation and renal accumulation (it is largely renally cleared), so use with caution and check the QTc. Indian brand: Amazeo (also Soltus).
- **Cariprazine (dopamine D3-preferring D2/D3 partial agonist, second-generation antipsychotic):** the strongest randomised negative-symptom signal, favoured over risperidone in predominant negative symptoms (Nemeth 2017). Dose: schizophrenia **1.5 to 6 mg/day** once daily (Stahl 2021). One caveat: its very long half-life means effects and side effects (akathisia, EPS) accumulate slowly, so titrate patiently.
- **Antidepressant augmentation (added to an antipsychotic):** may reduce affective flattening, alogia and avolition, but evidence is inconsistent and modest (Maudsley 2021). One caveat: reserve it for where a depressive component genuinely contributes, and choose an agent that will not compound the antipsychotic's side effects through pharmacokinetic or pharmacodynamic interaction.

11.5 Non-pharmacological approaches: the mainstay for functional deficit

Why these carry the load. Because no drug reliably treats the primary deficit, the mainstay of managing the functional impact of negative symptoms is non-pharmacological: **cognitive remediation**, social-skills training and broader psychosocial rehabilitation. Cognitive remediation is systematic training to enhance attention, memory, executive function and social cognition, and it improves cognition, symptoms and function in schizophrenia, at least in the short term (APA 2020). Its benefits on real-world functioning are most robust when it is delivered as a component of, or adjunct to, wider psychiatric rehabilitation rather than as a stand-alone exercise (APA 2020). Social-skills training and psychosocial rehabilitation, including supported employment, target the disability that avolition and social withdrawal produce, and are developed as programmes in the rehabilitation topics.

COMMON TRAP

Escalating pharmacology, adding drug after drug, in a patient whose problem is enduring primary negative symptoms. Once secondary causes are excluded, the evidence base points toward psychosocial rehabilitation and cognitive remediation for the functional deficit, not a fourth medication. Chasing a pharmacological cure for the pure deficit wastes time and adds side effects.

11.6 The Indian context

INDIA

The Indian Psychiatric Society schizophrenia guideline places psychosocial rehabilitation, family intervention and community-based care at the centre of managing the chronic disability of which negative symptoms are the core, in line with the District Mental Health Programme (DMHP) community model of care delivery. Amisulpride is widely available and inexpensive in India (marketed as Amazeo, among others), which makes the low-dose negative-symptom strategy practical here. Where the treatment plan reduces a high-EPS agent, the olanzapine long-acting injectable is available in India as Tolaz, but note its post-injection syndrome risk requires the mandated post-dose observation period; it is a delivery choice for adherence, not a treatment for the negative symptoms themselves. Verify the exact IPS recommendations and any local availability against the current guideline before quoting them.

MNEMONIC

SECONDARY: Symptoms (positive), EPS/parkinsonism, Cheerless (depression), Off stimulation, Narcotics/substances, Deprivation/institution, Ask before you call it primaRY

Before labelling negative symptoms primary, sweep the reversible causes: active positive *Symptoms*, drug-induced *EPS*/parkinsonism, a *Cheerless* depressive episode, being *Off* stimulation, *Narcotics* or other substance use, and environmental *Deprivation*. Only what survives that sweep is the enduring primary deficit.

PEARL

Clozapine ranks best for negative symptoms in network meta-analysis, but a real confound is its very low liability for parkinsonism: some of its apparent negative-symptom advantage is simply the absence of the bradykinesia that mimics expressive deficits with other agents (Maudsley 2021). The lesson generalises: much of what looks like a drug treating negative symptoms is a drug not causing secondary ones.

HOLD THIS

Separate secondary negative symptoms (from positive symptoms, depression, drug-induced parkinsonism, understimulation or substance use, all reversible) from primary negative symptoms (the enduring deficit), and treat the secondary cause first; for the primary deficit no drug reliably works, so offer a better-signal agent (amisulpride 50 to 300 mg/day, cariprazine 1.5 to 6 mg/day) or an antidepressant where depression contributes, and make cognitive remediation and psychosocial rehabilitation the mainstay.

Psychosocial rehabilitation and psychological treatment

12 · Psychosocial rehabilitation: principles and components

Why this matters. Medication controls the positive symptoms of schizophrenia, but it does not by itself return a patient to work, relationships and an independent life. That return, function and **recovery**, is delivered by **psychosocial rehabilitation**, and this is the single conceptual point the examiner tests: rehabilitation is not an optional extra bolted on once the psychosis settles, it is a core, planned part of treatment from the outset. Antipsychotics and rehabilitation address different targets, symptoms versus disability, and neither substitutes for the other (Kaplan & Sadock 2024). A management answer that stops at the drug has answered half the question.

The illness itself, its phenomenology, aetiology, diagnostic criteria and course, is owned by the Schizophrenia: aetiology, phenomenology, classification and course notes and is not re-taught here; what this topic teaches is the framework and the **components of rehabilitation**. Modern practice frames rehabilitation inside the **recovery model**, which reorients the goal from symptom-elimination alone to a life of hope, agency and meaning beyond the illness (Anthony 1993, Tasman 2015). We take the principle first, then the components, then the assessment and delivery.

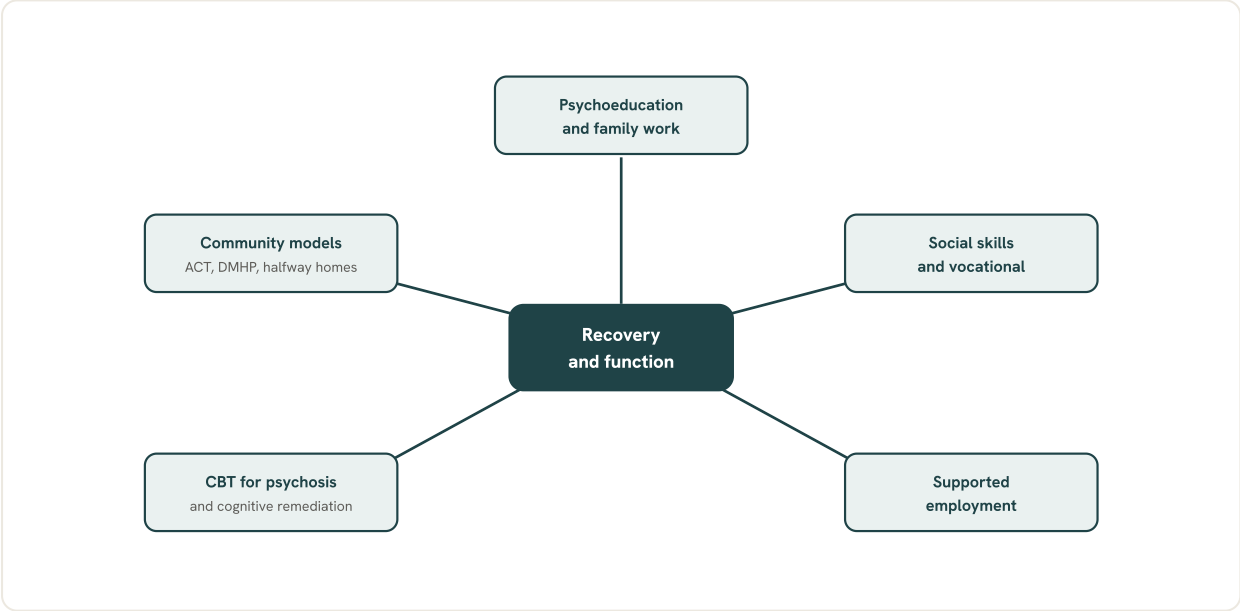


Fig 9.9 The components of psychosocial rehabilitation. Medication controls symptoms, but function and recovery come from the psychosocial half: psychoeducation and family work in high-expressed-emotion households, social skills training and supported employment, the psychological therapies, and the community and Indian service models. These are core to the plan, not an afterthought.

12.1 The core principle: medication controls symptoms, rehabilitation delivers function

The governing principle is a division of labour. Antipsychotic treatment reduces hallucinations, delusions and disorganisation and prevents relapse, the maintenance argument developed in the maintenance topic, but it leaves largely untouched the **disability** that drives long-term outcome: the negative symptoms, cognitive deficits, and lost social and occupational skills that keep a

person out of work and isolated even when frankly psychotic symptoms have gone (Kaplan & Sadock 2024). Function and recovery come from **rehabilitation**, not from medication alone. Because of this, guidelines treat psychosocial interventions as a required component of the plan for essentially every patient, offered alongside pharmacotherapy rather than after it (APA 2020). The practical corollary is that rehabilitation planning begins early, in parallel with drug treatment, not once symptoms have settled.

RULE **Rehabilitation is where function and recovery come from; medication alone does not deliver them.** Drugs treat symptoms, rehabilitation treats disability, and both belong in the plan from the start.

TRAP **Treating rehabilitation as an afterthought once symptoms settle.** Deferring psychosocial work until the psychosis is gone wastes the window in which function can be rebuilt and leaves recovery half-done.

12.2 The recovery model: hope, agency and a life beyond the illness

The **recovery model** is the frame within which rehabilitation is now delivered. Its foundational definition, from Anthony, describes recovery as "a deeply personal, unique process of changing one's attitudes, values, feelings, goals, skills and roles ... a way of living a satisfying, hopeful and contributing life even with limitations caused by the illness" (Anthony 1993, in Tasman 2015). The key move is the separation of **personal recovery** (a subjective, self-defined process of rebuilding a meaningful life) from clinical recovery (symptom remission): a person can be in recovery while symptoms persist, and symptom-free while not yet recovered. Anthony's own gloss captures the division of responsibility precisely: "recovery is what people with disabilities do; treatment, case-management and rehabilitation are what helpers do to facilitate recovery" (Anthony 1993).

The most widely used articulation of what personal recovery contains is the CHIME framework: Connectedness, Hope and optimism, Identity, Meaning, and Empowerment (agency) (Leamy et al. 2011). Hope is treated as vital, encompassing the patient's own outlook and that of the staff around them; empowerment is the restoration of agency and control over one's own care and life (Tasman 2015). For the examiner, the recovery model contributes three testable ideas: **hope** as a therapeutic stance, **agency** and self-determination as goals in their own right, and **a life beyond the illness**, chosen roles and relationships, as the true end-point of rehabilitation rather than mere symptom control.

MNEMONIC

CHIME

The five processes of personal recovery: **C**onnectedness, **H**ope (and optimism), **I**dentity, **M**eaning, **E**mpowerment (agency). Rehabilitation succeeds when it moves these, not only the symptom scores.

12.3 Psychoeducation and family work

Psychoeducation gives the patient and family a working understanding of the illness, its treatment and the early signs of relapse, converting them from passive recipients into active partners in care. Delivered to families, structured family intervention (family psychoeducation) is one of the best-evidenced psychosocial treatments in schizophrenia: it reduces expressed emotion in the home and, most importantly, lowers the relapse rate, and it is a recommended component across guidelines (APA 2020, RANZCP and PORT in Tasman 2015). The core ingredients are illness education, communication and problem-solving skills for the family, and crisis planning, typically over an extended period rather than a single session. Family work is therefore not merely supportive, it is an active relapse-prevention intervention, which is why it earns a guideline recommendation on the same footing as drug treatment.

GOOD TO REMEMBER

- **Psychoeducation:** structured teaching of the patient and family about the illness, treatment and relapse signs; the feature is shared understanding and partnership in care; the first step is to include the family early, not just the patient.
- **Family intervention (family psychoeducation):** extended family programme with illness education plus communication and problem-solving training; the discriminator is that it lowers expressed emotion and reduces relapse; the first step is to offer it to families of patients living with or in close contact with relatives (APA 2020).

12.4 Social-skills training and vocational training

Social skills training uses instruction, modelling, role-play and structured practice with feedback to rebuild the interpersonal behaviours, conversation, assertiveness, self-care, that schizophrenia erodes; the deficits it targets are persistent and largely independent of positive symptoms (Mueser et al. 1991, in Tasman 2015), which is precisely why a drug does not fix them. On the occupational side, **vocational training** aims at competitive employment, and the pivotal shift here is from the old "train-then-place" sheltered-workshop model to the "place-then-train" model of supported employment, best exemplified by Individual Placement and Support (IPS). IPS places the patient in a real, competitive, paid job rapidly according to their own preference and then provides on-the-job coaching, and it consistently outperforms traditional prevocational training on employment outcomes (APA 2020). Both social skills training and supported employment are guideline-recommended components (APA 2020, Statements 18 and 23).

GOOD TO REMEMBER

- **Social skills training:** behavioural teaching of interpersonal and self-care skills via modelling, role-play and feedback; the feature is targeting persistent, symptom-independent social deficits; the first step is structured practice, not advice alone.
- **Supported employment (Individual Placement and Support, IPS):** rapid placement into competitive paid work by patient preference, then on-the-job support; the discriminator is "place-then-train" beating "train-then-place"; the first step is a real job matched to preference, with coaching that follows (APA 2020).

12.5 Cognitive interventions

Cognition, attention, working memory, processing speed and executive function, is impaired in most patients and is a stronger predictor of real-world functioning than positive symptoms, yet responds poorly to antipsychotics (Kaplan & Sadock 2024). Cognitive remediation targets these deficits directly through repeated, structured drill and strategy training, usually computer-assisted, and improves cognitive performance with functional gains that are larger when it is paired with other rehabilitation rather than delivered alone (APA 2020, Statement 22). It is distinct from cognitive behavioural therapy for psychosis (CBTp), which targets the distress and appraisal of residual delusions and hallucinations rather than neurocognition; CBTp is a recommended psychological intervention in its own right (APA 2020, Statement 16). Keeping the two apart, remediation for cognition, CBTp for symptom-related distress, is a common exam discriminator.

GOOD TO REMEMBER

- **Cognitive remediation:** structured drill and strategy training for neurocognitive deficits; the discriminator is that it targets attention, memory and executive function, not delusions; the first step is to pair it with broader rehabilitation for functional benefit (APA 2020).
- **Cognitive behavioural therapy for psychosis (CBTp):** psychological therapy for the distress and appraisal of residual psychotic symptoms; the discriminator is symptom-related distress rather than cognition; the first step is to offer it as an adjunct to medication, not a replacement (APA 2020).

12.6 Supported housing and community support

Stable housing and assertive community follow-up are the structural components that hold the rest together. Supported housing provides secure accommodation with graded support, allowing patients to live in the community rather than in institutions, and is regarded as a core rehabilitation service though the formal evidence base is thinner than for the interventions above (Tasman 2015). Assertive community treatment (ACT) delivers care through a multidisciplinary team with a low caseload that takes services to the patient in their own setting rather than waiting for attendance; the original model recommended each team include a vocational rehabilitation expert and, ideally, peer support workers who are themselves patients in recovery (Killaspy & Rosen 2011, in Tasman 2015). ACT is targeted at the patients who use services most heavily and are hardest to engage, and it reduces hospitalisation and improves engagement (APA 2020, Statement 19). These community components cross-reference the practical management of the acute and first episode, developed in the first-episode management topic.

GOOD TO REMEMBER

- **Supported housing:** secure community accommodation with graded support; the feature is community living over institutional care; the first step is to match the level of support to the patient's assessed need.
- **Assertive community treatment (ACT):** multidisciplinary team, low caseload, care delivered in the patient's own setting; the discriminator is for the heaviest-service-using, hardest-to-engage patients; the first step is proactive outreach rather than clinic-based waiting (APA 2020).

12.7 Assessment of disability and needs

Rehabilitation is driven by a formal **assessment of disability and needs**, not by a generic package. The clinician profiles the patient's strengths and deficits across domains, self-care, social, occupational, cognitive, and their environmental supports and barriers, then works with the patient to set the goals that matter to them. A structured needs assessment such as the Camberwell Assessment of Need (CAN) is commonly used to map met and unmet needs across housing, occupation, social relationships and health so that resources are directed where the gap actually is (Tasman 2015). This assessment step is what makes rehabilitation individualised: the same diagnosis in two patients produces two different plans because their disabilities, environments and personal goals differ.

WORKED EXAMPLE

Two patients have identical residual schizophrenia. One lives with a supportive family and wants to return to a clerical job; his plan foregrounds supported employment (IPS) and cognitive remediation. The other is unemployed, socially isolated and disengaged from services; her plan foregrounds assertive community treatment, supported housing and social skills training. The needs assessment, not the diagnosis, generated two different rehabilitation plans (Tasman 2015).

12.8 Delivery: multidisciplinary, staged and individualised

Rehabilitation is delivered by a **multidisciplinary team**, psychiatrist, clinical psychologist, psychiatric social worker, occupational therapist, nurse and increasingly peer support workers, because no single discipline covers the range of components (Tasman 2015). It is **staged**: goals are matched to the phase of illness, with stabilisation and engagement first, then skills-building, then community integration and role resumption, so that a patient is not pushed into competitive employment before basic engagement is secure. And it is **individualised**: the plan is built around the specific goals and needs identified in assessment and revised as the patient progresses, which is exactly the recovery-model insistence that each person's recovery is a unique process (Anthony 1993, Tasman 2015). The examiner rewards the phrase "multidisciplinary, staged and individualised" as the delivery principle.

RULE **Deliver rehabilitation multidisciplinary, staged and individualised.** Assess needs first, match the component to the illness phase and the patient's own goals, and revise as they progress.

INDIA

Community rehabilitation in India runs largely through the District Mental Health Programme (DMHP), the service-delivery arm of the National Mental Health Programme, which integrates basic mental health care, including follow-up and community support, into the general health system at district level. The Indian Psychiatric Society (IPS) schizophrenia guideline endorses psychoeducation, family intervention and psychosocial rehabilitation as core components alongside pharmacotherapy, consistent with the international position, while recognising that formal supported-employment and assertive-community-treatment services are less widely available and that the family remains the principal locus of long-term community support in Indian practice.

GOOD TO REMEMBER

- **The principle:** medication treats symptoms, psychosocial rehabilitation treats disability and delivers function and recovery; both are core to the plan, offered from the start (Kaplan & Sadock 2024, APA 2020).
- **Recovery model:** personal recovery = hope, agency and a meaningful life beyond the illness (CHIME: Connectedness, Hope, Identity, Meaning, Empowerment); distinct from clinical remission (Anthony 1993).
- **Components of rehabilitation:** psychoeducation and family work; social-skills and vocational training (supported employment / IPS); cognitive interventions (remediation, CBTp); supported housing and community support (ACT).
- **Assessment and delivery:** formal assessment of disability and needs (for example CAN) drives an individualised plan delivered by a multidisciplinary team, staged to the phase of illness.

HOLD THIS

Medication controls symptoms but psychosocial rehabilitation delivers function and recovery, so it is a core not optional part of every plan: framed by the recovery model (hope, agency, a life beyond the illness), built from psychoeducation and family work, social-skills and vocational training, cognitive interventions, and supported housing and community support, driven by an assessment of disability and needs, and delivered multidisciplinary, staged and individualised.

13 · Psychoeducation and family interventions

Antipsychotic medication holds relapse at bay only while it is taken and only for the person prescribed it; the **psychoeducation** and **family intervention** topic is where the examiner tests whether you understand the *other half* of relapse prevention, the psychosocial half that acts on adherence and on the emotional climate the patient recovers into. Two ideas carry the page. The first is that giving the patient and the family an accurate model of the illness, its treatment and its early warning signs improves adherence and reduces relapse. The second is the **expressed emotion** story: families high in criticism, hostility or emotional over-involvement (a high-ee household) predict relapse, and a structured family intervention that educates, teaches communication and problem-solving and lowers that emotional temperature is one of the single best-evidenced psychosocial treatments in the whole of psychiatry (Companion 2010, APA 2020).

How to use this page. Fix the two levers separately: psychoeducation (an information and skills intervention for patient and family) and the expressed-emotion evidence base (why the family climate matters and how a structured family intervention modifies it). The illness itself, its phenomenology, aetiology, criteria and course, is not re-taught here; it belongs to the Schizophrenia: aetiology, phenomenology, classification and course notes, and this page assumes it. The trap the examiner is watching for is the reflex to *blame* the family: high expressed emotion is a target for support, not a fault, and the whole intervention is framed as helping relatives cope, never as accusing them of causing the relapse.

13.1 Psychoeducation: what it is and why it works

An information-and-skills intervention, not a leaflet. Psychoeducation is the systematic, planned delivery of information about the illness and its treatment to the patient and, where they

are involved, the family, combined with training in the skills to act on that information (APA 2020). The content that a good programme conveys is standardised: the diagnosis and symptoms, the rationale for medication and its adverse effects, stress and coping, the crisis plan, and above all the *early warning signs* of relapse and what to do when they appear (APA 2020, Bauml 2006). It is not a one-off handover of a pamphlet; it is delivered over multiple structured sessions, individually or in groups, often alongside family members, in a manner that aims to build hope, reassurance and a sense of mastery rather than simply reciting a prognosis.

Why it changes outcome. Psychoeducation reduces relapse and readmission principally by improving *adherence*, the single most common reversible cause of relapse, and by equipping patient and family to recognise an incipient relapse early enough to act (Xia 2011, APA 2020). Even relatively brief programmes, of ten sessions or fewer, reduce relapse rates over the following 9 to 18 months, an effect comparable to that of much lengthier treatment (Companion 2010, Pekkala 2002). In clinical trials a **12-session** programme is the usual format, with briefer courses of ten sessions or fewer also studied (APA 2020).

RULE **Teach the early warning signs.** The highest-yield content of any psychoeducation programme is the patient's and family's own relapse signature and the agreed action, because catching a relapse early is what converts information into prevented admission.

13.2 The early-warning-signs and adherence mechanism

Adherence is the proximal target. The reason psychoeducation earns its place in every guideline is mechanistic: relapse in schizophrenia is most often driven by stopping medication, and an accurate shared model of *why* the drug is needed (including that it is prophylactic, not merely symptomatic) is the most modifiable lever on adherence. The maintenance and adherence principles behind this sit in the maintenance topic; here the point is that psychoeducation is the intervention that operationalises them for the patient and the household. Behavioural techniques (cueing, packaging, reminders) improve adherence further and are complementary rather than alternative (Companion 2010).

TRAP **Do not front-load the worst prognosis onto a newly diagnosed patient.** Education can harm, particularly in the newly diagnosed hearing about poor outcomes, and family interventions can even raise expressed emotion in already low-expressed-emotion families; pitch the information to build coping, not despair (Companion 2010).

13.3 Expressed emotion: the construct and how it is measured

The emotional climate of the household, operationalised. Expressed emotion is a measured attribute of a key relative's attitude towards the patient, comprising three components: *critical comments*, *hostility* and *emotional over-involvement* (Companion 2010, Tasman 2015). A household is rated **high ee** if the relative exceeds threshold on criticism or shows hostility or marked emotional over-involvement; the shorthand that a family shows high criticism, hostility or emotional over-involvement is exactly the definition of a high-ee household. The reference instrument is the Camberwell Family Interview (Vaughn & Leff 1976), a semi-structured interview of the relative from which critical comments are counted and hostility and over-

involvement rated; the briefer Five Minute Speech Sample (Magana 1986) is the practical field alternative.

It predicts relapse across disorders, not only schizophrenia. High expressed emotion is a robust, replicated predictor of relapse in schizophrenia and, with an even larger effect, in mood and eating disorders (Butzlaff & Hooley 1998). Note the direction-of-causation caveat the examiner may probe: expressed emotion is partly a *response* of relatives to the difficulty of living with a severe illness, and high expressed emotion is less evident in relatives of first-episode than of multiply-relapsing patients, so it is best read as a modifiable relational risk marker rather than a simple external cause (Companion 2010).

Critical comments
Statements of dislike or disapproval of the patient's behaviour, counted over the interview; the commonest high-expressed-emotion component.

Hostility
Generalised rejection or criticism of the patient as a person rather than of a specific behaviour.

Emotional over-involvement
Over-protective, self-sacrificing or intrusively over-concerned attitudes, including excessive distress and over-identification with the patient.

13.4 The expressed-emotion evidence: Brown and the contact threshold

The founding observation. The classic prospective study is Brown et al (1972): patients recovering from an episode of schizophrenia who returned to live with a relative prone to make critical comments relapsed far more often over the following 12 months than those living with a more tolerant, accepting relative, **58% versus 16%** (Companion 2010). Two moderators emerged and are examinable. First, antipsychotic medication *buffered* the effect, so pharmacotherapy and family climate act on relapse together, not in competition. Second, the ill effect of high expressed emotion was mitigated when the patient was in face-to-face contact with the high-expressed-emotion relative for less than **35 hours** a week, so reduced contact, in effect a degree of social distance, was protective (Companion 2010). A later systematic review of 27 studies confirmed the effect as robust, strongest in chronic patients (Butzlaff & Hooley 1998).

58% vs 16%	<35 h/wk	27
RELAPSE AT 12 MO, HIGH VS LOW EE (BROWN 1972)	FACE-TO-FACE CONTACT THAT IS PROTECTIVE	STUDIES IN THE EE META-ANALYSIS (BUTZLAFF 1998)

13.5 Family intervention: the Leff trial and what it contains

Modifying the climate changes the relapse rate. If high expressed emotion drives relapse, then an intervention that lowers it should prevent relapse, and the landmark test is Leff et al (1982). Patients living in high-expressed-emotion households, all on depot antipsychotics, were randomised to routine care or to a package of factual education for the relatives, a relatives' group to share experience, and family sessions in the home aimed at reducing expressed emotion and face-to-face contact. At 9 months the relapse rate was **50% in controls versus 9%** in the treated group, and the only two treated patients who relapsed were those in whom neither expressed

emotion nor contact had actually fallen (Companion 2010). This both proved that a structured family intervention prevents relapse and reinforced that reduced expressed emotion and contact are the operative levers.

The three ingredients of a family intervention. A family intervention is systematic, extends well beyond simply conveying information, and is future- rather than past-focused (APA 2020). Every effective programme combines three elements: *education* about the illness and its treatment; *communication training* and structured *problem-solving* skills for the household; and explicit work to *lower expressed emotion* and stress and to strengthen support (APA 2020, Companion 2010). Across at least 25 trials these reliably reduce relapse; no single therapeutic model is clearly superior, which has led to the view that education may be the common active ingredient (Companion 2010, Pitschel-Walz 2001).

RULE **Offer family intervention wherever the patient is in ongoing contact with relatives.** A structured family intervention in a high-expressed-emotion household is one of the strongest relapse-prevention tools available and is guideline-recommended for any patient in regular family contact (APA 2020).

TRAP **Do not blame the family.** High expressed emotion is a target for support, not a fault; it is largely a coping response to a hard illness, and the intervention is framed as helping relatives cope, never as accusing them of causing the relapse.

13.6 Practical delivery: format, dose and duration

Single-family or multi-family, over months. Family interventions are delivered either as *single-family* work (one household, often including the patient, sometimes led by a member of the care team so a liaison develops between team, patient and relatives) or as *multi-family groups* that bring several families together and add mutual support and shared learning (APA 2020, McFarlane 2016). They are not brief: the benefit is greatest when more than **10** sessions are delivered over a period of at least **7 months** (APA 2020, McDonagh 2017). This "months, not weeks" dosing is a common examinable discriminator, distinguishing a genuine family intervention from a single family meeting.

FEATURE	PSYCHOEDUCATION	FAMILY INTERVENTION
Core aim	Accurate illness model, adherence, early warning signs	**Lower expressed emotion, add communication and problem-solving skills**
Recipient	Patient, and/or family	**Family (with or without the patient)**
Format	Individual or group; can be brief	**Single-family or multi-family group**
Typical course	About 12 sessions (10 or fewer also effective)	**More than 10 sessions over at least 7 months**
Chief benefit	Reduced relapse via adherence and early detection	**Reduced relapse and readmission; lower carer burden**

Psychoeducation and family intervention overlap in content but differ in target and dose; the family intervention is the longer, skills-based, expressed-emotion-lowering programme (APA 2020, Companion 2010).

The boundary condition. These approaches are by definition of no value to patients who have lost contact with family or do not wish relatives involved; conversely, provided the patient-directed intervention is comprehensive, formal family involvement is not always mandatory (Companion 2010, Pitschel-Walz 2001). Most patients, however, do want family involved (APA 2020).

13.7 The Indian family-centred setting

Family as co-therapist, not visitor. In Indian practice the patient overwhelmingly lives within, and is cared for by, the family, so the family is present, informed and involved as a matter of course rather than by special arrangement; this makes psychoeducation and family intervention the natural, high-value backbone of psychosocial care rather than an add-on. Delivering education to the whole household, using the family to supervise and support adherence, and coaching relatives to lower criticism and over-involvement fit the setting directly and are strongly endorsed by the Indian guideline (IPS 2025).

INDIA

The District Mental Health Programme (DMHP), launched in 1995 under the National Mental Health Programme, is the community delivery vehicle through which psychoeducation and family work reach patients at district level. Practical family-centred care leans on the co-resident family to hold adherence and watch for early warning signs. A widely taught cross-cultural observation is that Indian families of patients with schizophrenia tend to show lower rates of high expressed emotion than Western samples, offered as one contributor to the better course of schizophrenia reported in developing-country cohorts; treat the precise percentages as needing verification and hold the qualitative point.

GOOD TO REMEMBER

- **Psychoeducation:** planned information plus skills for patient and family (diagnosis, medication rationale, coping, and above all early warning signs); reduces relapse mainly by improving adherence; usual format about 12 sessions, briefer courses also effective; caveat, avoid front-loading the worst prognosis onto the newly diagnosed.
- **Expressed emotion (EE):** a rated relative attribute of critical comments, hostility and emotional over-involvement, measured by the Camberwell Family Interview or the Five Minute Speech Sample; high EE predicts relapse; caveat, it is a modifiable relational marker and partly a coping response, not a blame.
- **Family intervention:** a systematic programme of education plus communication and problem-solving skills plus expressed-emotion lowering; among the best-evidenced psychosocial relapse-prevention tools; dose to hold, more than 10 sessions over at least 7 months; single-family or multi-family group; caveat, offer wherever the patient is in ongoing family contact.

HOLD THIS

High expressed emotion (criticism, hostility, emotional over-involvement) predicts relapse; a structured family intervention that educates, teaches communication and problem-solving, and lowers expressed emotion is one of the best-evidenced psychosocial relapse-prevention treatments, dosed over months, not weeks.

14 · Social skills training and vocational rehabilitation

Pharmacotherapy controls positive symptoms but does little for the enduring **social and functional disability** that keeps people with schizophrenia out of relationships and work. The recovery-oriented plan therefore couples the antipsychotic with structured psychosocial rehabilitation, and two of its most exam-favoured components are social skills training and vocational rehabilitation. The illness itself, its negative-symptom and cognitive substrate, is owned by the Schizophrenia: aetiology, phenomenology, classification and course notes; here we take the deficits as given and ask how to remediate them behaviourally.

Why examiners love it. The single highest-yield fact is a paradigm shift: vocational rehabilitation moved from the old prevocational "train then place" ladder to the evidence-based supported employment "place then train" model, of which Individual Placement and Support (IPS) is the exemplar. Knowing which one wins, and why, separates a rehearsed answer from a vague one.

14.1 Social skills training: what it is

Definition. Social skills training is a structured, behavioural teaching method that breaks down conversational, self-care and community-living skills into components and trains them one at a time to counter the social deficits of schizophrenia (Companion to Psychiatric Studies; Kaplan & Sadock 2024). It is didactic and skills-focused, not insight-focused: the therapist teaches a discrete social behaviour the way a coach teaches a motor skill.

Targets. Typical goals are everyday behaviours a resident can name in a viva: making eye contact, smiling at appropriate times, actively listening, sustaining a conversation, assertiveness, and appropriate verbal and nonverbal communication, extending to self-care and independent community living (APA 2021).

14.2 The four learning steps: model, rehearse, feedback, reinforce

Mechanism. Social skills training is delivered through a repeating behavioural loop: **instruction and modelling** (the skill is demonstrated), **role-play and rehearsal** (the patient practises it), **corrective feedback and positive reinforcement** (performance is shaped), then **homework** to transfer the skill to real settings (APA 2021; Companion to Psychiatric Studies). It is usually run in a group format so members can practise on each other and receive social reinforcement.

MNEMONIC

M-R-F-G

Model the skill, **R**ehearse it in role-play, give **F**eedback and reinforcement, set **G**eneralisation homework. The four moving parts of every social skills training session.

14.3 Evidence and the honest limits of social skills training

What it does. Social skills training improves social function and can improve negative symptoms and core illness symptoms more than usual care, with reduced relapse and rehospitalisation in some studies (McDonagh et al. 2017, in APA 2021). **The limit.** The strength of evidence is modest, which is why the APA grades it a *suggestion*, not a strong recommendation (APA 2021), and skill gains generalise to daily life only if homework and in-vivo practice are built in. Frame it as a useful adjunct for the patient whose stated goal is better social functioning, not a stand-alone cure.

RULE **Skills are taught, not talked about.** Social skills training works through modelling, rehearsal, feedback and homework; a discussion group without behavioural rehearsal is not social skills training.

14.4 Vocational rehabilitation: the scale of the problem

Why it matters. Impaired work role is one of the most disabling features of schizophrenia, feeding poverty and loss of self-efficacy. In the United States fewer than **15%** of patients are employed, yet **50 to 75%** state that competitive employment is a primary goal (Kaplan & Sadock 2024). Vocational rehabilitation, the systematic effort to help the patient obtain and keep paid work, has always been a centrepiece of psychiatric rehabilitation, but the historically dominant approach was the wrong one.

<15%	50 to 75%	~40	2 to 3x
OF US PATIENTS EMPLOYED	WANT COMPETITIVE WORK	RCTS FAVOUR IPS	EMPLOYMENT RATE VS COMPARISON

The vocational gap and the evidence base for supported employment (Kaplan & Sadock 2024).

14.5 The paradigm shift: train then place versus place then train

The old model. Traditional vocational rehabilitation used **prevocational** "train then place" ladders: extensive pre-employment assessment, counselling, day centres, sheltered workshops and transitional employment intended to build the patient up to a presumed threshold of "work readiness" *before* any real job (Kaplan & Sadock 2024). Evaluations found these stepwise models did not improve competitive-employment rates; most patients became discouraged, disengaged or stalled in the preparatory phase.

The new model. From the late 1980s the field shifted to "place then train", termed supported employment: the patient is helped into a real competitive job first, with training and support delivered *on the job*. Anyone who wants to work is helped, without screening for readiness, and support continues once employed (Kaplan & Sadock 2024).

FEATURE	PREVOCATIONAL "TRAIN THEN PLACE"	SUPPORTED EMPLOYMENT "PLACE THEN TRAIN"
Sequence	Prepare, then place	**Place first, train on the job**
Readiness screen	Extensive pre-employment assessment	**Zero exclusion, no readiness screen**
Intermediate steps	Sheltered workshops, transitional work	None; direct to competitive job
Job type	Sheltered or preparatory	**Competitive, at or above minimum wage**
Support	Ends before real job	Ongoing follow-along, time-unlimited
Competitive-employment outcome	Not improved over usual care	**2 to 3 times higher**

The train-then-place to place-then-train shift; the evidence favours the right-hand column (Kaplan & Sadock 2024).

RULE **Place then train beats train then place.** Supported employment (IPS) achieves better competitive-employment outcomes than prevocational preparation for open-market work.

TRAP **Waiting for "work readiness".** Assuming a patient must be symptom-free before any vocational step contradicts the evidence; IPS uses zero exclusion and starts the job search regardless of residual symptoms.

14.6 Individual Placement and Support: the eight principles

What IPS is. IPS, also called evidence-based supported employment, is the manualised model of supported employment developed in the 1990s for severe mental illness (Kaplan & Sadock 2024). It emphasises the patient's own preferences, a rapid job search without lengthy pre-employment training, and individualised on-the-job support. Its eight fidelity principles are the examinable core.

Zero exclusion

Anyone who wants to work is helped, regardless of symptoms, cognition, work history or substance use.

Competitive employment

The goal is a real job in the open labour market, at or above minimum wage, not a sheltered post.

Rapid job search

Direct job seeking rather than lengthy assessment; a job is applied for within about 30 days, first job typically found within 4 months.

Job development

The employment specialist builds employer relationships to match jobs to the client's skills and preferences.

Integration with treatment

The employment specialist sits inside the clinical or ACT team, not in a separate agency.

Client preferences

Placements follow the patient's stated interests; preference-matched jobs last longer.

Ongoing support

Follow-along support is time-unlimited and continues after the patient is employed.

Benefits counselling

Individualised advice on how work affects welfare or disability benefits, to correct fears of losing them.

14.7 The evidence base for supported employment

Strength. Nearly **40** randomised controlled trials show IPS produces higher employment rates, greater earnings, more hours worked and longer job tenure; competitive-employment rates are **2 to 3 times** those of comparison vocational programmes (Kaplan & Sadock 2024). The European EQOLISE trial replicated the finding outside the United States, with over **50%** of patients working at some point during follow-up (Burns et al. 2007). **Safety.** High work expectations do *not* destabilise patients or raise relapse; employed patients report better self-esteem and quality of life (Kaplan & Sadock 2024). Interventions that do not target placement directly, including counselling and medication alone, have little effect on employment.

> **HOLD THIS**
> Supported employment, place then train (IPS), beats prevocational train-then-place for competitive work; its founding principle is zero exclusion, so you never wait for a patient to become symptom-free before starting the job search.

14.8 Place in the recovery-oriented plan

Integration, not sequence. Neither skills nor work is a graduation prize awarded after symptom control; both run alongside the antipsychotic as part of a recovery-oriented plan aimed at function and personal goals, not just symptom scores. Social skills training and vocational rehabilitation sit beside family psychoeducation, cognitive remediation and assertive community treatment; the employment specialist is embedded in the clinical team (Shorter Oxford Textbook of Psychiatry; Kaplan & Sadock 2024). Cognitive remediation and family intervention are covered in their own management topics; here the point is that vocational and social rehabilitation are woven into the same team, not bolted on afterwards.

14.9 The Indian context

Where the evidence meets Indian practice. Formal IPS supported-employment services are still scarce in India, and much community-based vocational rehabilitation runs through sheltered workshops, occupational-therapy units and, above all, family-supported work within the household or family business. The District Mental Health Programme under the National Mental Health Programme carries community rehabilitation intent, but competitive supported employment is far from routine. The examinable Indian answer holds two things at once: sheltered and family-supported work remain the realistic default here, while the guideline-level evidence still favours supported employment on the place-then-train model wherever it can be offered.

INDIA

Vocational rehabilitation in India leans on sheltered workshops and family-supported work embedded in the joint-family and small-business economy, with the District Mental Health Programme providing the community scaffold. State the local reality, then name supported employment (IPS) as the evidence-based direction of travel.

COMMON TRAP

Do not describe social skills training as a talking or support group. It is a behavioural teaching method: without modelling, role-play rehearsal, feedback and homework it is not social skills training, and the marks are in naming those components.

GOOD TO REMEMBER

- **Social skills training:** structured behavioural teaching of social, self-care and community-living skills; delivered by modelling, role-play rehearsal, feedback and homework, usually in a group; APA graded it a suggestion (2C) for the patient whose goal is better social functioning.
- **Vocational rehabilitation:** the systematic effort to help the patient obtain and keep paid work; the old prevocational "train then place" ladder (sheltered workshops, transitional employment) did not improve competitive-employment rates.
- **Supported employment:** the "place then train" model; help anyone who wants to work into a real competitive job first, with on-the-job support; the discriminator is zero exclusion and no readiness screen.
- **Individual Placement and Support (IPS):** the evidence-based manualised form of supported employment; eight principles (zero exclusion, competitive employment, rapid job search, job development, treatment integration, client preferences, ongoing support, benefits counselling); nearly 40 RCTs, 2 to 3 times higher employment than comparison; the caveat is that it needs the employment specialist embedded in the clinical team to work.

15 · CBT for psychosis and cognitive remediation

Why this matters. Two psychological therapies sit inside the schizophrenia treatment plan alongside the drug, and the examiner tests them precisely because a candidate who answers "management" with medication alone has answered half the question. **CBT for psychosis** works on the residual positive symptoms the antipsychotic leaves behind, the distress and conviction of persistent delusions and voices, while **cognitive remediation** works on the neurocognitive deficits, attention, memory and executive function, that no antipsychotic corrects. Both are guideline-endorsed adjuncts, both have modest and debated effect sizes, and the single commonest error is to confuse the two: CBTp is for symptom-related distress, remediation is for cognition.

The disorder itself, its phenomenology, aetiology, criteria and course, is owned by the Schizophrenia: aetiology, phenomenology, classification and course notes and is not re-taught here; the cognitive domain of the illness and the framing of cognition as a treatment target are developed there. What this topic teaches is the two therapies: what each is, what it targets, the size and the controversy of its evidence, and where each sits in the guidelines. We take **cognitive**

behaviour therapy for psychosis first, then cognitive remediation, then the discriminator that keeps them apart.

15.1 CBT for psychosis: what it is and what it targets

Cognitive behaviour therapy for psychosis (CBTp) is a structured, collaborative psychological therapy adapted from standard CBT for use with people who have psychotic symptoms. Its three signature moves are: it **normalises** psychotic experiences by placing them within a range of ordinary experience, for example hearing a loved one's voice in grief, so the experience is less alien and less frightening; it helps the patient **test the evidence** for delusional beliefs, guiding them to generate their own healthier and more realistic alternative explanations rather than the clinician arguing the delusion down; and it works to **reduce the distress and the impact** of persistent positive symptoms and to improve functioning, using behavioural self-monitoring, coping strategies and graded task assignment (APA 2020, Kingdon & Turkington 2019). The therapeutic stance is deliberately non-judgemental and non-confrontational: the target is not the belief's truth-value in the abstract but the patient's distress, appraisal and conviction, so cbtp is offered as an adjunct to medication for persistent distressing symptoms, never as a replacement for it (APA 2020).

RULE **CBTp is an evidence-based adjunct for persistent distressing symptoms, not a replacement for medication.** It runs alongside the antipsychotic, working on distress, appraisal and conviction, never instead of the drug.

15.2 The evidence base and the guideline position

CBTp is a recommended psychological intervention across guidelines. The APA gives it a strong recommendation, "APA recommends that patients with schizophrenia be treated with cognitive-behavioral therapy for psychosis", rated 1B (APA 2020, Statement 16), and NICE recommends offering CBTp to everyone with schizophrenia, with a suggested minimum of **16 sessions** (NICE 2014, in APA 2020). The pivotal meta-analysis behind the symptom claim is Jauhar and colleagues' review of **34 randomised controlled trials**, which found CBTp more effective than usual care on overall symptoms measured on the PANSS and BPRS, with a standardised mean difference of **-0.33** (95% CI -0.47 to -0.19) (Jauhar et al. 2014, in APA 2020). CBTp also improves global, social and occupational functioning in the short term, up to about **6 months**, but these functional gains are generally not maintained beyond that once the course ends (McDonagh et al. 2017, in APA 2020). CBTp can be delivered individually or in groups, in any setting and any phase, though some initial symptom reduction usually helps the patient engage.

15.3 The modest effect size and the debate over it

The effect size is real but modest, and it is genuinely contested, which the examiner rewards a candidate for knowing. Two points anchor the controversy. First, the magnitude: an SMD of about -0.33 for overall symptoms is a small effect, and the APA itself rates the strength of evidence only as moderate for the outcomes that show a benefit and low or insufficient for the rest, with essentially no meaningful effect on negative symptoms (APA 2020). Second, the sensitivity to blinding: the symptom effect is smaller, though it remains statistically significant,

when the analysis is restricted to trials with blinded outcome assessment (95% CI -0.27 to -0.03), and at least one meta-analysis raised the possibility of publication bias (Jauhar et al. 2014, in APA 2020). The honest summary for a viva is that CBTp produces a small, blinding-sensitive improvement in positive symptoms and short-term function, that it is safe with minimal harms, and that it therefore earns its place as an adjunct even though its effect is modest and disputed rather than large and settled.

-0.33	34	16
CBTP OVERALL-SYMPTOM SMD (JAUHAR 2014)	RCTS IN THE CBTP META-ANALYSIS	MIN SESSIONS SUGGESTED (NICE)

The high-yield numbers for CBTp: a small, blinding-sensitive symptom effect, from a large but heterogeneous evidence base, delivered over a defined minimum course.

GOOD TO REMEMBER

- **CBT for psychosis (CBTp, cognitive behaviour therapy for psychosis):** what it is, a structured collaborative therapy that normalises psychotic experiences, tests the evidence for delusional beliefs and reduces the distress and impact of persistent positive symptoms; the discriminator, it targets symptom-related distress and conviction, not neurocognition; the first step, offer it as an adjunct to medication for persistent distressing symptoms, never as a replacement (APA 2020, Statement 16, recommends 1B).

15.4 Cognitive remediation: what it is and what it targets

Cognitive remediation (also called cognitive remediation therapy, CRT) is a behavioural, training-based intervention that targets the neurocognitive deficits of schizophrenia directly: attention, memory, executive function, and increasingly social cognition and metacognition, with the goal of durable and generalisable improvement (Wykes & Spaulding 2011, in Tasman 2015). The analogy Tasman uses is physiotherapy after a broken leg: the skill lost to the illness is regained through structured exercise. It is delivered individually or in groups, increasingly computer-assisted, and comes in two methodological flavours: **drill and practice**, which teaches a skill through repetition alone, and **drill and practice plus strategy**, which adds explicit learning of strategies to bypass a specific cognitive limitation (Tasman 2015). It is distinct from cognitive compensation or adaptation, which does not try to repair the deficit but supplies external aids such as calendars, alarms and checklists, the "glasses for vision" approach. This cross-references the cognitive domain and the framing of cognition as a core treatment target developed in the Schizophrenia: aetiology, phenomenology, classification and course notes.

15.5 Cognitive remediation: effect on cognition and transfer to function

The evidence is best summarised as a small-to-moderate effect on cognition that transfers to real-world function best when the training is paired with broader rehabilitation. The landmark meta-analysis is McGurk and colleagues', **26 randomised controlled trials** in **1,151 patients**, which concluded that cognitive remediation produces moderate improvements in neurocognitive performance and, critically, that functional outcomes improve when the remediation is combined with psychiatric rehabilitation (McGurk et al. 2007, in Kaplan & Sadock 2024). The APA echoes this: cognitive remediation gives moderate improvement in specific aspects of cognition and small positive effects on social, occupational and global function, with the psychosocial benefit

"particularly robust when cognitive remediation is used as a component of or adjunct to other forms of psychiatric rehabilitation rather than being delivered as a stand-alone intervention" (APA 2020, Statement 22). The caution is real: some gains reflect practice on the trained tasks and may not generalise, so drill without transfer is a known failure mode. This is exactly why the guideline pairs it with rehabilitation and why the APA rates it a suggestion, 2C, rather than a strong recommendation (APA 2020).

TRAP **Expecting cognitive remediation to transfer to function without pairing it with rehabilitation.** Drill alone can improve the trained task and still leave real-world function untouched; the functional gain comes when remediation is embedded in rehabilitation.

26	1,151	2C
RCTS IN THE REMEDIATION META-ANALYSIS	PATIENTS POOLED (MCGURK 2007)	APA STRENGTH FOR REMEDIATION (SUGGESTS)

Cognitive remediation: a moderate cognitive effect from a sizeable evidence base, carried to a weaker guideline recommendation because functional transfer depends on pairing with rehabilitation.

GOOD TO REMEMBER

- **Cognitive remediation (cognitive remediation therapy, CRT):** what it is, drill-and-strategy training of the neurocognitive deficits (attention, memory, executive function); the discriminator, it targets cognition, not the distress of delusions or voices, with a small-to-moderate effect on cognition; the first step, pair it with psychiatric rehabilitation so the cognitive gain transfers to function rather than staying on the trained task (Wykes et al. 2011, APA 2020, Statement 22, suggests 2C).

15.6 Keeping the two apart: the exam discriminator

The single most examined point is the clean separation of the two therapies by their target. CBTp targets the **distress, appraisal and conviction** of persistent positive symptoms, the residual delusions and hallucinations; cognitive remediation targets **neurocognition**, the attention, memory and executive-function deficits that predict functional outcome and respond poorly to drugs. They are not interchangeable and they are not competitors: a single patient with distressing residual voices and marked cognitive impairment can appropriately receive both, each aimed at a different problem. A useful contrast table anchors the discriminator for recall.

FEATURE	CBT FOR PSYCHOSIS (CBTP)	COGNITIVE REMEDIATION (CRT)
Primary target	**Distress and appraisal of persistent positive symptoms**	**Neurocognitive deficits: attention, memory, executive function**
Core method	Normalise, test the evidence for beliefs, reduce distress and impact	Drill and practice, or drill plus strategy training
Effect size	Small, blinding-sensitive (SMD about -0.33 on symptoms)	Small-to-moderate on cognition; functional transfer needs rehab
APA guideline strength	**Recommends (1B)**	**Suggests (2C)**
Key caveat	Modest and debated; not a replacement for medication	Gains may not generalise unless paired with rehabilitation

The clean split the examiner tests: CBTp for symptom-related distress, remediation for cognition; both adjuncts to medication, neither a substitute.

15.7 Placement in the plan and delivery

Both therapies are adjuncts layered onto the pharmacological plan, not alternatives to it. CBTp can be started in any phase and any setting, but usually needs some initial symptom reduction for the patient to engage, and requires a therapist with proper CBTp training and supervision; the commonest real-world barrier is simply availability of trained staff (APA 2020). Cognitive remediation is best placed inside a broader rehabilitation package rather than run alone, for the transfer reason above, and its main barrier is again programme availability, which online and computer-assisted delivery is beginning to address (APA 2020). Both fold into the psychosocial rehabilitation plan whose principles and other components, family work, supported employment, assertive community treatment, are developed in the psychosocial rehabilitation topic. Where medication resistance is the driver, the review of psychosocial treatments, including whether CBTp has been offered, is an explicit step in the treatment-resistant pathway (APA 2020).

INDIA

The Indian Psychiatric Society schizophrenia guideline endorses structured psychosocial interventions, psychoeducation, family intervention and rehabilitation, as core components of care alongside pharmacotherapy, consistent with the international position. In Indian practice, formal CBTp and structured cognitive-remediation programmes are far less widely available than antipsychotic treatment and family-based support, so the realistic plan for most settings foregrounds medication, psychoeducation and family work, with CBTp and remediation offered where a trained therapist and a rehabilitation programme actually exist rather than assumed to be universally accessible.

PEARL

The tidiest way to hold the pair: **CBTp changes how the patient relates to the symptom; remediation changes the machinery underneath.** One works on the distress and conviction of a delusion or voice, the other exercises attention, memory and executive function. Neither replaces the antipsychotic, and remediation only reaches function when it rides on rehabilitation.

HOLD THIS

CBT for psychosis is an evidence-based adjunct that normalises psychotic experiences, tests the evidence for delusions and reduces the distress of persistent positive symptoms, with a small blinding-sensitive effect (recommended, APA 1B); cognitive remediation drills attention, memory and executive function with a small-to-moderate cognitive effect that transfers to function only when paired with rehabilitation (suggested, APA 2C); both are adjuncts to medication, never replacements, and the discriminator is target, distress for CBTp, cognition for remediation.

16 · Community models and the Indian services

Why this matters. Once the acute episode is treated and the patient is discharged, the question the examiner asks is not "which drug" but "who delivers care, where, and to whom". **Community psychiatry** is the answer: a shift of the locus of care from the mental hospital to the patient's own setting, and the models that operationalise it. The two testable ideas are a Western service model, **assertive community treatment** and the case-management family that sits around it, and the Indian service architecture built on the National Mental Health Programme and its **district mental health** arm. A management answer that names the drug but cannot name the service that keeps a disengaged patient in treatment has answered only half the question.

This topic teaches the service scaffolding, not the illness. The phenomenology, aetiology, criteria and course of schizophrenia are owned by the Schizophrenia: aetiology, phenomenology, classification and course notes and are not re-taught here; the individual rehabilitation components (supported employment, social skills training, cognitive remediation) sit in the psychosocial rehabilitation topic. What this topic adds is the *delivery vehicle*: how care is organised as a team, a caseload and a district-level programme. We take assertive community treatment first, then case management, then the Indian models, then telepsychiatry and the non-governmental sector.

16.1 Assertive community treatment: the team that goes to the patient

Assertive community treatment (ACT) is a community-care model in which a **multidisciplinary team** delivers treatment, rehabilitation and support directly in the patient's own environment rather than waiting for the patient to attend a clinic (Kaplan & Sadock 2024). Its defining features are a **low, shared caseload**, **assertive outreach**, services provided directly by the team rather than brokered out, time-unlimited care and around-the-clock coverage. The caseload per worker is **about ten to fifteen**, in deliberate contrast to standard case management, and the caseloads are shared across the whole team rather than held by one clinician, so care continues when any one worker is away (Tasman 2015). K&S describe ACT as a program with mobile mental-health teams providing an array of treatment, rehabilitation and housing services available 24 hours a day, whose goal is to keep the person with serious mental illness out of hospital and functioning in the community (Kaplan & Sadock 2024).

The target is not everyone. ACT is reserved for the **most disabled, hardest-to-engage and most frequently-admitted** patients, the "revolving-door" group, for whom ordinary clinic-based follow-up repeatedly fails. In this group ACT reliably **reduces admissions and improves**

engagement and adherence, and it improves housing stability, employment, quality of life and satisfaction; where its outcomes have been compared head-to-head with intensive case management the clinical differences are small, so the benefit is largely about engagement and reduced hospital use rather than symptom change (Tasman 2015). The APA guideline recommends ACT specifically for patients with a history of poor engagement leading to frequent relapse or homelessness (APA 2020, Statement 19).

RULE **Assertive community treatment targets the high-need, frequently-admitted patient, not everyone.** Low shared caseload plus assertive outreach is a scarce, intensive resource aimed at the disengaged revolving-door group; it reduces admissions and improves engagement.

TRAP **Transplanting a Western caseload model without adapting it to the Indian family-and-district reality.** A 24/7 team-based, low-caseload service is resource-heavy; in India the family is the de-facto case manager and the district is the unit of delivery, so the model must be adapted, not copied.

16.2 Case management and its models: broker versus clinical/intensive

Case management is the broader family of models for coordinating care across services for a person with serious mental illness; ACT is best understood as its most intensive, team-delivered form. The models differ mainly in who does the work and how large the caseload is.

MODEL	HOW CARE IS DELIVERED	CASELOAD / TARGET
Broker case management	Case manager **arranges and links** the patient to services (assesses, refers, coordinates) but does not deliver clinical care directly; the thinnest model	Large caseload; the classic "broker" who brokers services out
Clinical case management	Case manager also **provides direct clinical care** (therapy, monitoring, medication support) as well as coordinating services	Moderate caseload; care not brokered out
Intensive case management (ICM) / intensive clinical case management (ICCM)	Clinical case management at **low caseload**; the case manager does *not* share the caseload (the point that separates it from ACT)	Caseload low, similar to ACT
Standard case management (SCM)	Conventional coordinated follow-up	Caseload **30 to 35 patients** per worker
Assertive community treatment (ACT)	Multidisciplinary team, direct care, assertive outreach, 24/7, **shared** caseload	Caseload **about ten to fifteen**; heaviest-service-using group

The case-management spectrum: from the broker who only links, through clinical and intensive models, to team-based ACT. The two exam discriminators are caseload size (ACT about ten to fifteen versus standard 30 to 35) and whether the caseload is shared (ACT) or held individually (ICCM).

The single line to hold: **ACT differs from intensive clinical case management chiefly in that ACT shares the caseload across a team while ICCM does not**, and both differ from standard case management by a much lower caseload (Tasman 2015). The broker model, which only

assesses and refers without delivering care, is the weakest and is largely superseded by clinical and assertive models.

16.3 The Indian frame: the National Mental Health Programme and community psychiatry

The Indian service architecture is not built on ACT teams but on a public-health, decentralised model. The National Mental Health Programme (NMHP) was launched in **1982** with three objectives: to ensure availability and accessibility of minimum mental-health care for all, to encourage application of mental-health knowledge in general health care and social development, and to promote community participation in mental-health service development. Its governing idea is **integration of basic mental-health care into general (primary) health care** delivered by trained non-specialist personnel, because specialist psychiatrists are far too few to reach the population directly. This is **community psychiatry** in the Indian public-health sense: not a mobile specialist team, but mental-health care pushed down the existing primary-care system.

INDIA

The District Mental Health Programme (DMHP), use "district mental health", was launched in **1995** as the delivery component of the NMHP, decentralising care to the **district** as the operational unit. Its prototype was the **Bellary model** in Karnataka (started 1985, catering to a population of about 1.5 million), which demonstrated that trained primary-care staff could deliver mental-health care at the district and primary-health-centre level. Successive plans expanded the DMHP across districts. The DMHP, use "dmhp", is the answer the examiner wants to the question "how does India decentralise psychiatric care", and it is the Indian analogue of the community-service question that ACT answers in the West.

16.4 The Indian service settings: day care and the halfway home

Within community psychiatry, Indian rehabilitation spans a graded ladder of settings "in a living, learning or working environment ranging from the inpatient psychiatric unit to day-care hospitals and half-way homes". Two of these settings are named service devices the examiner tests.

Day care centre / day hospital

A non-residential setting the patient attends during the day for supervised treatment, activity and rehabilitation, returning home at night; it delivers structured care and monitoring without the cost and dependency of an inpatient bed, and bridges the gap between the ward and full community living.

Halfway home

A supported, transitional residential facility for the patient who is no longer acutely ill but not yet ready for fully independent living; it provides supervised accommodation and rehabilitation "halfway" between hospital and home, rebuilding self-care, social and occupational skills before discharge to the community.

The phrase to reproduce is that the day care, use "day care", centre and the halfway home, use "halfway home", occupy the middle of the rehabilitation ladder: more support than living at home, less restriction than a hospital ward. In Indian practice, where families are usually

available, these settings are often used to give the family respite and the patient graded exposure to community demands rather than as permanent placements.

16.5 Telepsychiatry and the non-governmental sector in India

Two features are specific to how community care is actually extended in India. **Telepsychiatry**, the delivery of psychiatric assessment and follow-up over a video/telecommunication link, is a strategy to overcome the severe shortage and uneven distribution of psychiatrists across a large, largely rural population: it lets a specialist in a medical college support a distant district or primary-health-centre team, and it is increasingly written into the DMHP and formalised through national telepsychiatry guidance. It extends specialist reach without moving the specialist, which is exactly the constraint the Indian system faces. **Non-governmental-organisation (NGO)-run rehabilitation** supplies much of the day-care, halfway-home, vocational and community-support capacity that the public sector cannot fully staff; voluntary agencies and self-help/family organisations are an explicit part of the NMHP's community-participation objective and, in practice, carry a large share of psychosocial rehabilitation in India. For the examiner, telepsychiatry and NGO-run rehabilitation are the two adaptations that make a Western community model workable in the Indian setting.

> **PEARL**
>
> The Western question "which community team?" and the Indian question "how do we reach the district?" are answered differently: ACT is a low-caseload specialist team that goes to the patient; the DMHP is a decentralised public-health programme that pushes care into primary care, backed by telepsychiatry for specialist reach and NGOs for rehabilitation capacity. Name the right model for the setting the examiner specifies.

16.6 Putting the models together: what to say in a management answer

In a discharge or long-term-management answer, the community-services paragraph should do three things. First, **match intensity to need**: reserve assertive community treatment (and its low, shared caseload) for the frequently-admitted, disengaged patient, and use ordinary or clinical case management for the rest. Second, **name the Indian delivery frame**: the National Mental Health Programme and its District Mental Health Programme decentralising care to the district and primary-health-centre level within community psychiatry, with the day care centre and halfway home as graded transitional settings. Third, **name the two Indian force-multipliers**: telepsychiatry to extend scarce specialist reach and NGO-run rehabilitation to supply community capacity, both leaning on the family as the ever-present real-world case manager. The ECT question for treatment-resistant or catatonic cases belongs to the ECT and neurostimulation notes and is not part of the community-services answer.

GOOD TO REMEMBER

- **Assertive community treatment (ACT):** what it is, a multidisciplinary team delivering care in the patient's own setting with assertive outreach; caseload about ten to fifteen, shared across the team, 24/7; the one thing to hold, it is for the most disabled and frequently-admitted patients and it reduces admissions and improves engagement (not for everyone) (Kaplan & Sadock 2024, Tasman 2015, APA 2020).
- **Case management (broker vs clinical/intensive):** what it is, coordination of care across services; the discriminator, the broker only links and refers, the clinical model also delivers care, and intensive/ACT run at low caseload; the one thing to hold, ACT shares the caseload while intensive clinical case management does not, and standard case management runs at 30 to 35 patients per worker (Tasman 2015).
- **National Mental Health Programme (NMHP):** what it is, India's 1982 programme to integrate mental-health care into general health care; the one thing to hold, its method is decentralisation and community participation, not specialist expansion.
- **District Mental Health Programme (DMHP):** what it is, the 1995 delivery arm of the NMHP decentralising care to the district; the discriminator, prototype was the Bellary model in Karnataka (1985); the one thing to hold, the district and primary-health-centre are the unit of delivery.
- **Day care centre:** what it is, non-residential daytime supervised treatment and rehabilitation with the patient going home at night; the one thing to hold, it bridges ward and community without an inpatient bed.
- **Halfway home:** what it is, supported transitional residential living between hospital and independent home; the one thing to hold, it rebuilds skills before full discharge and gives the family graded handover.
- **Telepsychiatry and NGO-run rehabilitation:** what they are, video-link specialist care and voluntary-sector rehabilitation capacity; the one thing to hold, they are the Indian adaptations that overcome specialist shortage and staffing gaps, working with the family as case manager.

HOLD THIS

Assertive community treatment is a low-caseload (about ten to fifteen, shared) multidisciplinary team with assertive outreach reserved for the most disabled, frequently-admitted patients, reducing admissions and improving engagement; India delivers community psychiatry instead through the National Mental Health Programme (1982) and its District Mental Health Programme (1995, Bellary prototype) decentralising care to the district, including the day care centres, halfway homes, telepsychiatry and NGO-run rehabilitation, and the family as the real case manager.

Antipsychotic adverse effects and emergencies

17 · Extrapyramidal side effects

Why this matters. The extrapyramidal side effects, the eps, are the signature motor toxicity of dopamine D2 blockade in the **nigrostriatal pathway**, and the examiner tests them in one disciplined way: by their onset timeline. The single most reliable way to tell the three acute reactions apart, and to separate them from the delayed one, is when they appear after the drug is started or the dose is raised. Acute dystonia strikes in hours, akathisia in days, drug-induced parkinsonism in weeks, and tardive dyskinesia only after months to years (Maudsley 2021,

Kaplan & Sadock 2024). Get the clock right and the diagnosis, and usually the management, follows.

This topic teaches the three acute-to-subacute reactions with their timing, features and first management step; tardive dyskinesia (months to years) is developed in the next topic. The receptor and pathway mechanics of D2 blockade are not re-derived here (they are owned by the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes); the illness itself is owned by the Schizophrenia: aetiology, phenomenology, classification and course notes. Here we apply the pharmacology at the bedside. The one governing sentence: eps come from too much nigrostriatal D2 blockade, and their timing is diagnostic.

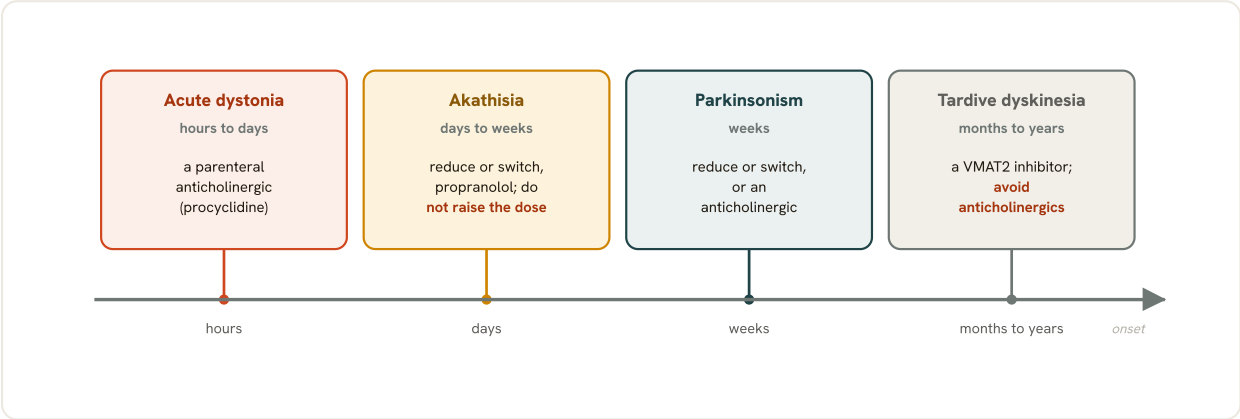


Fig 9.10 The extrapyramidal timeline, ordered by onset. Acute dystonia strikes in hours, akathisia in days, parkinsonism in weeks, and tardive dyskinesia after months to years. The management differs: an anticholinergic helps dystonia and parkinsonism but worsens tardive dyskinesia, akathisia is treated by reducing the dose and never by raising it, and established tardive dyskinesia responds to a VMAT2 inhibitor.

17.1 The unifying mechanism and the onset timeline

All the classical eps arise from blockade of dopamine D2 receptors in the nigrostriatal pathway, which shifts the striatal dopamine-acetylcholine balance toward relative cholinergic excess (Stahl 2021). This is why the acute reactions are commonest with high-potency first-generation agents (haloperidol) at higher D2 occupancy, and why anticholinergic drugs relieve dystonia and parkinsonism. The four disorders are best learned as points on a single clock measured from starting the drug or raising the dose: acute dystonia within hours to a few days, akathisia within days to weeks, drug-induced parkinsonism within weeks, and tardive dyskinesia only after months to years (Maudsley 2021). The timeline is the spine of the whole topic and the fastest route to the answer in a viva.

RULE **Timing dates the reaction.** Acute dystonia is hours, akathisia is days, parkinsonism is weeks, and tardive dyskinesia is months to years; when in doubt, put the reaction on the clock from the last dose change.

17.2 Acute dystonia: sustained spasm within hours

Acute dystonia is a sustained, often painful muscle spasm that appears within hours of starting a high-potency antipsychotic, or within minutes if the drug is given intramuscularly or intravenously (Maudsley 2021). The spasm is of any muscle group but the classic sites are the eyes rolling upward (oculogyric crisis), the head and neck twisted to one side (torticollis), the jaw,

tongue and pharynx (impairing speech and swallowing), and, most dangerously, the larynx (laryngeal dystonia), which can threaten the airway. In extreme cases the back arches (opisthotonos). It is commonest in young men who are antipsychotic-naive and on a high-potency agent (Maudsley 2021, Kaplan & Sadock 2024). It is frightening, and because patients often report it as an allergy, it drives non-adherence unless explained.

Management. The first step is a parenteral anticholinergic, given intramuscularly or intravenously because the patient may be unable to swallow. Benztropine **1 to 2 mg** IM or IV, or an antihistaminic-anticholinergic such as diphenhydramine **50 mg** IM or IV, or promethazine, produces rapid relief; the response to the intravenous route is seen within about 5 minutes and to the intramuscular route within about 20 minutes (Kaplan & Sadock 2024, Maudsley 2021). Laryngeal dystonia is an emergency and is treated at once. After the acute episode, reduce the dose or switch to a lower-potency or second-generation agent, and consider short-term prophylactic anticholinergic cover if a high-potency first-generation drug must continue.

GOOD TO REMEMBER

- **Acute dystonia:** feature, sustained painful spasm (oculogyric crisis, torticollis, jaw, tongue, laryngeal); discriminator, onset within hours to days, young man on a high-potency agent, and the muscle is held in spasm rather than restless or tremulous; first management step, parenteral anticholinergic (benztropine 1 to 2 mg IM/IV, or diphenhydramine 50 mg, or promethazine), treating laryngeal dystonia as an emergency.

17.3 Akathisia: inner restlessness within days to weeks

Akathisia, from the Greek meaning "never to sit down", is a subjective, unpleasant inner restlessness with a compulsion or urge to move, appearing within days to weeks of starting the antipsychotic or increasing the dose (Kaplan & Sadock 2024, Maudsley 2021). The subjective dysphoria is the core; the objective signs are foot-stamping when seated, constantly crossing and uncrossing the legs, rocking from foot to foot when standing, and pacing. It is genuinely distressing and is an established suicide-risk factor, having been linked to suicidal ideation and to aggression (Maudsley 2021). Its great danger is diagnostic: it is readily mistaken for psychotic agitation, and if the antipsychotic is then raised the akathisia worsens.

Management. The principle is the opposite of raising the drug. Reduce the antipsychotic dose, or switch to an agent with a lower liability for akathisia (olanzapine, quetiapine and clozapine carry the lowest risk; haloperidol among the highest); add a beta-blocker, low-dose propranolol **30 to 80 mg/day**, which is the most commonly used adjunct, or a benzodiazepine such as clonazepam or lorazepam (Kaplan & Sadock 2024, Maudsley 2021). Anticholinergics are generally unhelpful for pure akathisia unless it is part of a wider eps spectrum (Maudsley 2021). Critically, do NOT raise the antipsychotic.

TRAP **Treating akathisia as psychotic agitation and raising the antipsychotic.** The extra dose worsens the very restlessness it was meant to calm; when a patient becomes more agitated after a dose increase, think akathisia and go down, not up.

GOOD TO REMEMBER

- **Akathisia:** feature, subjective inner restlessness with an urge to move plus observable pacing, rocking and leg-crossing; discriminator, onset within days to weeks, dysphoric and worse after a dose increase (unlike agitation, which the drug should calm), and a recognised suicide-risk factor; first management step, reduce the dose or switch, add propranolol 30 to 80 mg/day or a benzodiazepine, and never raise the antipsychotic.

17.4 Drug-induced parkinsonism: bradykinesia, rigidity and tremor within weeks

Drug-induced parkinsonism (pseudoparkinsonism) is the antipsychotic-induced triad of bradykinesia, rigidity and tremor, appearing days to weeks after starting the drug or raising the dose (Maudsley 2021). Bradykinesia gives decreased facial expression, a flat monotone voice, slow movement and difficulty initiating movement; there may be bradyphrenia (slowed thinking), a coarse resting tremor and increased salivation. It is more common in the elderly, in women and in those with pre-existing neurological damage (Maudsley 2021). The examiner's favourite point is that its mask-like face, monotone and slowness are readily mistaken for depression or for the negative symptoms of schizophrenia, so it is under-recognised.

Management. Reduce the antipsychotic dose, switch to an agent with a lower propensity for parkinsonism (a second-generation agent such as quetiapine or olanzapine), or add an anticholinergic such as trihexyphenidyl **2 to 10 mg/day** or benztropine (Maudsley 2021, Kaplan & Sadock 2024). Most patients do not need long-term anticholinergics; review the need at least every 3 months, and do not dose them at night, since symptoms are usually absent during sleep (Maudsley 2021).

GOOD TO REMEMBER

- **Drug-induced parkinsonism:** feature, bradykinesia, rigidity and tremor with mask-like face and monotone voice; discriminator, onset within weeks, symmetrical, and easily mistaken for depression or negative symptoms (so it is under-recognised); first management step, reduce the dose or switch to a lower-eps agent, or add an anticholinergic (trihexyphenidyl 2 to 10 mg/day or benztropine), reviewed at least every 3 months.

17.5 Putting the reactions side by side

The table sets the acute-to-subacute eps against the delayed reaction on the four axes an examiner tests: effect, onset, features and management. Read the onset column downward as the clock that dates the diagnosis. Tardive dyskinesia is included only to complete the timeline; its phenomenology and treatment are developed in the next topic.

EFFECT	ONSET	FEATURES	MANAGEMENT
Acute dystonia	**Hours to days (minutes if IM/IV)**	Sustained spasm: oculogyric crisis, torticollis, laryngeal; young men, high-potency agent	Parenteral anticholinergic (benztropine 1 to 2 mg IM/IV, diphenhydramine 50 mg, or promethazine)

EFFECT	ONSET	FEATURES	MANAGEMENT
Akathisia	**Days to weeks**	Subjective inner restlessness, urge to move, pacing; distressing, suicide-risk factor	Reduce dose or switch; propranolol 30 to 80 mg/day or a benzodiazepine; NOT raising the antipsychotic
Drug-induced parkinsonism	**Weeks**	Bradykinesia, rigidity, tremor; mask-like face, monotone; mimics depression/negative symptoms	Reduce dose, switch to lower-eps agent, or anticholinergic (trihexyphenidyl 2 to 10 mg/day, benztropine)
Tardive dyskinesia	**Months to years**	Choreoathetoid orofacial and limb movements; developed in the next topic	Withdraw anticholinergic, reduce or switch (clozapine best supported), VMAT2 inhibitor; see next topic

The eps by onset timeline: hours (dystonia), days (akathisia), weeks (parkinsonism), months to years (tardive dyskinesia), the clock that dates the diagnosis.

17.6 India and practical points

The acute anticholinergics used for dystonia and parkinsonism are cheap and available in Indian practice: trihexyphenidyl (benzhexol) is the everyday oral anticholinergic, and promethazine and diphenhydramine cover the parenteral acute-dystonia need where injectable benztropine is not stocked. High-potency first-generation agents remain in wide use on cost grounds, so acute dystonia in a young man on injectable haloperidol (marketed as Serenace) is a scenario a resident will actually meet. Among the second-generation agents, verified Indian brands include olanzapine as Oleanz and quetiapine as Qutipin, the two lower-akathisia switch options; risperidone (marketed as Sizodon) is intermediate.

INDIA

For acute dystonia where injectable benztropine is unavailable, parenteral promethazine or diphenhydramine is the practical Indian substitute, and oral trihexyphenidyl (benzhexol) is the workhorse for drug-induced parkinsonism. Because high-potency first-generation agents such as haloperidol (Serenace) stay in routine use, keep a parenteral anticholinergic readily to hand when starting them, especially in a young, antipsychotic-naive man.

17.7 The one distinction that decides management

The whole topic reduces to reading the movement and the clock together, because the two errors that hurt patients are opposite in direction. Miss akathisia behind "psychotic agitation" and you raise the drug and make it worse; miss parkinsonism behind "depression or negative symptoms" and you under-treat a reversible motor effect. Both are avoided by asking, first, when did this start relative to the last dose change, and second, is the patient restless-and-driven (akathisia), spasm-held (dystonia) or slow-and-stiff (parkinsonism). That single discrimination, plus the onset clock, is what the examiner is testing.

Hours	Days to weeks	Weeks	30 to 80 mg/day
ACUTE DYSTONIA ONSET	AKATHISIA ONSET	PARKINSONISM ONSET	PROPRANOLOL FOR AKATHISIA

HOLD THIS

Date the reaction by the clock from the last dose change: acute dystonia in hours (parenteral anticholinergic), akathisia in days (reduce or switch, add propranolol, never raise the drug), parkinsonism in weeks (reduce, switch or anticholinergic), tardive dyskinesia in months to years.

18 · Tardive dyskinesia

Why this matters. **Tardive dyskinesia** is the adverse effect that most defines the long-term risk of antipsychotic prescribing, and the examiner returns to it because it inverts the logic that governs the acute movement disorders. Where acute dystonia, parkinsonism and akathisia arrive early and are eased by lowering dopamine blockade or adding an anticholinergic, tardive dyskinesia arrives late, is potentially irreversible, and is made worse, not better, by an anticholinergic. The whole topic hinges on holding that reversal and on knowing the one class of drug, the **vmat2** inhibitor, that is genuinely evidence-based for the established disorder (Kaplan & Sadock 2024, Maudsley 2021).

This is a management topic: the phenomenology and course of schizophrenia itself belong to the Schizophrenia: aetiology, phenomenology, classification and course notes, and the dopamine-pathway and receptor mechanics that explain why chronic D2 blockade produces a hyperkinetic movement disorder belong to the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes. Here we recognise it, screen for it, weigh the risk factors, and treat it.

18.1 The features: a late-onset, potentially irreversible movement disorder

Tardive dyskinesia is a late-onset, potentially irreversible choreoathetoid **abnormal involuntary movement** disorder that emerges after months to years of antipsychotic exposure (Kaplan & Sadock 2024). "Tardive" means late: unlike the acute extrapyramidal syndromes that appear within hours to weeks, tardive dyskinesia by convention requires a sustained period of exposure, and it may persist or progress even after the offending drug is withdrawn, which is what makes prevention and early detection so much more important than late rescue. The movements are involuntary, repetitive and purposeless, and the patient is often unaware of them.

RULE **Late, choreoathetoid, and possibly permanent.** Tardive dyskinesia follows months to years of exposure, is a choreoathetoid abnormal involuntary movement, and may be irreversible, so the whole game is prevention and early detection, not late treatment.

18.2 The phenomenology: where the movements are and what they look like

The classic and earliest picture is orofacial-lingual-buccal: lip-smacking, puckering and pursing, chewing and lateral jaw movements, tongue protrusion and writhing ("fly-catcher" tongue), and grimacing. Beyond the face the disorder extends to chorea of the limbs and trunk, with piano-playing finger movements, choreoathetoid writhing of the hands and feet, and truncal rocking or

pelvic thrusting; respiratory dyskinesia and irregular breathing can also occur. The movements typically worsen with emotional arousal, lessen with voluntary action over the affected part, and disappear in sleep. Recognising the orofacial-lingual-buccal pattern is the single most exam-relevant discriminator, because it is the presentation the AIMS was built to capture.

Orofacial-lingual-buccal movements
Lip-smacking and puckering, chewing, tongue protrusion and writhing, grimacing; the earliest and most characteristic pattern.

Chorea of the limbs and trunk
Piano-playing finger and toe movements, choreoathetoid writhing of hands and feet, truncal rocking and pelvic thrusting.

Choreoathetoid
A blend of chorea (rapid, irregular, flowing) and athetosis (slow, sinuous, writhing); the defining quality of the tardive movements.

18.3 Screening and quantification: the AIMS

Tardive dyskinesia is screened for and quantified with the Abnormal Involuntary Movement Scale (AIMS), the standard structured examination that rates involuntary movements across facial, oral, extremity and trunk regions on a graded scale together with global severity and the patient's awareness and distress (Stahl 2021). Guidance is to examine patients periodically for the development of abnormal movements using a neurological examination and the AIMS, so that emerging tardive dyskinesia is caught while it is mild and potentially reversible rather than after it has become established. The scale is a monitoring instrument, not a diagnostic test on its own: the diagnosis is clinical, made in a patient with the requisite exposure once other causes of dyskinesia are excluded.

WORKED EXAMPLE

A woman in her sixties on long-term haloperidol is noticed at follow-up to have subtle lip-smacking and tongue movements she has not remarked on. Rather than "just her dentures", the correct step is a structured AIMS examination, review of the antipsychotic (dose reduction or switch where the illness allows), and, because the movements are established, consideration of a vmat2 inhibitor. Reaching for an anticholinergic here would be the classic error.

18.4 The risk factors

The risk factors cluster into patient factors and drug factors, and the examiner expects both. Patient factors: older age (the strongest and most consistent), female sex, diabetes and an affective (mood) illness, and early or prominent extrapyramidal symptoms after starting the drug, which flag a susceptible nigrostriatal system. Drug factors: longer duration of exposure and higher cumulative dose, and the use of first-generation (typical) agents, which carry a substantially higher tardive dyskinesia risk than second-generation agents (Kaplan & Sadock 2024). The composite high-risk patient the textbooks describe is an older woman with a mood disorder on a first-generation antipsychotic who developed extrapyramidal symptoms early.

DOMAIN	RISK FACTOR
Patient	**Older age (strongest)**
	Female sex
	Diabetes
	Affective (mood) illness
	Early extrapyramidal symptoms after starting the drug
Drug	Longer duration of exposure
	Higher cumulative dose
	First-generation (typical) agents

Tardive dyskinesia risk factors: older age and first-generation agents are the two most consistently emphasised, one patient and one drug factor.

18.5 Management overview: prevention first, then reduce or switch, then treat

Management runs in three tiers and the order is deliberate. First, prevention: use the lowest effective dose, prefer second-generation agents over first-generation ones where clinically appropriate, and detect early through periodic AIMS screening, because an established disorder may not reverse. Second, once tardive dyskinesia is present, reduce or switch the antipsychotic where the illness allows: a switch to clozapine or quetiapine is the classic manoeuvre, since these lowest-D2-affinity agents are least likely to drive the movements and clozapine in particular may improve tardive symptoms (Maudsley 2021, Kaplan & Sadock 2024). Third, add an evidence-based drug treatment: a vmat2 inhibitor. Throughout, one thing is never done, which is to add an anticholinergic, because anticholinergics worsen tardive dyskinesia.

MNEMONIC

PREVENT, SWITCH, VMAT2 (never anticholinergic)

PREVENT with the lowest effective dose, second-generation agents and early AIMS detection; SWITCH or reduce the antipsychotic, classically to clozapine or quetiapine; treat the established disorder with a VMAT2 inhibitor; and never reach for an anticholinergic, which worsens it.

18.6 The VMAT2 inhibitors: valbenazine and deutetrabenazine

The evidence-based drug treatment for established tardive dyskinesia is a vmat2 inhibitor. VMAT2 (the vesicular monoamine transporter 2) packages dopamine and other monoamines into presynaptic vesicles; inhibiting it depletes the dopamine available for release, dampening the dopaminergic overactivity that drives the movements (Kaplan & Sadock 2024). Two agents are specifically evidence-based and approved for tardive dyskinesia. Valbenazine is a highly selective, once-daily VMAT2 inhibitor that produced significantly greater reductions in AIMS scores than placebo in randomised trials (Hauser 2017, Kaplan & Sadock 2024). Deutetrabenazine is a deuterated form of tetrabenazine given twice daily with food, also with randomised evidence of AIMS improvement. The older agent, tetrabenazine, is the first-generation VMAT2 inhibitor: it

has a short half-life (active metabolites about 2 to 8 hours) requiring multiple daily dosing and carries more depression and parkinsonism, so where available the newer agents are generally preferred (Maudsley 2021, Kaplan & Sadock 2024). All three can prolong the QT interval and carry warnings around depression and suicidality; VMAT2 inhibitor doses are lowered in hepatic impairment.

40 to 80	12 to 48	2 to 10 h
VALBENAZINE MG ONCE DAILY (TD)	DEUTETRABENAZINE MG/DAY, 2 DIVIDED (TD)	TETRABENAZINE HALF-LIFE

RULE **The VMAT2 inhibitors, valbenazine and deutetrabenazine, are the evidence-based treatment for established tardive dyskinesia.** They are the drugs approved and trial-supported specifically for tardive dyskinesia; tetrabenazine is the older, less-preferred option.

TRAP **Do not give an anticholinergic for tardive dyskinesia; it worsens it.** Anticholinergics help acute dystonia and drug-induced parkinsonism, but in tardive dyskinesia they aggravate the movements, so they are exactly the wrong reflex here.

18.7 Why the anticholinergic reflex fails here

The trap is worth its own paragraph because it is the commonest single error and the cleanest discriminator between the tardive and the acute syndromes. Acute dystonia and drug-induced parkinsonism arise from a relative dopaminergic deficit against unopposed cholinergic tone in the striatum, so an anticholinergic (benztropine, trihexyphenidyl) restores the balance and relieves them. Tardive dyskinesia is the opposite state, a hyperkinetic disorder linked to dopaminergic supersensitivity, so blocking cholinergic tone tips the balance further towards the dyskinesia and makes it worse. This is why the correct pharmacological lever is a VMAT2 inhibitor, which reduces dopamine availability, and why any prescribed anticholinergic should if anything be withdrawn when tardive dyskinesia appears.

COMMON TRAP

Reflexively prescribing benztropine or trihexyphenidyl for any antipsychotic-associated movement. For acute dystonia and parkinsonism that is right; for tardive dyskinesia it worsens the movements. The tardive patient needs antipsychotic review plus a VMAT2 inhibitor, not an anticholinergic.

INDIA

In Indian practice the affordable and available levers dominate: prevention through the lowest effective dose and preferential second-generation prescribing, periodic clinical and AIMS screening, and antipsychotic reduction or a switch (classically to clozapine, marketed as Sizopin, or to quetiapine, marketed as Qutipin) where the illness allows. The VMAT2 inhibitors valbenazine and deutetrabenazine are not routinely available or affordable in most Indian settings at the time of writing, which makes prevention and early detection, not late rescue, the practical backbone of care.

GOOD TO REMEMBER

- **Tardive dyskinesia:** FEATURE, a late-onset, potentially irreversible choreoathetoid abnormal involuntary movement (orofacial-lingual-buccal movements, chorea of the limbs and trunk) after months to years of antipsychotic exposure. DISCRIMINATOR, it is worsened by an anticholinergic (unlike acute dystonia and parkinsonism, which improve). FIRST MANAGEMENT STEP, screen and quantify with the AIMS, then review the antipsychotic (lowest effective dose, reduce or switch where possible).
- **Valbenazine:** WHAT, a selective VMAT2 inhibitor, evidence-based for established tardive dyskinesia. DOSE, **40 to 80 mg once daily** (Stahl). CAVEAT, QT prolongation and a warning for depression/suicidality; lower the dose in hepatic impairment.
- **Deutetrabenazine:** WHAT, a deuterated VMAT2 inhibitor, evidence-based for tardive dyskinesia. DOSE, **12 to 48 mg/day** in two divided doses, taken with food (Stahl). CAVEAT, QT prolongation and depression/suicidality warning; lower the dose in hepatic impairment.
- **Tetrabenazine:** WHAT, the older first-generation VMAT2 inhibitor, the less-preferred option. DOSE/CAVEAT, short half-life (**2 to 10 hours**) needing multiple daily dosing (Kaplan & Sadock); more depression and parkinsonism than the newer agents.

HOLD THIS

Established tardive dyskinesia is treated with a VMAT2 inhibitor (valbenazine or deutetrabenazine) after reducing or switching the antipsychotic; an anticholinergic worsens it, which is the reverse of acute dystonia and parkinsonism.

19 · Neuroleptic malignant syndrome

Why this matters. Neuroleptic malignant syndrome is the antipsychotic emergency the examiner will not forgive you for missing. It is rare, with an estimated incidence of the order of **0.02 to 0.16 per cent** of antipsychotic-treated patients, but it kills, with a reported mortality of about **5.6 per cent** overall and up to **20 per cent** in advanced cases (Maudsley 2021, Kaplan & Sadock 2024). The whole of its management turns on one reflex: recognise it early and stop the drug. This topic teaches the features, the investigations and the management; it deliberately does not re-teach the illness itself, which is owned by the Schizophrenia: aetiology, phenomenology, classification and course notes.

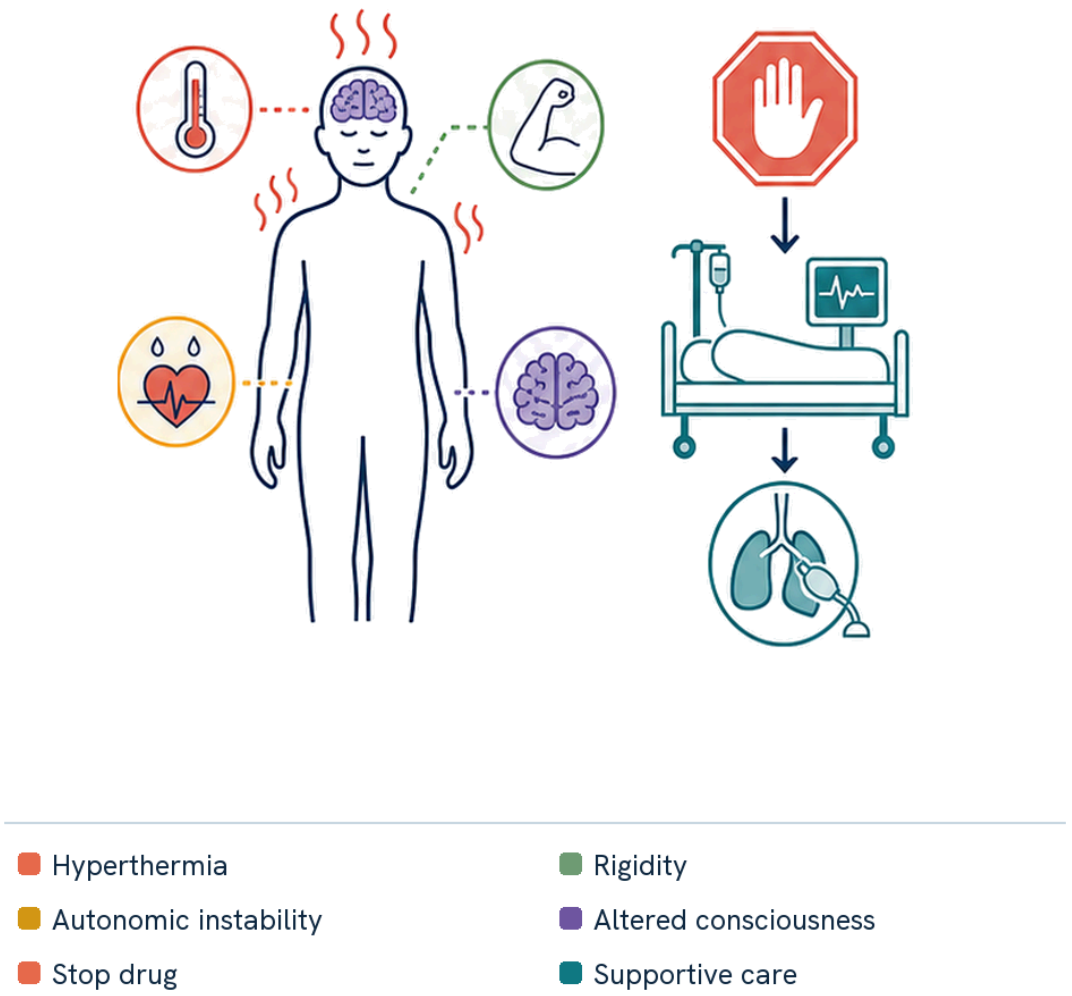


Fig 9.11 The clinical pattern of neuroleptic malignant syndrome: hyperthermia, severe rigidity, autonomic instability and altered consciousness demand immediate withdrawal of the offending drug and urgent supportive management.

Neuroleptic malignant syndrome, the nms, is an idiosyncratic reaction to dopamine D2 blockade, best understood as an acute disorder of thermoregulation and neuromotor control produced by an abrupt hypodopaminergic state in the **striatum and hypothalamus** (Kaplan & Sadock 2024). The receptor and pathway mechanics of D2 antagonism are not re-derived here (they are owned by the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes); here we apply that pharmacology at the bedside. The one governing sentence: any antipsychotic-treated patient with fever and rigidity is nms until proven otherwise, and the first move is to stop the drug.

19.1 The clinical tetrad and its timing

The classic presentation is a tetrad, worth memorising as a block. First, lead-pipe rigidity: a generalised, uniform (not cogwheel) increase in tone that is the motor signature of the syndrome and the source of the heat and the muscle breakdown. Second, hyperthermia: a true pyrexia, often marked, driven by muscular heat generation and impaired hypothalamic heat loss. Third,

autonomic instability: labile or high blood pressure, tachycardia and profuse diaphoresis. Fourth, an altered mental state, ranging from confusion and fluctuating consciousness to stupor and coma (Maudsley 2021, Kaplan & Sadock 2024). The syndrome typically evolves over **1 to 3 days** (roughly 24 to 72 hours), and characteristically appears early in treatment, after a recent dose increase, or with a high-potency agent (Maudsley 2021). Presentation is heterogeneous, and atypical cases lacking hyperthermia or rigidity are described, particularly with second-generation agents, so a high index of suspicion is the safeguard.

RULE **Fever and rigidity on an antipsychotic is nms until proven otherwise.** Stop the drug first and investigate second; do not wait for the creatine kinase before acting.

19.2 Risk factors: who and when

The risk is concentrated at predictable points. Drug factors dominate: high-potency first-generation agents (haloperidol above all), parenteral administration, a recent or rapid dose increase, high doses, antipsychotic polypharmacy, and intermittent non-adherence with re-exposure (Maudsley 2021, Kaplan & Sadock 2024). Patient factors add to it: dehydration, exhaustion, psychomotor agitation, pre-existing catatonia, an organic brain disorder, adjunctive lithium, a low serum iron, and a past history of nms. Demographically, young adult males are over-represented, while the outcome is more often lethal in older patients (Maudsley 2021). The practical lesson is that nms clusters around the agitated, dehydrated young man just started on, or recently escalated on, injectable high-potency haloperidol, which is exactly the patient a resident manages on an acute ward.

19.3 Investigations: the creatine kinase and its company

The signature laboratory finding is a markedly raised creatine kinase, often above **1000 units/L** and sometimes into the tens of thousands, released from the rigid, breaking-down muscle (Maudsley 2021, Kaplan & Sadock 2024). It is accompanied by a leukocytosis and frequently by deranged liver function tests. One caveat the examiner likes: asymptomatic creatine kinase rises are common with antipsychotics and with any agitation or intramuscular injection, so a raised creatine kinase supports but does not by itself diagnose nms, and it is the clinical picture that decides (Maudsley 2021). The dangerous downstream sequelae are what make the bloods urgent: the muscle breakdown causes rhabdomyolysis, which with the myoglobinuria and dehydration produces acute kidney injury, and in severe cases disseminated intravascular coagulation supervenes. Monitor renal function, electrolytes, coagulation and creatine kinase serially.

19.4 The differential: what else is rigid and febrile

The exam value of nms is in telling it apart from its mimics. Serotonin syndrome shares hyperthermia, autonomic instability and altered mental state, but is distinguished by neuromuscular hyperactivity of a different quality, clonus and hyperreflexia rather than lead-pipe rigidity, and by a serotonergic drug and a faster onset (over hours). Malignant hyperthermia is an anaesthetic reaction to volatile agents and depolarising muscle relaxants; there are no direct data linking it to nms, but antipsychotics are used cautiously in patients with a malignant hyperthermia history (Kaplan & Sadock 2024). Malignant catatonia can be clinically

indistinguishable from nms and shares its rigidity, hyperthermia and autonomic storm; as an entity it is owned by the Other psychotic disorders, delusional syndromes and catatonia notes, and it appears here only to be named in the nms differential. Also exclude a central nervous system infection (meningitis, encephalitis) and, in a febrile patient, a straightforward chest or other infection, which is precisely the trap below.

TRAP **Calling it "just EPS" or "just a chest infection" and continuing the antipsychotic.** Rigidity plus fever plus a raised creatine kinase is not ordinary parkinsonism and not a simple pneumonia; missing nms behind either label and leaving the drug running is the classic fatal error.

19.5 Management: stop the drug, support aggressively

The first and non-negotiable step is to **stop the antipsychotic immediately**, and stop any other contributing dopamine antagonist (Maudsley 2021, Kaplan & Sadock 2024). Everything else is built on that. The second pillar is aggressive supportive care in a high-dependency or intensive-care setting: active cooling, generous intravenous rehydration to protect the kidneys from the rhabdomyolysis, correction of electrolytes, and close monitoring of temperature, pulse and blood pressure, with ventilatory support or dialysis in severe cases (Kaplan & Sadock 2024). Supportive care alone, started early, is often enough in mild cases. Reduce environmental and pharmacological aggravants, treating dehydration and stopping adjunctive lithium.

19.6 Pharmacological options: dantrolene, bromocriptine and benzodiazepines

Where the picture is more severe, specific agents are added, on limited evidence and with guideline recommendations that vary widely (Maudsley 2021). The muscle relaxant dantrolene acts directly on skeletal muscle to reduce the rigidity and heat generation, with benefit sometimes seen within minutes to hours (Kaplan & Sadock 2024). The dopamine agonist bromocriptine counteracts the underlying hypodopaminergic state. Benzodiazepines (for example a lorazepam test dose) are useful, particularly where catatonic features are present, and are a recommended treatment. Dopamine agonists and dantrolene are often combined. For refractory cases, and where malignant catatonia cannot be excluded, electroconvulsive therapy is effective even after pharmacotherapy has failed; the technique itself is not taught here and is owned by the ECT and neurostimulation notes (Maudsley 2021, Kaplan & Sadock 2024).

GOOD TO REMEMBER

- **Dantrolene:** a direct-acting skeletal-muscle relaxant (reduces calcium release from the sarcoplasmic reticulum) for the rigidity and hyperthermia; a regimen is 0.8 to 2.5 mg/kg intravenously every 6 hours, up to a maximum of 10 mg/kg/day, then oral 100 to 200 mg/day once the patient can swallow (Kaplan and Sadock 2024); the caveat to hold is hepatotoxicity, so watch liver function.
- **Bromocriptine:** an oral dopamine agonist that reverses the hypodopaminergic state; start at 2.5 mg two to three times daily and build to the therapeutic 20 to 30 mg/day given in *four* divided doses, ceiling 45 mg/day; the caveat is that it may worsen psychosis and lower blood pressure.
- **Benzodiazepines:** for example lorazepam as a 1 to 2 mg parenteral test dose; useful adjunct, especially with catatonic features; the caveat is respiratory depression and sedation, so monitor consciousness.

19.7 The features and management at a glance

The table pins the tetrad, the key investigations and the management steps in one place, with the discriminator that separates each feature from its benign mimic in the highlighted column. Read the management column top to bottom as the running order: stop the drug, support, then add specific agents.

DOMAIN	FEATURE	DISCRIMINATOR	FIRST MANAGEMENT STEP
Motor	Lead-pipe rigidity	**Uniform (not cogwheel) tone, generalised, not relieved by anticholinergics**	Stop the antipsychotic; dantrolene if severe
Temperature	Hyperthermia	**True pyrexia driven by muscle heat, not a source of infection**	Active cooling; stop the drug
Autonomic	Autonomic instability	**Labile or high BP, tachycardia, diaphoresis**	Supportive monitoring in a high-dependency setting
Mental state	Altered mental state	**Fluctuating consciousness, confusion to stupor/coma**	Supportive care; exclude CNS infection
Laboratory	Raised creatine kinase, leukocytosis	**Creatine kinase often >1000 units/L; supports but does not alone diagnose**	IV fluids, monitor renal function (rhabdomyolysis, AKI, DIC)

The nms tetrad plus the laboratory signature, each with its discriminator and its first management step, the first of which is always to stop the drug.

19.8 Restarting an antipsychotic afterwards

Most patients still need an antipsychotic, and cautious rechallenge carries an acceptable risk (Maudsley 2021). Wait until the features of nms have resolved completely, stopping the drug for at least **5 days** and preferably longer (Maudsley 2021); Kaplan & Sadock advise waiting at least **2 weeks** after symptoms resolve (Kaplan & Sadock 2024). Correct the prior risk factors first, rehydrate and avoid concomitant lithium. Then begin with a very small dose and titrate slowly with close monitoring of temperature, pulse and blood pressure, choosing an agent structurally unrelated to the culprit and of lower dopamine affinity, that is, a low-potency or second-generation agent such as quetiapine or clozapine. Avoid high-potency first-generation drugs and avoid all depot or long-acting injectable preparations, because the drug cannot be withdrawn quickly if nms recurs (Maudsley 2021).

RULE **Rechallenge low and slow, never by depot.** After full resolution and at least 5 days off, restart a low-potency or second-generation oral agent at a tiny dose with close observation, and never with a long-acting injectable.

INDIA

The scenario a resident actually meets is nms in an agitated, dehydrated young man recently started on injectable high-potency haloperidol (marketed as Serenace), still widely used on cost grounds. For safe rechallenge the lower-potency second-generation switch options are readily available: quetiapine (marketed as Qutipin), olanzapine (marketed as Oleanz), and clozapine (marketed as Sizopin) where a structurally unrelated, low-affinity agent is wanted. Depot and long-acting injectable preparations are avoided after nms because they cannot be withdrawn quickly.

1 to 3 days	>1000 units/L	5 days	~5.6 per cent
TYPICAL EVOLUTION OF NMS	CREATINE KINASE (OFTEN)	MINIMUM OFF-DRUG BEFORE RECHALLENGE	OVERALL MORTALITY

PEARL

Lead-pipe rigidity plus true hyperthermia plus a creatine kinase in the thousands, evolving over a couple of days in someone recently started or escalated on a high-potency antipsychotic, is nms until proven otherwise. The rigidity is uniform and unrelieved by anticholinergics, which is what separates it from ordinary drug-induced parkinsonism.

HOLD THIS

Any antipsychotic-treated patient with fever and rigidity is neuroleptic malignant syndrome until proven otherwise: stop the drug immediately, support aggressively (cooling, fluids, high-dependency monitoring), add dantrolene and bromocriptine (and benzodiazepines, ECT for refractory cases) if severe, and rechallenge later low and slow with a low-potency or second-generation agent, never a depot.

20 · Metabolic syndrome and the monitoring schedule

Why this matters. The antipsychotics that control psychosis also, for many patients, quietly engineer a cardiometabolic catastrophe: **weight gain**, dyslipidaemia, insulin resistance and type 2 diabetes that together constitute the **metabolic syndrome**. This burden is not a footnote to treatment; it is the principal driver of the fifteen-to-twenty-year mortality gap between people with schizophrenia and the general population, most of that excess being cardiovascular (Maudsley 2021, Tasman 2015). The examiner tests one competence above all here: whether you know the **monitoring schedule** and will actually take a metabolic baseline before you prescribe. This is a schedule-heavy topic, and the intervals are the marks.

The illness itself, its phenomenology, aetiology, criteria and course, is owned by the Schizophrenia: aetiology, phenomenology, classification and course notes and is not re-taught here; the receptor pharmacology behind why H1 and 5HT2C blockade drive appetite, and the CYP metabolism of individual agents, belong to the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and are applied, not re-derived. What this topic teaches is the metabolic burden, its measurement, its verified monitoring schedule, and its management.

	Baseline	6 weeks	12 weeks	Annually
Weight and BMI	●	●	●	●
Waist circumference	●	–	–	●
Fasting glucose or HbA1c	●	–	●	●
Lipid profile	●	–	●	●
Blood pressure	●	–	●	●

● measure at this visit – not required this visit Schedule per the standard guidance; verify locally.

Fig 9.12 The metabolic monitoring schedule. Weight is tracked most closely, at baseline, six and twelve weeks and then at least annually; waist at baseline and annually; and fasting glucose or HbA1c, lipids and blood pressure at baseline, twelve weeks and annually. Olanzapine and clozapine carry the highest metabolic risk, so a baseline before starting is not optional.

20.1 The burden: why the metabolic hit dominates the mortality gap

People with schizophrenia die roughly fifteen to twenty years earlier than the general population, and the largest single contributor is cardiovascular disease, not suicide (Maudsley 2021). Around half of all people with schizophrenia meet criteria for obesity, a relative risk of nearly two against the general population, and while genetic and lifestyle factors contribute, antipsychotic-induced weight gain is in large measure responsible (Tasman 2015). The chain is mechanistic: weight gain and central adiposity drive insulin resistance, which drives dyslipidaemia and ultimately type 2 diabetes, and each step compounds cardiovascular risk. Antipsychotics can also, rarely, precipitate diabetic ketoacidosis or hyperosmolar hyperglycaemic states de novo, sometimes without preceding obesity, which is why glucose is monitored in every patient and not only the visibly overweight (Stahl 2021).

PEARL

The headline the examiner wants is that the mortality gap in schizophrenia is driven mainly by cardiovascular disease, and antipsychotic-induced weight gain and metabolic syndrome are a modifiable slice of it. Monitoring is not box-ticking, it is the intervention that lets you catch and reverse the process before it becomes irreversible cardiac disease.

20.2 The weight-gain league table: olanzapine and clozapine worst, aripiprazole/lurasidone/ziprasidone most weight-neutral

Not all antipsychotics carry equal metabolic risk, and the ranking is examinable. A classic meta-analysis of ten-week weight change at standard doses found mean gains of **4.45 kg** with clozapine, **4.15 kg** with olanzapine, **2.10 kg** with risperidone and **0.04 kg** with ziprasidone (Allison et al. 1999, in Tasman 2015). Over a year the hierarchy holds: aripiprazole and ziprasidone around 1 kg, amisulpride about 1.5 kg, quetiapine and risperidone 2 to 3 kg, and olanzapine more than 6 kg, with clozapine at least as bad as olanzapine (Newcomer & Haupt

2006, in Tasman 2015). Lurasidone, among the newer agents, causes the least weight gain (De Hert et al. 2012). The practical output is that where a patient is metabolically vulnerable you preferentially choose a **weight-neutral agent**: **aripiprazole, lurasidone or ziprasidone** are the most weight-neutral of the commonly used drugs, while **olanzapine and clozapine carry the highest risk** and demand the tightest monitoring.

ANTIPSYCHOTIC	RELATIVE METABOLIC / WEIGHT-GAIN RISK	QUANTIFIED SIGNAL (VERIFIED)
Clozapine	**Highest (worst)**	~4.45 kg at 10 weeks; at least as much long-term as olanzapine
Olanzapine	**Highest (worst)**	~4.15 kg at 10 weeks; >6 kg over 1 year
Quetiapine	Intermediate	~2 to 3 kg over 1 year (like risperidone)
Risperidone / paliperidone	Intermediate	~2.10 kg at 10 weeks; 2 to 3 kg over 1 year
Amisulpride	Lower-intermediate	~1.5 kg over 1 year
Aripiprazole	**Most weight-neutral**	~1 kg over 1 year; largely lipid/glucose neutral
Ziprasidone	**Most weight-neutral**	~0.04 kg at 10 weeks; ~1 kg over 1 year
Lurasidone	**Most weight-neutral**	Least weight gain among newer agents

Weight-gain hierarchy: clozapine and olanzapine are worst; aripiprazole, ziprasidone and lurasidone are the most weight-neutral. Figures from Allison et al. 1999 and Newcomer & Haupt 2006 (in Tasman 2015).

GOOD TO REMEMBER

- **Olanzapine:** second-generation (atypical) antipsychotic, D2/5HT2A antagonist with high H1 affinity; oral 5 to 20 mg/day (verify per patient); the one caveat to hold is that it is among the worst two agents for weight gain and metabolic syndrome, so it mandates the tightest metabolic monitoring. Indian brand: Oleanz.
- **Clozapine:** the only agent licensed for treatment-resistant schizophrenia (owned by the treatment-resistance topic); metabolically it is at least as bad as olanzapine for weight gain, dyslipidaemia and diabetes; the caveat is that its haematological monitoring never displaces metabolic monitoring, both run in parallel. Indian brand: Sizopin (or Lozapin).
- **Aripiprazole:** D2 partial agonist, second-generation; oral 10 to 30 mg/day (verify per patient); the point to hold is that it is one of the most weight-neutral agents and a reasonable metabolic-sparing switch target. Indian brand: Arip (or Arip MT).
- **Lurasidone / ziprasidone:** second-generation antipsychotics; both are among the most weight-neutral options; the caveat is that weight-neutrality does not exempt them from monitoring, because obesity prevalence in this population is high regardless of drug.

20.3 Defining the metabolic syndrome: the five components and their thresholds

The **metabolic syndrome** is a cluster diagnosis, not a single number, and you should be able to name its components. It is defined by central obesity plus a combination of the cardiometabolic

abnormalities: raised **waist** circumference, raised fasting glucose, raised triglycerides, low HDL cholesterol and raised blood pressure. In the widely quoted NCEP ATP III framing, three or more of five criteria establish the syndrome, and the abdominal-obesity threshold is a **waist** circumference above **102 cm** (40 inches) in men or above **88 cm** (35 inches) in women (Newcomer 2007, in Tasman 2015). The parameters you actually measure to capture it are **waist** circumference, BMI, fasting glucose or **hba1c**, and lipids, with blood pressure completing the set.

Central obesity (waist)

Waist circumference >102 cm (men) or >88 cm (women); measured at the umbilicus (Stahl 2021, Tasman 2015).

BMI

Weight (kg) / height (m) squared; overweight 25 to 29.9, obese 30 or above (verified WHO cut-offs).

Dysglycaemia

Impaired fasting glucose (fasting plasma glucose 100 to 125 mg/dL) or diabetes (fasting plasma glucose 126 mg/dL or above); fasting glucose or hba1c both acceptable measures (Stahl 2021).

Dyslipidaemia

Raised triglycerides and/or low HDL cholesterol on a fasting lipid profile (Maudsley 2021).

Hypertension

Raised blood pressure (thresholds vary by criteria set; NICE and local hypertension guidance apply).

GOOD TO REMEMBER

- **Metabolic syndrome:** feature, a cluster of central obesity, dysglycaemia, dyslipidaemia and raised blood pressure (three or more of five criteria, NCEP ATP III); discriminator from simple weight gain, it is the constellation, not the number, and the waist threshold is >102 cm in men or >88 cm in women; first management step, lifestyle intervention plus consider switching to a weight-neutral agent and treat each risk factor medically.

20.4 The metabolic baseline: what to record before the first dose

Every schedule begins at the same non-negotiable point: a metabolic baseline taken before, or as soon as possible after, the first dose. Before starting an antipsychotic, record weight and BMI, waist circumference, pulse and blood pressure, a fasting blood glucose plus **hba1c**, and a fasting lipid profile, alongside a personal and family history of diabetes, obesity, dyslipidaemia, hypertension and cardiovascular disease (Maudsley 2021, Stahl 2021). Without this baseline you cannot later tell antipsychotic-induced change from pre-existing disease, and you cannot demonstrate that a rise happened on your watch. The baseline is the single most commonly omitted step in real practice and the easiest mark to lose.

TRAP **Starting an antipsychotic without a metabolic baseline.** No baseline means no way to attribute later weight, glucose or lipid change to the drug, and it is the classic omission the examiner is probing; take weight/BMI/waist, fasting glucose/HbA1c, lipids and blood pressure before the first dose.

20.5 The monitoring schedule: baseline, then early (6 and 12 weeks), then annually

The **metabolic monitoring** principle across guidelines is the same shape: **baseline, then early re-checks in the first weeks, then annually** once stable, with more frequent checks for the highest-risk drugs and patients. The verified NICE schedule, reproduced in the Maudsley, measures weight weekly for the first six weeks, then at twelve weeks, one year and annually; waist circumference annually; pulse and blood pressure at twelve weeks, one year and annually; and fasting blood glucose, **hba1c** and blood lipids at twelve weeks, one year and annually (Maudsley 2021). The Maudsley's own summary table places blood lipids and weight at baseline, then at three months, then yearly, and plasma glucose at baseline, at four to six months, then yearly, with clozapine and olanzapine re-checked three-monthly through the first year (Maudsley 2021). The ADA/APA-derived US schedule that Stahl uses is stated cell by cell: BMI monthly for three months then quarterly; blood pressure, fasting plasma glucose and fasting lipids within three months then annually, earlier and more often for those with diabetes or who gain more than five percent of initial weight (Stahl 2021). All three agree on the crunchy summary: baseline, an early check in the first six to twelve weeks, then at least annual review.

Baseline	6 wk	12 wk	Annually
WEIGHT/BMI/WAIST, FASTING GLUCOSE+HBA1C, LIPIDS, BP BEFORE DOSE	EARLY RE-CHECK (WEIGHT WEEKLY TO 6 WK, NICE)	GLUCOSE/HBA1C, LIPIDS, BP, WEIGHT (NICE)	FULL PANEL THEREAFTER ONCE STABLE

PARAMETER	BASELINE	EARLY (FIRST WEEKS)	12 WEEKS	1 YEAR / ANNUALLY
Weight / BMI	**Yes**	Weekly to 6 weeks (NICE); monthly x3 (ADA/APA)	Yes	Yes, then annually
Waist circumference	**Yes**	(with weight where possible)	-	Annually
Fasting glucose or HbA1c	**Yes**	Maudsley: at 4 to 6 months	Yes (NICE)	Yes, then annually
Fasting lipids	**Yes**	Maudsley: at 3 months	Yes (NICE)	Yes, then annually
Blood pressure	**Yes**	During titration	Yes (NICE)	Yes, then annually
Highest-risk drugs (clozapine, olanzapine)	Yes	More frequent	3-monthly through first year	Then yearly (Maudsley)

Verified monitoring schedule, harmonised from NICE (in Maudsley 2021), the Maudsley summary table, and the ADA/APA schedule in Stahl 2021. The convergent rule is baseline, early re-check at 6 to 12 weeks, then annual; clozapine and olanzapine monitored more frequently.

WORKED EXAMPLE

A 24-year-old man is to start olanzapine for a first episode. Before the first dose you record weight, BMI and waist, pulse and blood pressure, a fasting glucose with HbA1c and a fasting lipid panel, and note his family history of diabetes. Because olanzapine is a high-risk agent you check weight in the early weeks, review the full metabolic panel at twelve weeks, and, given his youth and the drug, keep glucose and lipids under closer-than-annual review through the first year. If he gains more than five percent of his baseline weight, you bring the next check forward rather than waiting for the annual review (Stahl 2021).

20.6 Management: prevent, intervene on lifestyle, add metformin, treat the risk factors

Management runs on four tiers, and the exam wants them in order. First, **prevention**: where the patient is metabolically vulnerable, choose a weight-neutral agent (aripiprazole, lurasidone or ziprasidone) rather than olanzapine or clozapine at the outset (Maudsley 2021). Second, **lifestyle intervention**: structured diet and exercise advice, plus counselling on smoking and alcohol, offered from the start and not only once weight has risen (Maudsley 2021, BAP/Cooper et al. 2016 in Shorter Oxford 2018). Third, **pharmacological**: adjunctive metformin is the best-evidenced drug intervention for antipsychotic-induced weight gain, with monitoring of renal function and B12 (Maudsley 2021); switching to a less obesogenic antipsychotic is the other lever, weighed against relapse risk. Fourth, **treat the established cardiometabolic risk factors**: manage diabetes, dyslipidaemia (statin where indicated) and hypertension according to standard medical guidelines, because reducing weight alone does not undo an established cardiovascular risk (Maudsley 2021). Where the patient is already on the worst-offending drug and cannot switch, all four tiers run together.

RULE **Metabolic monitoring is baseline, early (6 and 12 weeks), then annual, and olanzapine and clozapine carry the highest risk.** Prevent with a weight-neutral agent where you can, intervene on lifestyle from the start, add metformin for antipsychotic weight gain, and treat each cardiometabolic risk factor medically.

GOOD TO REMEMBER

- **Metformin (for antipsychotic weight gain):** what it is, a biguanide used off-label as the best-evidenced adjunct for antipsychotic-induced weight gain; the caveat to hold is that it requires monitoring of renal function and B12 (Maudsley 2021).
- **Antipsychotic-induced weight gain:** feature, progressive weight gain, often early and appetite-driven (H1/5HT2C mechanism); discriminator, dose- and drug-dependent, worst with clozapine and olanzapine; first management step, lifestyle intervention plus consider switching to a weight-neutral agent, and add metformin if weight gain persists.

INDIA

The Indian IPS schizophrenia guideline endorses routine baseline and follow-up metabolic monitoring, and in the Indian setting real-world monitoring rates are low (Poojari et al. 2020, cited in Maudsley 2021), so the baseline is the practical failure point to guard. The olanzapine long-acting injectable is marketed in India as Tolaz LA (Torrent), and carries the same metabolic monitoring obligation as oral olanzapine plus its own three-hour post-injection observation for post-injection delirium/sedation syndrome. Verify current thresholds against IPS and NICE at the point of care.

HOLD THIS

Take a metabolic baseline before the first dose, then re-check weight/glucose/lipids/BP early (by 6 to 12 weeks) and at least annually, monitor olanzapine and clozapine most closely, and manage with prevention, lifestyle, metformin and treatment of each risk factor.

21 · Hyperprolactinaemia, QTc prolongation and the cardiac effects

Why this matters. Two of the antipsychotic harms an examiner will always test are silent until they are looked for: the endocrine harm of raised prolactin and the cardiac harm of a lengthened QT interval. Both flow directly from the same D2 blockade that treats the psychosis, both are agent-specific so the answer is largely a matter of knowing which drug does what, and both are managed by the same governing move, switch to a safer agent or add a sparing one. Hyperprolactinaemia (hyperprolactinemia) is common, under-reported and does long-term damage to bone; QTc (qtc) prolongation is rarer but lethal, because it is the road to torsades de pointes and sudden death (Maudsley 2021, Kaplan & Sadock 2024).

This topic teaches the endocrine and cardiac adverse effects only. The receptor pharmacology and the tuberoinfundibular dopamine pathway are not re-derived here (they are owned by the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes); the illness itself is owned by the Schizophrenia: aetiology, phenomenology, classification and course notes. Here we apply the pharmacology at the bedside: recognise the effect, name the offending agent, and act.

21.1 Hyperprolactinaemia: the mechanism

Dopamine tonically inhibits prolactin (prolactin) release from the anterior pituitary lactotrophs, acting through D2 receptors in the tuberoinfundibular pathway. An antipsychotic that blocks those D2 receptors removes the brake, and prolactin rises (Maudsley 2021, Stahl 2021). The elevation is roughly dose-related, and for most agents the D2 occupancy that raises prolactin sits very close to the occupancy needed for antipsychotic efficacy, which is why hyperprolactinaemia is so common. A drug that spares prolactin does so either because it is a partial agonist at D2 (aripiprazole, which behaves as a dopamine agonist at the pituitary and can actually lower prolactin) or because it occupies pituitary D2 receptors only loosely and transiently (quetiapine, clozapine). The pituitary sits outside the blood-brain barrier, so drugs that are actively pumped out of the brain but not the pituitary (amisulpride, and to a large degree paliperidone and risperidone) raise prolactin disproportionately (Maudsley 2021).

RULE **A raised prolactin is a tuberoinfundibular D2 effect.** Confirm it is drug-related, then switch to a prolactin-sparing agent or add aripiprazole; treat the symptoms and the long-term bone risk, not the number alone.

21.2 Which agents raise prolactin, and which spare it

The single highest-yield fact is the agent grouping. The worst offenders are risperidone and its active metabolite paliperidone, amisulpride, sulpiride, and the high-potency first-generation antipsychotics (haloperidol, the phenothiazines); risperidone and amisulpride can raise prolactin more than the typicals do (Maudsley 2021, Leucht 2013). The prolactin-sparing agents are aripiprazole (and the other partial agonists brexpiprazole, cariprazine), quetiapine and clozapine, which raise prolactin only rarely; olanzapine and ziprasidone are intermediate, giving a modest dose-related rise. This ordering is worth memorising verbatim because it drives every switch decision.

PROLACTIN EFFECT	AGENTS	NOTE
Marked rise (worst)	Risperidone, paliperidone, amisulpride, sulpiride; high-potency typicals (haloperidol, phenothiazines)	Risperidone and amisulpride can exceed the typicals
Modest, dose-related rise	Olanzapine, ziprasidone	Intermediate liability
Sparing (little or no rise)	Aripiprazole, brexpiprazole, cariprazine, quetiapine, clozapine	Aripiprazole can lower prolactin (partial D2 agonist)

Antipsychotic effect on prolactin: the switch target is always a drug from the sparing row (Maudsley 2021).

GOOD TO REMEMBER

- **Risperidone / paliperidone:** second-generation D2/5HT2A antagonists (risperidone as Sizodon; paliperidone as Paliris); the leading cause of antipsychotic hyperprolactinaemia among the atypicals, so ask about galactorrhoea and menstrual change at every review.
- **Amisulpride:** substituted benzamide, selective D2/D3 antagonist (marketed as Amazeo), oral dose about **400 to 800 mg/day** for positive symptoms; a potent prolactin-raiser because it acts preferentially on pituitary D2 outside the blood-brain barrier, and adjunctive aripiprazole may not fully normalise amisulpride-induced hyperprolactinaemia.
- **Aripiprazole:** D2 partial agonist (marketed as Arip / Arip MT); prolactin-sparing and the first-choice add-on to correct raised prolactin, adjunct dose **5 mg/day**; the one caveat is akathisia.
- **Quetiapine:** loosely-binding D2/5HT2A antagonist (marketed as Qutipin); prolactin-sparing, a sound switch target when raised prolactin is the problem; hold the caveat of sedation and postural drop rather than prolactin.

21.3 The clinical consequences of raised prolactin

Hyperprolactinaemia is often superficially asymptomatic, the patient does not spontaneously complain, which is exactly why it is missed (Maudsley 2021). When symptomatic, persistent elevation suppresses the hypothalamic-pituitary-gonadal axis and produces galactorrhoea, menstrual disturbance and amenorrhoea in women, sexual dysfunction (loss of libido, arousal and orgasmic difficulty) in both sexes, breast growth and, occasionally, gynaecomastia in men.

The consequence that matters most in the long term is a fall in bone mineral density from chronic hypogonadism, which raises fracture risk, and there is a debated small increase in breast-cancer risk (Maudsley 2021, De Hert 2016). Because prolactin also rises with stress, pregnancy, lactation, seizures, renal impairment and, importantly, a prolactinoma, the sample should be taken early in the morning with venepuncture stress minimised, and a very high level must be worked up rather than assumed drug-related.

Galactorrhoea

Inappropriate milk secretion from HPG-axis suppression; volunteered rarely, so ask.

Amenorrhoea / oligomenorrhoea

Menstrual disturbance from hypogonadism; a red flag for symptomatic hyperprolactinaemia.

Sexual dysfunction

Reduced libido, arousal and orgasm; multifactorial but prolactin is one driver.

Bone-density loss

The key long-term harm; chronic hypogonadism lowers bone mineral density and raises fracture risk.

21.4 Interpreting the prolactin level and managing it

Measure plasma prolactin at baseline in all patients, and again if hyperprolactinaemia is suspected or a prolactin-elevating agent is being used. On the Maudsley interpretation, a normal prolactin is about **0 to 25 ng/ml** in women and **0 to 20 ng/ml** in men; a level of **25 to 118 ng/ml** is elevated; and a highly elevated level of **over 118 ng/ml** (over 2500 mIU/L) should prompt referral to rule out a prolactinoma (Maudsley 2021). Treatment is driven by symptoms and long-term risk, not by the number in isolation. If treatment is needed, the first choice is to switch to an agent with a lower prolactin liability, accepting that any switch risks destabilising the illness; where a switch is inappropriate or fails, add adjunctive aripiprazole **5 mg/day**, which lowers prolactin dose-dependently. Where aripiprazole cannot be used, verified second-line options are vitamin B6 (pyridoxine) **600 mg/day** and, less preferably, a dopamine agonist such as cabergoline or bromocriptine (each carrying a theoretical risk of worsening psychosis). Address the bone risk directly: weight-bearing exercise, smoking cessation, and adequate calcium and vitamin D (Maudsley 2021).

0 to 25 ng/ml	25 to 118 ng/ml	>118 ng/ml	5 mg/day
NORMAL PROLACTIN, WOMEN	ELEVATED	HIGHLY ELEVATED: RULE OUT PROLACTINOMA	ADJUNCTIVE ARIPIPRAZOLE

GOOD TO REMEMBER

- **Hyperprolactinaemia:** feature, galactorrhoea, amenorrhoea, sexual dysfunction and long-term bone-density loss, often asymptomatic; discriminator, on a marked prolactin-raiser (risperidone, paliperidone, amisulpride, high-potency typical) with a raised morning level, once stress, pregnancy and a prolactinoma (level over 118 ng/ml) are excluded; first management step, switch to a prolactin-sparing agent, or add aripiprazole 5 to 10 mg/day, and manage the bone risk.

21.5 QTc prolongation: the mechanism and the agents

Many antipsychotics block the cardiac potassium channel IKr (the hERG channel), which slows ventricular repolarisation and produces QT prolongation on the ECG (Maudsley 2021, Kaplan & Sadock 2024). Because the raw QT shortens as heart rate rises, it is corrected for rate and reported as the QTc. The danger of a long QTc is torsades de pointes (torsades), a polymorphic ventricular tachycardia that can degenerate into ventricular fibrillation and sudden cardiac death. The risk is agent-specific. The highest-effect antipsychotics are pimozide and sertindole; thioridazine is the classic and most notorious offender, withdrawn from routine use precisely because it caused substantial QTc prolongation, torsades and sudden death (Kaplan & Sadock 2024). Also carrying meaningful, moderate effect are ziprasidone, high-dose haloperidol (especially given intravenously), chlorpromazine, amisulpride and quetiapine. The low-effect or no-effect agents include aripiprazole, brexpiprazole, cariprazine, lurasidone and olanzapine (Maudsley 2021).

QT EFFECT	ANTIPSYCHOTICS	EXAM HANDLE
High effect	Pimozide, sertindole; thioridazine (classic offender, restricted)	ECG mandatory; thioridazine and pimozide are the named "avoid / monitor" drugs
Moderate effect	Ziprasidone, haloperidol (worst high-dose and IV), chlorpromazine, amisulpride, quetiapine	Haloperidol IV or high-dose carries an explicit sudden-death warning
Low / no effect	Aripiprazole (~8 ms), brexpiprazole, cariprazine, lurasidone, olanzapine	The switch targets when QTc is the problem

Antipsychotic effect on QTc: pimozide and sertindole highest, thioridazine the classic offender; move toward the low/no-effect row (Maudsley 2021).

GOOD TO REMEMBER

- **Thioridazine:** low-potency phenothiazine; the classic high-QTc offender associated with substantial QTc prolongation, torsades and sudden death, now reserved for refractory cases with an ECG before and during treatment.
- **Pimozide:** high-potency diphenylbutylpiperidine; high QTc effect (and seizures) at higher doses, so an ECG is mandatory and dose is kept low.
- **Ziprasidone:** second-generation D2/5HT2A antagonist; a moderate, dose-related QTc effect, so it is avoided in cardiac risk and co-prescription with other QT-prolonging drugs.
- **Haloperidol:** high-potency butyrophenone (marketed as Serenace); QTc, torsades and sudden-death risk is greatest with intravenous use and at doses higher than recommended, so keep IV use monitored and dose modest.

21.6 The QTc thresholds and monitoring with an ECG

Learn the numbers exactly. The upper limit of normal QTc is **440 ms** in men and **470 ms** in women; a QTc **over 500 ms** is clearly associated with an increased risk of arrhythmia and is the threshold that mandates action; a QTc **over 650 ms** may be more likely than not to induce torsades (Maudsley 2021). The management ladder follows those bands. Below 440 ms (men) or 470 ms (women), no action is needed unless the T-wave morphology is abnormal. Between the

normal limit and 500 ms, consider reducing the dose or switching to a lower-effect agent and repeat the ECG. Above 500 ms, repeat the ECG, stop the suspected causative drug, switch to a lower-effect agent, and refer to a cardiologist immediately; abnormal T-wave morphology at any QTc also prompts urgent review. Measure the QTc with an ECG in all patients on admission (before or at the start of treatment), and at the annual physical health check if there is a previous abnormality or a known additional risk factor (Maudsley 2021, APA 2021).

440 ms	470 ms	>500 ms	>650 ms
UPPER NORMAL QTC, MEN	UPPER NORMAL QTC, WOMEN	ACT: STOP / SWITCH, REFER	MAY INDUCE TORSADES

21.7 Additive risk: other QT drugs and electrolytes

QTc risk is additive, and this is where residents come unstuck. Stacking a QT-prolonging antipsychotic on top of another QT-prolonging drug multiplies the danger: the common culprits are macrolide and quinolone antibiotics (erythromycin, clarithromycin), antimalarials (chloroquine, quinine), class Ia and III antiarrhythmics (quinidine, sotalol, amiodarone), methadone, and other psychotropics (Maudsley 2021). Electrolyte disturbance is the other multiplier: hypokalaemia, hypomagnesaemia and hypocalcaemia all prolong QTc, and hypokalaemia is especially common in acute psychotic admissions (poor intake, vomiting, refeeding). Bradycardia, congenital long-QT syndrome, ischaemic heart disease, myocardial infarction, female sex and extremes of age add further risk. The practical rule before adding any drug to an antipsychotic is to ask whether it prolongs QT and to check potassium and magnesium first.

TRAP **Stacking two QT-prolonging drugs without checking the QTc and electrolytes.** Adding a macrolide, an antiarrhythmic or a second QT-prolonging antipsychotic to an existing one, in a patient who may be hypokalaemic, is how a preventable torsades happens; check the ECG and potassium/magnesium first.

21.8 The other cardiac effect concerns

Beyond the QT interval, two further cardiac effect concerns are examined. The first is clozapine-associated myocarditis (and cardiomyopathy), an inflammatory injury of the heart muscle that typically presents in the first weeks of clozapine treatment with tachycardia, fever, chest pain, dyspnoea, a rising troponin and CRP, and ECG or echocardiographic change; it is a reason to stop clozapine and is developed in full in the clozapine topic, so it is cross-referenced here rather than re-taught. The second is postural (orthostatic) hypotension from alpha-1 adrenergic blockade, prominent with low-potency phenothiazines (chlorpromazine), clozapine and quetiapine, and worst on initiation and dose titration; it causes dizziness and falls, particularly in the elderly, and is managed by slow titration, splitting or lowering the dose, and advising the patient to stand up slowly (Maudsley 2021, Kaplan & Sadock 2024).

GOOD TO REMEMBER

- **QTc prolongation / torsades:** feature, a lengthened QTc on the ECG risking torsades de pointes and sudden death; discriminator, worst with pimozide, sertindole, thioridazine, ziprasidone and high-dose or IV haloperidol, and amplified by other QT drugs and by low potassium or magnesium; first management step, if QTc over 500 ms stop the causative drug, switch to a lower-effect agent, correct electrolytes and refer to cardiology.
- **Clozapine myocarditis:** feature, early inflammatory cardiac injury (tachycardia, fever, chest pain, dyspnoea, raised troponin/CRP); discriminator, onset in the first weeks of clozapine; first management step, stop clozapine and refer, see the clozapine topic.
- **Postural hypotension:** feature, a drop in standing blood pressure with dizziness and fall risk from alpha-1 blockade; discriminator, worst on initiation and titration with chlorpromazine, clozapine and quetiapine; first management step, titrate slowly, lower or split the dose, advise standing up slowly.

INDIA

Verified Indian brands keep the endocrine-and-cardiac decisions concrete at the bedside: risperidone (Sizodon) and paliperidone (Paliris) are the common prolactin-raisers to switch away from, aripiprazole (Arip) and quetiapine (Qutipin) the sparing targets, and haloperidol (Serenace) the high-potency typical whose intravenous and high-dose QTc risk applies in the emergency room. Baseline ECG before starting a moderate or high QT-effect agent, and a serum potassium and magnesium before adding any second QT-prolonging drug, are low-cost, high-value habits in Indian practice.

PEARL

Both harms in this topic are "silent-until-sought and agent-specific". The endocrine harm is found by asking about galactorrhoea, periods and libido and checking a morning prolactin; the cardiac harm is found by an ECG and a potassium. In both, the fix is the same shape: switch to a safer agent, or in the case of prolactin, add aripiprazole.

HOLD THIS

Raised prolactin means a tuberoinfundibular D2 effect (worst with risperidone, paliperidone, amisulpride), so switch to a sparing agent or add aripiprazole 5 to 10 mg/day; a QTc over 500 ms (normal 440 ms men, 470 ms women) means stop the drug, correct potassium and magnesium, and refer, and never stack two QT-prolonging drugs without checking the ECG and electrolytes first.

22 · Discriminate: the adverse-effect and emergency differential

Why this matters. A hyperthermic, rigid or agitated patient on psychotropics is a differential, not a diagnosis, and the examiner rewards the trainee who separates the look-alikes on the correct single discriminator rather than reaching for a reflex label. The raw entity of neuroleptic malignant syndrome is developed alongside; here the payoff is the interleaved **differential** that tells it apart from the three syndromes it is most often confused with, each of which is fatal if managed as the wrong one (Kaplan & Sadock 2024). Kaplan & Sadock name the exact company

nms keeps: "conditions with clinical similarity to NMS include serotonin syndrome, malignant hyperthermia, drug toxicity, heat stroke, and malignant catatonia" (Kaplan & Sadock 2024).

The discipline is to run one axis at a time across all four entities: the **trigger drug**, the quality of the motor sign, the reflexes, the pupils, the bowel sounds, and the tempo. Read that way, four syndromes that share fever and altered mental state pull cleanly apart. The receptor and pathway mechanics of dopamine blockade and serotonergic and muscarinic excess are not re-derived here (they are owned by the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes); this topic applies them at the bedside as discriminators. The disorder that the patient carries underneath, its phenomenology and course, belongs to the Schizophrenia: aetiology, phenomenology, classification and course notes.

	NMS	Serotonin syndrome	Malignant catatonia	Anticholinergic toxicity
Trigger	antipsychotic	serotonergic drug	psychiatric illness	anticholinergic load
Onset	1 to 3 days	hours	days	hours
Muscle tone	lead-pipe rigidity	rigidity, tremor	waxy or rigid	normal
Reflexes	hyporeflexia	clonus, hyperreflexia	variable	normal
Pupils, skin	normal, sweating	dilated, sweating	sweating	dilated, dry, flushed
The one discriminator	rigidity, very high CK	clonus, hyperreflexia	catatonic signs first	dry skin, no bowel sounds

Malignant catatonia as an entity is developed in the Other psychotic disorders, delusional syndromes and catatonia notes.

Fig 9.13 The hyperthermic-rigid emergency differential. Rigidity with hyporeflexia and a very high creatine kinase is neuroleptic malignant syndrome; clonus and hyperreflexia after a serotonergic drug is serotonin syndrome; catatonic signs that precede the picture point to malignant catatonia; and hot, dry, flushed skin with absent bowel sounds is anticholinergic toxicity. The discriminator, not the fever they share, makes the diagnosis.

22.1 Neuroleptic malignant syndrome: rigidity with hyporeflexia, over days

Trigger and signature. Neuroleptic malignant syndrome follows antipsychotic exposure (dopamine D2 blockade, or abrupt withdrawal of a dopamine agonist), and its motor signature is lead-pipe rigidity: a uniform, generalised increase in tone with hyporeflexia or normal reflexes, never the brisk hyperreflexia of serotonergic excess (Kaplan & Sadock 2024). The tempo is slow: it evolves over **1 to 3 days** (about 24 to 72 hours), and the muscle breakdown drives a very high creatine kinase, often above **1000 units/L** and sometimes into the tens of thousands. The single discriminator to hold is rigidity with hyporeflexia and a days-long onset in an antipsychotic-treated patient with a very high creatine kinase. Pupils are typically normal and bowel sounds are unremarkable. The raw entity, its investigations and its full management are developed alongside.

22.2 Serotonin syndrome: clonus with hyperreflexia, over hours

Trigger and signature. Serotonin syndrome follows a serotonergic drug, usually the initiation or dose increase of a serotonergic agent, or the combination of two (an SSRI with an MAOI, tramadol, linezolid, or a triptan); the raw entity is developed in the mood-disorders pharmacology notes, and here it is the key nms mimic. Its motor signature is neuromuscular

hyperactivity of a wholly different quality: clonus (spontaneous, inducible, or ocular), hyperreflexia, myoclonus and tremor, greater in the lower limbs (Kaplan & Sadock 2024). It adds dilated pupils (mydriasis), hyperactive bowel sounds with diarrhoea, and a rapid onset, over **hours** rather than days. The single discriminator is clonus with hyperreflexia coming on within hours of a serotonergic drug. Diagnosis rests on the Hunter Serotonin Toxicity Criteria (clonus being the pivotal sign) or the older Sternbach criteria, and the specific antidote is the serotonin antagonist cyproheptadine (Kaplan & Sadock 2024).

RULE **Rigidity with hyporeflexia is neuroleptic malignant syndrome; clonus with hyperreflexia is serotonin syndrome.** The reflexes and the quality of the motor sign, read together with the tempo (days versus hours), separate the two before any blood result returns.

22.3 Malignant catatonia: the mimic that can be indistinguishable

Trigger and signature. Malignant catatonia is the most treacherous look-alike, because it can be clinically indistinguishable from neuroleptic malignant syndrome and can precede it; indeed nms is regarded by some as a drug-induced form of malignant catatonia (Kaplan & Sadock 2024). It carries the same hyperthermia, rigidity and autonomic storm, but is distinguished by antecedent and accompanying **catatonic signs**, that is, a preceding phase of excitement, stupor, mutism, negativism, posturing or waxy flexibility, often before any antipsychotic was given. As an entity it is owned by the Other psychotic disorders, delusional syndromes and catatonia notes; it appears here only as the mimic to name in the differential. The practical consequence is decisive: a benzodiazepine (lorazepam) challenge and electroconvulsive therapy treat malignant catatonia, whereas a dopamine antagonist can worsen it, which is why the catatonic history must be sought before an antipsychotic is given to a rigid, febrile patient. The technique of electroconvulsive therapy is not taught here and is owned by the ECT and neurostimulation notes.

22.4 Anticholinergic toxicity: hot and DRY, "mad as a hatter"

Trigger and signature. Anticholinergic toxicity follows an anticholinergic load, from antimuscarinic antiparkinsonian agents (trihexyphenidyl, benztropine), low-potency antipsychotics, tricyclics, antihistamines and their combinations, and it is the great pretender because it also produces hyperthermia and delirium (APA 2021, Kaplan & Sadock 2024). The discriminator is the skin and the secretions: the patient is **hot but DRY**, with flushing, dilated pupils, urinary retention, **absent bowel sounds** and a florid delirium with visual hallucinations, and the creatine kinase is normal to only mildly raised, because there is no lead-pipe rigidity to break the muscle down. The classic teaching phrase is "hot, dry, red, mad" (hot as a hare, dry as a bone, red as a beet, mad as a hatter, blind as a bat). Muscle tone is not rigid, which alone separates it from neuroleptic malignant syndrome; the dry skin separates it from the drenching diaphoresis of both nms and serotonin syndrome. Kaplan & Sadock warn that "in some cases, anticholinergic toxicity may be mistaken for an exacerbation of psychosis, and the antipsychotic dose may be increased inappropriately" (Kaplan & Sadock 2024).

MNEMONIC

HOT, DRY, RED, MAD

The anticholinergic toxidrome: hot (hyperthermia), dry (dry skin and mucosae, the pivotal discriminator against the sweaty nms and serotonin syndrome), red (flushing), and mad (delirium), rounded out by dilated pupils, urinary retention and absent bowel sounds. If the febrile patient is sweating, it is not anticholinergic toxicity.

22.5 The one discriminator per entity

Stripping each syndrome to its single most decisive sign is what makes the differential usable under pressure. For each, one axis carries the diagnosis: the reflexes for the two neuromuscular emergencies, the catatonic history for the third, and the dry skin for the fourth. Everything else is corroboration.

PEARL

Bowel sounds triage the febrile, altered patient faster than any blood test: hyperactive points to serotonin syndrome, absent points to anticholinergic toxicity, and unremarkable with lead-pipe rigidity points to neuroleptic malignant syndrome. Pair that with the reflexes (brisk with clonus versus depressed) and the tempo (hours versus days) and the four-way differential resolves at the bedside.

22.6 The emergency differential grid

The table runs the six axes across all four entities, with the single discriminator for each highlighted in the final column. Read it column by column when a hyperthermic, rigid or agitated patient arrives: the trigger drug narrows the field, the motor sign and the reflexes separate nms from serotonin syndrome, the catatonic history flags malignant catatonia, and the dry skin with absent bowel sounds flags anticholinergic toxicity.

ENTITY	TRIGGER	RIGIDITY VS CLONUS	REFLEXES	PUPILS	BOWEL SOUNDS	THE ONE DISCRIMINATOR
Neuroleptic malignant syndrome	Antipsychotic (D2 block) or dopamine-agonist withdrawal	Lead-pipe rigidity	Hyporeflexia / normal	Normal	Normal	**Rigidity with hyporeflexia, days-long onset, very high creatine kinase (>1000 units/L)**
Serotonin syndrome	Serotonergic drug (start, increase, or combination)	Clonus, myoclonus (no lead-pipe rigidity)	Hyperreflexia	Dilated	Hyperactive (diarrhoea)	**Clonus with hyperreflexia, rapid (hours) onset**

ENTITY	TRIGGER	RIGIDITY VS CLONUS	REFLEXES	PUPILS	BOWEL SOUNDS	THE ONE DISCRIMINATOR
Malignant catatonia	Often none (may precede any antipsychotic)	Rigidity, can be indistinguishable from nms	Variable	Variable	Variable	**Antecedent catatonic signs (stupor, mutism, posturing, negativism); responds to lorazepam / ECT**
Anticholinergic toxicity	Anticholinergic load (antimuscarinics, TCAs, antihistamines)	Not rigid	Normal	Dilated	Absent	**Hyperthermia with DRY skin, flushing, urinary retention, delirium; creatine kinase normal to mild**

The four hyperthermic or rigid or agitated look-alikes across six axes, each keyed on its single discriminator; skin (dry versus sweaty), reflexes and bowel sounds carry the most diagnostic weight (Kaplan & Sadock 2024, APA 2021).

TRAP **Giving an anticholinergic to a hyperthermic, rigid patient before separating nms from anticholinergic toxicity.** Reaching for benztropine or promethazine "for the rigidity" in a patient who is actually in anticholinergic delirium pours petrol on the fire, and a warm sweaty nms patient does not benefit from an antimuscarinic either; separate the two on the dry-skin discriminator first.

Hours
SEROTONIN SYNDROME ONSET

1 to 3 days
NEUROLEPTIC MALIGNANT SYNDROME ONSET

>1000 units/L
CREATINE KINASE IN NMS (OFTEN); NORMAL-TO-MILD IN ANTICHOLINERGIC

INDIA

The everyday Indian anticholinergic load is trihexyphenidyl (benzhexol), routinely co-prescribed with high-potency first-generation agents such as haloperidol (marketed as Serenace), plus parenteral promethazine used for acute dystonia; stacking these on a low-potency antipsychotic is how a resident meets anticholinergic delirium on the ward. The reflex to add "one more anticholinergic for the stiffness" is exactly the trap, so the dry-skin discriminator must be checked before any antimuscarinic is given to a hot, rigid patient.

GOOD TO REMEMBER

- **Neuroleptic malignant syndrome:** feature, lead-pipe rigidity with hyperthermia and autonomic instability over 1 to 3 days; discriminator, rigidity with hyporeflexia and a very high creatine kinase; first step, stop the antipsychotic and support (cooling, IV fluids, high-dependency monitoring).
- **Serotonin syndrome:** feature, neuromuscular hyperactivity with hyperthermia over hours; discriminator, clonus with hyperreflexia, dilated pupils and hyperactive bowel sounds after a serotonergic drug; first step, stop the serotonergic agent, support, and give cyproheptadine.
- **Malignant catatonia:** feature, hyperthermia and rigidity that can be indistinguishable from nms; discriminator, antecedent catatonic signs (stupor, mutism, posturing); first step, a lorazepam challenge and consideration of ECT, and avoid a dopamine antagonist.
- **Anticholinergic toxicity:** feature, hyperthermia with delirium; discriminator, DRY skin, flushing, dilated pupils, urinary retention, absent bowel sounds ("hot, dry, red, mad") with a normal-to-mild creatine kinase; first step, stop the anticholinergic agents and give supportive care (physostigmine only in specialist hands).

HOLD THIS

Four hyperthermic look-alikes, four discriminators: rigidity with hyporeflexia over days is neuroleptic malignant syndrome, clonus with hyperreflexia over hours is serotonin syndrome, antecedent catatonic signs is malignant catatonia, and hot-but-DRY with absent bowel sounds and delirium is anticholinergic toxicity; never give an anticholinergic to a rigid febrile patient until you have separated nms from anticholinergic toxicity on the dry-skin sign.

Apply and consolidate

23 · Apply: four worked management vignettes

Everything in the preceding topics converges here into four short clinical decisions, each a **vignette** written as scenario, then reasoning, then plan. This is the format the examiner actually rewards: not a recital of doses but a defended choice, where the drug or the emergency step falls out of a weighing of efficacy against harm and a named discriminator. Nothing new is taught; the four moves are the four commonest management questions in the paper, worked to their answer.

How to use this page. Each of the four sub-topics is one worked example: a **first-episode** drug choice, a **treatment-resistant** case moving to clozapine, an acute **rigidity-and-fever** differential, and a maintenance **monitoring** case. The illness itself, its criteria and course, is not re-taught: it is owned by the Schizophrenia: aetiology, phenomenology, classification and course notes. The receptor pharmacology, dopamine pathways and CYP metabolism behind the drugs belong to the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; here the pharmacology is applied, not derived. Every dose, range and threshold below is verified against the cited source; anything not confirmable is flagged, not guessed.

23.1 Vignette 1: first-episode drug choice, weighing the adverse-effect profile

The decision. The first prescribing decision in a drug-naive young patient is not "which drug is strongest" but "which adverse-effect profile can this particular person live with", because among

the non-clozapine antipsychotics there is no clear efficacy winner, only minor individual advantages, so the choice is driven almost entirely by tolerability and by the **metabolic** versus extrapyramidal versus hyperprolactinaemia trade-off (Maudsley 2021, Leucht 2013). The reasoning below is the worked example the examiner wants.

WORKED EXAMPLE

Case: a 21-year-old man, antipsychotic-naive, first episode of a schizophrenia-spectrum psychosis, physically well, normal weight, keen to return to college, no cardiac history. **Reasoning.** He is drug-naive and therefore dose-sensitive, so whatever is chosen starts low and titrates slowly against response and tolerability. Efficacy will not separate the reasonable options, so the choice turns on the harm he can least afford. A young man who wants to study and stay engaged will be lost by heavy sedation and by weight gain, so a markedly metabolic agent (olanzapine) is a poor first choice despite good efficacy; a strongly prolactin-raising or EPS-prone agent risks sexual dysfunction and motor side effects that also drive covert non-adherence. **Plan.** Take a full baseline first (weight, height and BMI, fasting glucose and lipids, blood pressure, ECG where indicated), then start a single antipsychotic at the lowest effective dose: a reasonable, defensible first choice is aripiprazole, weight-neutral and prolactin-sparing, at **10 mg/day** (a valid first-episode starting dose), or risperidone **2 mg/day** if a more sedating, more familiar agent is wanted, accepting its dose-related prolactin rise. Titrate slowly, run an adequate trial before judging response, and decide the drug with the patient. This is shared decision-making, not a default.

RULE **First episode: choose on adverse effects, start low.** Efficacy does not separate the non-clozapine agents, so pick the one whose harm profile the patient can live with, take the baseline, then start at the lowest effective dose in a dose-sensitive drug-naive brain.

TRAP **Reaching for the strongest drug or the loading dose.** Starting a metabolically heavy agent, or front-loading a high dose in a drug-naive patient, buys adverse effects and non-adherence for no efficacy gain; "lowest effective" is not homeopathic, but the first episode is where over-dosing loses the alliance.

23.2 Vignette 2: treatment resistance, confirming it and moving to clozapine

The decision. The move to clozapine is earned, not assumed: it is triggered the moment true **treatment resistance** is confirmed, and the classic error is a third same-class switch instead. The definition is failure of two adequate antipsychotic trials, each at an adequate dose (about 600 mg chlorpromazine-equivalent) for an adequate duration (at least 6 weeks), with adherence confirmed and misdiagnosis and pseudo-resistance excluded (Maudsley 2021, APA 2020, Kane 1988). This worked example walks the confirmation, then sets up the monitoring.

WORKED EXAMPLE

Case: a 29-year-old woman with persistent positive symptoms of at least moderate severity despite two antipsychotics. **Reasoning: confirm resistance first.** Were both trials genuinely adequate: an adequate dose (about **600 mg/day** chlorpromazine-equivalent) for an adequate duration (at least **6 weeks** at optimum dose, which is the TRRIP resistance minimum, not the looser 4-to-6-week general switching rule)? Was adherence real (target 80% or more, checked, not assumed, since covert non-adherence is the commonest fake resistance)? Is the diagnosis right, and are substance use, an untreated depression and inadequate psychosocial support excluded? Only when all of that is cleared is this true resistance, not pseudo-resistance. **Plan.** Move to clozapine, not a third me-too antipsychotic. Response is usually seen across **150 to 900 mg/day** (UK average around 450 mg/day; maximum 900 mg/day), titrated slowly against tolerability and plasma level (Maudsley 2021). Set up the mandatory haematological monitoring before the first dose: baseline full blood count, then FBC **weekly for 18 weeks**, then two-weekly to one year, then monthly. Hold the two neutrophil cut-offs as the safety spine: stop clozapine if the neutrophil count falls below **1.5 x10^9/L**, and refer to specialist medical care if it falls below **0.5 x10^9/L** (Maudsley 2021). Baseline an ECG (myocarditis and QT risk), give a gastrointestinal history for the hypomotility risk, and warn of the transient benign fever of early titration.

RULE **Two adequate failed trials means clozapine.** Confirm adequacy of dose, duration and adherence and exclude pseudo-resistance, then move to clozapine, never to a third antipsychotic of the same broad class.

TRAP **Stopping clozapine for a benign transient neutropenia.** The action threshold is a neutrophil count below 1.5 x10^9/L; a mild dip that stays above it, or benign ethnic neutropenia, is not an automatic stop, and pulling the one drug that works on a misread count harms the patient.

23.3 Vignette 3: acute rigidity and fever, the NMS differential

The decision. A patient on an antipsychotic who becomes rigid and febrile is neuroleptic malignant syndrome until proven otherwise, and the whole of management is: recognise it, stop the drug, support the patient. The reasoning is a three-way differential against serotonin syndrome and malignant catatonia, each separated by a named discriminator (Maudsley 2021, Kaplan & Sadock 2024). Malignant catatonia as an entity is owned by the Other psychotic disorders, delusional syndromes and catatonia notes; it appears here only inside this differential.

ENTITY	KEY FEATURE	DISCRIMINATOR	FIRST STEP
NMS	Lead-pipe rigidity, hyperthermia, autonomic instability, altered consciousness; CK often >1000 units/L	**Uniform lead-pipe rigidity + a dopamine-blocker trigger, evolving over 1 to 3 days**	Stop the antipsychotic, supportive care
Serotonin syndrome	Hyperthermia, autonomic instability, altered mental state, neuromuscular hyperactivity	**Clonus and hyperreflexia (not lead-pipe rigidity) + a serotonergic drug, faster onset (hours)**	Stop the serotonergic agent, supportive care
Malignant catatonia	Rigidity, hyperthermia, autonomic storm, may be clinically indistinguishable from NMS	**Often a preceding psychiatric excitement/catatonic phase; may occur without a dopamine-blocker trigger; responds to ECT**	Supportive care; benzodiazepines/ECT (owned by the ECT notes)

The rigidity-and-fever differential: the discriminator column carries the exam answer, and the first step for NMS is always to stop the drug and support (Maudsley 2021, Kaplan & Sadock 2024).

WORKED EXAMPLE

Case: a 34-year-old man, five days into an escalated dose of a high-potency antipsychotic, brought in confused, with a temperature of 39.5 degrees, generalised stiffness and labile blood pressure. **Reasoning.** The rigidity is uniform and lead-pipe, not the clonus-and-hyperreflexia of serotonin syndrome, and there is a clear dopamine-blocker trigger with the characteristic 1-to-3-day evolution, so this is NMS, not serotonin syndrome; there is no preceding catatonic excitement and no serotonergic drug. A creatine kinase, which is often above **1000 units/L** in NMS, supports the picture but does not by itself make the diagnosis (asymptomatic rises are common). **Plan.** The first step is not a drug: **stop the antipsychotic immediately** and start supportive care (cooling, fluids and rehydration, correction of electrolytes, and monitoring for renal failure from rhabdomyolysis). Only then consider specific pharmacology (dantrolene, bromocriptine, benzodiazepines) for severe or refractory cases. When restarting later, wait a minimum of **5 days** off the drug and preferably longer, then rechallenge with a lower-potency or second-generation agent (Maudsley 2021).

TRAP **Missing NMS behind "just rigid from the antipsychotic".** Fever plus a raised creatine kinase plus autonomic instability is not ordinary parkinsonism; a stiff, febrile patient on a dopamine blocker is NMS until proven otherwise, and the cost of the miss is death.

23.4 Vignette 4: adverse-effect monitoring on maintenance, and what to change

The decision. A stable patient on a maintenance antipsychotic is not "done": the silent harms (metabolic, prolactin, cardiac) are what shorten this population's life, so the maintenance job is to run the **monitoring schedule**, read it, and change the drug when a threshold is crossed (Maudsley 2021, APA 2020). This worked example runs the three tracks and lands the switch decision.

1.5 to 0.5	3 mo then yearly	440 / 470 ms	>500 ms
CLOZAPINE NEUTROPHIL CUT-OFFS (X10^9/L): STOP, THEN REFER	GLUCOSE AND LIPIDS AFTER BASELINE (MAUDSLEY)	UPPER-NORMAL QTC, MEN / WOMEN	QTC THAT MANDATES ACTION

WORKED EXAMPLE

Case: a 42-year-old man, well for two years on maintenance olanzapine, comes for review having gained weight, and separately a woman on risperidone reports galactorrhoea and amenorrhoea. **Reasoning: run three tracks.** *Metabolic*: weight, waist and BMI are recorded frequently for the first three months then at least yearly, and fasting glucose (or HbA1c) and a fasting lipid panel are taken at baseline, at 3 months, then yearly (more often, 3-monthly in the first year, for olanzapine and clozapine) (Maudsley 2021). His weight gain on a high-metabolic-risk agent is a signal to act. *Prolactin*: the woman's galactorrhoea and amenorrhoea point to hyperprolactinaemia; treatment is driven by the symptoms and the long-term bone risk, not by the number in isolation, and a level over **2500 mIU/L** prompts referral to exclude a prolactinoma. *Cardiac*: check the QTc against the upper-normal bands, **440 ms** in men and **470 ms** in women, with a QTc **over 500 ms** mandating action. **Plan: what to change.** For the metabolic case, offer lifestyle advice and switch toward a weight-neutral agent (aripiprazole) or add a metabolic-sparing adjunct; for the prolactin case, once a prolactinoma is excluded, switch to a prolactin-sparing agent (aripiprazole) or add adjunctive aripiprazole; for a QTc over 500 ms, stop or switch the offending QT-prolonging agent (haloperidol at high dose or IV is the worst offender) and correct electrolytes.

RULE **Maintenance is monitoring plus a switch.** Run the metabolic, prolactin and cardiac tracks on schedule; when weight climbs, prolactin is symptomatic, or the QTc crosses its band, the action is to switch to a sparing agent, not to keep watching.

HOLD THIS

Four moves, four discriminators: first episode, choose on the adverse-effect profile and start low; treatment resistance, confirm two adequate failed trials then move to clozapine with its neutrophil monitoring; acute rigidity and fever, call it NMS until proven otherwise, stop the drug and support; maintenance, run the metabolic, prolactin and cardiac monitoring and switch to a sparing agent when a threshold is crossed.

GOOD TO REMEMBER

- **Aripiprazole (first-episode and switch target):** a dopamine D2 partial agonist (mechanism owned by the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes); a valid first-episode starting dose is 10 mg/day; the one thing to hold is that it is weight-neutral and prolactin-sparing, which is exactly why it is the first-choice switch or add-on for antipsychotic-induced metabolic burden or hyperprolactinaemia.
- **Risperidone (a reasonable first-episode alternative):** a second-generation D2/5-HT2A antagonist; a valid first-episode starting dose is 2 mg/day; the one caveat is its dose-related rise in prolactin, so ask about galactorrhoea, menstrual change and sexual dysfunction at review.
- **Clozapine (the treatment-resistance answer):** the only agent with proven superiority in true resistance; response usually across 150 to 900 mg/day (UK average around 450 mg/day, maximum 900 mg/day); the monitoring parameter to hold is the neutrophil count, FBC weekly for 18 weeks then two-weekly to one year then monthly, stop below 1.5 x10^9/L and refer below 0.5 x10^9/L (Maudsley 2021).
- **NMS (the rigidity-and-fever emergency):** feature, lead-pipe rigidity + hyperthermia + autonomic instability + altered consciousness, CK often >1000 units/L; discriminator from serotonin syndrome, uniform rigidity (not clonus/hyperreflexia) with a dopamine-blocker trigger over 1 to 3 days; first step, stop the antipsychotic and give supportive care, wait a minimum of 5 days before a lower-potency rechallenge.
- **Hyperprolactinaemia (the maintenance endocrine harm):** feature, galactorrhoea, amenorrhoea and sexual dysfunction from tuberoinfundibular D2 blockade; discriminator, symptom-driven with a level over 2500 mIU/L prompting a prolactinoma referral; first step, once a prolactinoma is excluded, switch to a prolactin-sparing agent (aripiprazole) or add adjunctive aripiprazole.
- **QTc prolongation (the maintenance cardiac harm):** feature, a lengthened QT interval on the road to torsades de pointes; discriminator, upper-normal 440 ms (men) and 470 ms (women), with over 500 ms the threshold that mandates action; first step, stop or switch the offending agent (haloperidol high-dose or IV is the worst) and correct electrolytes (Maudsley 2021).

INDIA

Clozapine monitoring in the Indian setting follows the same neutrophil logic but is run through the treating psychiatrist and local laboratory rather than a mandatory national registry, so the discipline of the schedule sits with the clinician; benign ethnic neutropenia is a genuine consideration when reading borderline counts. The Indian Psychiatric Society (IPS) schizophrenia guideline endorses the same core pathway: confirm resistance across two adequate trials, then move to clozapine. Where an early long-acting injectable is chosen to secure adherence, olanzapine long-acting injection is marketed in India as Tolaz (Torrent), with its binding constraint the post-injection syndrome that mandates a supervised post-injection observation period after every dose. Verify the local brand and formulation before naming one; generic prescribing dominates and is affordable.

Figure. A four-panel decision map, one panel per vignette (first-episode choice by adverse-effect axis; the confirm-resistance-then-clozapine ladder with neutrophil cut-offs; the NMS-versus-serotonin-versus-catatonia discriminator triangle; the three maintenance monitoring tracks with their switch thresholds), is flagged for a concept figure.

24 · Consolidate: mnemonic, retrieval and synthesis

Everything in this chapter has been laid out in bands: the plan and the algorithm, drug choice and the receptor trade-off, treatment resistance and clozapine, psychosocial rehabilitation, and the adverse effects and emergencies. This closing topic does not add facts; it fuses them. The examinable payoff of the whole note is the ability to unpack one seed cue into the entire management chapter, to recall each band cold under viva pressure, and to redraw the structure of treatment from a blank page. Consolidation is the step that turns a read note into a retrievable one, and on a management question it is where marks are won or lost: the examiner rewards the candidate who can place a patient on the algorithm, defend a drug against its adverse-effect trade-off, recognise resistance and reach clozapine, and spot the emergency, all from one chained cue.

How to use this page. Three tools, in order. First, the master **mnemonic** that chains the whole chapter so a single cue unpacks the note, the payoff of the seed planted in the orientation topic. Second, a set of **answer-free recall prompts**: the single highest-yield revision technique for this material is **active recall**, so test yourself against these before you re-read anything. Third, a **synthesis map** to redraw from memory, the four-branch skeleton on which every drug, adverse effect and emergency hangs. Do not treat this as a summary to skim; treat it as a set of exercises to perform. The illness itself, its phenomenology, aetiology, criteria and course, is not re-taught here; it belongs to the Schizophrenia: aetiology, phenomenology, classification and course notes.

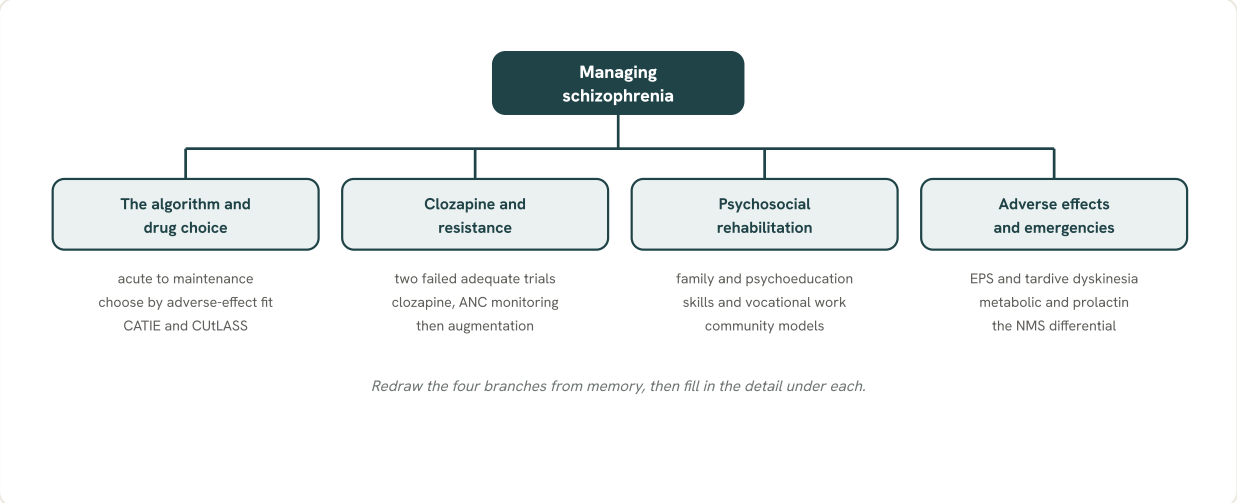


Fig 9.14 The whole-chapter synthesis map. Managing schizophrenia has four branches: the treatment algorithm and drug choice, clozapine and treatment resistance, psychosocial rehabilitation, and the adverse effects and their emergencies. Cover the detail, redraw the four branches from memory, then reconstruct what sits under each.

24.1 The master mnemonic: the whole chapter on one seed

The seed unpacked. The chapter runs as one management sequence, and one master mnemonic chains it so that a single cue delivers the entire note: *choose* the drug, *maintain* it, *resist*ance turns you to clozapine, *rehabilitate* across all phases, then *watch the harms*. This is the payoff of the seed set at orientation: *CHOOSE, MAINTAIN, RESIST, REHABILITATE, WATCH THE HARMS*, in reading order. Fix the five links and every later topic slots onto its band; the harms link is the longest, because the adverse effects and emergencies carry the most marks. The box below

unpacks every letter of the chain, chaining the plan and the algorithm from acute to maintenance, drug choice and the receptor trade-off, treatment resistance and clozapine, psychosocial rehabilitation, and the adverse effects and emergencies.

MNEMONIC

"CHOOSE, MAINTAIN, RESIST, REHABILITATE, WATCH THE HARMS": the management chain. CHOOSE = the plan (locus, focus, modus), the algorithm (acute, stabilisation, maintenance) and drug choice on the D2-versus-adverse-effect trade-off. MAINTAIN = long-term, lowest effective dose, the LAI for adherence. RESIST = two failed adequate trials, then clozapine, then augmentation. REHABILITATE = family work, CBT for psychosis, skills and vocational rehabilitation. WATCH THE HARMS = EPS and tardive dyskinesia, metabolic, prolactin and QTc, then NMS and clozapine neutropenia.

Unpack it link by link. **CHOOSE** is the plan and the algorithm: set the biopsychosocial plan as *locus* (least-restrictive care), *focus* (the symptoms set by the phase) and *modus* (every mode of treatment), run the algorithm forward through the acute, stabilisation and maintenance phases, and choose a single antipsychotic on the receptor trade-off, more D2 blockade buys antipsychotic effect but also extrapyramidal and prolactin harm, while broader receptor action buys metabolic harm (the receptor and pathway mechanics are owned by the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; here we apply them). An adequate trial is 4 to 6 weeks at optimum dose (Maudsley 2021). **MAINTAIN** is the maintenance phase: continue long-term at the lowest effective dose for relapse prevention, reaching for a long-acting injectable where adherence is the limiting problem. **RESIST** is the treatment-resistance branch: non-response across two adequate antipsychotic trials turns the algorithm to clozapine, the one drug with evidence in refractory illness, and only then to augmentation (developed in the treatment-resistance and clozapine topics; ECT for augmentation, resistance and catatonia belongs to the ECT and neurostimulation notes). **REHABILITATE** is the psychosocial modus that runs across all phases: family intervention and psychoeducation to reduce high expressed emotion, CBT for psychosis, and social-skills and vocational rehabilitation, because the drug alone does not restore function. **WATCH THE HARMS** is the safety spine and the highest-yield band: the movement disorders (acute extrapyramidal side-effects and tardive dyskinesia), the metabolic syndrome, hyperprolactinaemia and QTc prolongation, and the two emergencies, neuroleptic malignant syndrome and clozapine-related neutropenia. One seed, the whole chapter.

RULE **One cue, five links.** If you can say "CHOOSE, MAINTAIN, RESIST, REHABILITATE, WATCH THE HARMS" and unpack each link into its topic, you can rebuild the entire management chapter without notes; that is the whole point of the seed.

TRAP **Memorising the acronym without the unpacking.** A mnemonic you cannot expand is a dead cue; drill the expansion (plan and algorithm, LAI, two failed trials to clozapine, the psychosocial limbs, and each named harm) until every link opens its own paragraph, or the chain buys you nothing in the viva.

24.2 Retrieval practice across the three bands

Why testing beats re-reading. The evidence on studying is unambiguous: **active recall** and spaced **retrieval practice** outperform passive re-reading and highlighting for durable memory. Use the prompts below as your first pass, not your last. **Cover the answers** that live in the topics above, attempt each prompt aloud or on paper from memory, and only then check yourself against the relevant topic. The prompts span the three bands, the algorithm and drug choice, resistance and clozapine, and the adverse effects and emergencies, so that a single sitting exercises the whole chapter. Do not print or peek at the answers first; the learning is in the effort of retrieval.

RETRIEVAL PRACTICE, COVER THE ANSWERS

These are answer-free recall prompts. This is **active recall**: **retrieval practice** works only if you attempt each one from memory before checking, so **cover the answers** in the topics above and write your own before you look.

1. State the three limbs of the biopsychosocial plan (locus, focus, modus) and say what sets the focus.
2. Name the three phases of the treatment algorithm in order and give the single target of each.
3. Define an adequate antipsychotic trial in duration and dose, and say why it matters before relabelling a patient resistant.
4. Give the staged escalation for acute agitation, from the first move to the last resort.
5. State the receptor trade-off that governs drug choice: what more D2 blockade buys you and what it costs you.
6. Contrast a first-generation with a second-generation antipsychotic on the two adverse-effect axes that separate them.
7. Name the single indication for a long-acting injectable in the maintenance phase.
8. Define treatment-resistant schizophrenia: how many adequate trials of how many drugs must fail.
9. Name the one drug licensed for treatment-resistant schizophrenia and the one blood parameter that must be monitored on it.
10. List the acute extrapyramidal side-effects and give the first management step for akathisia.
11. Distinguish tardive dyskinesia from an acute dystonia on timing and on the effect of the offending drug.
12. Name the components of antipsychotic-induced metabolic syndrome and the parameters recorded at baseline.
13. State the clinical tetrad of neuroleptic malignant syndrome and the single first management step.
14. Distinguish neuroleptic malignant syndrome from serotonin syndrome and from malignant catatonia on the two features that separate them.
15. Name the two antipsychotic emergencies that are true medical emergencies and the immediate action for each.

RULE **Attempt before you check.** The learning is in the effortful retrieval, not in reading the answer; a prompt you look up without trying teaches almost nothing.

24.3 The synthesis map: redraw the chapter from memory

One skeleton, four branches. The final consolidation exercise is to draw the synthesis map of the whole chapter on a blank page: a central node, managing schizophrenia, with four branches, the algorithm and drug choice; clozapine and resistance; psychosocial rehabilitation; and adverse effects and emergencies. Off *the algorithm and drug choice* hang the three phases from acute to maintenance and the receptor-versus-adverse-effect trade-off that picks the molecule; off *clozapine and resistance* hang the two-failed-trials definition, clozapine and its haematological

monitoring, and then augmentation; off *psychosocial rehabilitation* hang family intervention and psychoeducation, CBT for psychosis, and skills and vocational work; off *adverse effects and emergencies* hang the extrapyramidal side-effects and tardive dyskinesia, the metabolic syndrome and prolactin and QTc, and the neuroleptic malignant syndrome and clozapine neutropenia emergencies. Rebuild this map from memory, and redraw from memory each week until the four branches and their twigs come without prompting, and you own the chapter; the mnemonic in 24.1 is the verbal form of this same synthesis map, and each recall prompt in 24.2 tests one twig of it.

HOLD THIS

The whole chapter is one seed, "CHOOSE, MAINTAIN, RESIST, REHABILITATE, WATCH THE HARMS", unpacking into four branches, the algorithm and drug choice, clozapine and resistance, psychosocial rehabilitation, and adverse effects and emergencies; recall it by active retrieval with the answers covered, and redraw the four-branch synthesis map from memory until every twig comes unprompted.

GOOD TO REMEMBER

- **Master mnemonic (CHOOSE, MAINTAIN, RESIST, REHABILITATE, WATCH THE HARMS):** the management chapter chained in reading order; central claim is that one seed cue unpacks the whole note (plan and algorithm, drug choice, resistance to clozapine, psychosocial rehabilitation, adverse effects and emergencies); the discriminator to hold is that the fifth link, the harms, is the longest and highest-yield on a management question.
- **Active recall and retrieval practice:** testing yourself from memory with the answers covered before re-reading; central claim is that effortful retrieval produces more durable memory than passive review; the discriminator is that the benefit depends on attempting each prompt before checking, so answer-free prompts are the correct format and the answers are never printed.
- **Synthesis map (Fig 9.14):** a central managing-schizophrenia node with four branches, the algorithm and drug choice, clozapine and resistance, psychosocial rehabilitation, and adverse effects and emergencies; central claim is that redrawing it from memory proves the structure is held, not just the facts; the discriminator is that it is the visual twin of the master mnemonic and of the recall-prompt set, so all three tools test the same skeleton.

Figure. The whole-chapter synthesis map, a central managing-schizophrenia node with its four branches, the algorithm and drug choice (acute to maintenance, choose by the receptor trade-off), clozapine and resistance (two failed adequate trials, clozapine and monitoring, then augmentation), psychosocial rehabilitation (family and psychoeducation, CBT for psychosis, skills and vocational work), and adverse effects and emergencies (extrapyramidal side-effects and tardive dyskinesia, metabolic and prolactin and QTc, the neuroleptic malignant syndrome differential and clozapine neutropenia), to be redrawn from memory, is drawn as Fig 9.10.

Previously asked

The treatment of schizophrenia is examined as heavily as the illness, and it splits cleanly along the three bands of these notes. The management and the drugs come as long essays with a diagnosis-and-manage stem and as short notes on the individual agents; rehabilitation is a

recurring full essay; and the adverse effects and emergencies are a perennial source of both the 25-mark movement-disorder case and a stream of short notes. The genuine questions below are grouped by the three bands.

? HOW THIS TERRITORY IS ACTUALLY TESTED

Q **Antipsychotic pharmacotherapy and management.** The recurring long-essay tail of the schizophrenia papers is the management, and it is also asked directly as "management of treatment-resistant schizophrenia" more than once. The drugs themselves come as short notes, "clozapine", "clozapine, adverse effects and management", and single agents such as "aripiprazole". Build the treatment algorithm and the two-failed-trials definition to answer these. long essay and short note, recurring

Q **Psychosocial rehabilitation and psychological treatment.** "Discuss rehabilitation in schizophrenia" is a repeated full essay, and the components come as their own short notes, "social skills training in schizophrenia", "psychoeducation", "therapeutic community", and "rehabilitation in psychiatry practice". The Indian service frame is asked as "community mental health in the Indian context" and "the national mental health plan and community psychiatry in India". long essay and short note, recurring

Q **Adverse effects and emergencies.** The classic 25-mark case is a patient on an antipsychotic and an antidepressant who develops involuntary movements, to investigate, diagnose, manage and explain the pathophysiology, and "neuroleptic malignant syndrome and its differential diagnosis" is asked as its own essay. The short notes are steady, "tardive dyskinesia", "antipsychotic drug-induced movement disorders", "drug-induced extrapyramidal reactions", "antipsychotic-induced metabolic syndrome", "adverse effects of atypical antipsychotics", "adverse effects of olanzapine", and "management of hyperprolactinaemia in psychiatry". long essay and short note, recurring

Prepare this material to be argued, not just recited: the treatment algorithm, the drug-choice and emergency-differential selectors, and the four worked vignettes in these notes are built to the way the topic is examined. The phenomenology, aetiology, criteria and course of the illness are developed in the Schizophrenia: aetiology, phenomenology, classification and course notes; malignant catatonia and the other psychotic disorders as entities live in the Other psychotic disorders, delusional syndromes and catatonia notes; these notes own the antipsychotics, the psychosocial treatment, and the adverse effects and their emergencies.

Quick review

The whole subject in one table	
THE PLAN AND THE ALGORITHM	A biopsychosocial plan on the LOCUS (where), FOCUS (target by phase) and MODUS (every mode of treatment) spine. Antipsychotics run acute to stabilisation to maintenance; acute agitation is managed by de-escalation first, then rapid tranquillisation and, least-restrictive, restraint. When two adequate trials fail, the illness is treatment-resistant and the next step is clozapine.
MECHANISM AND RECEPTORS	All effective antipsychotics block dopamine D2; the antipsychotic effect maps to about 65 to 80 percent striatal D2 occupancy, above which extrapyramidal risk rises without added benefit. The 5-HT2A to D2 balance defines the atypicals. The receptor profile predicts the harm: D2 for extrapyramidal effects and prolactin, H1 for sedation and weight, M1 anticholinergic, alpha-1 postural hypotension.
TYPICAL ANTIPSYCHOTICS	First-generation agents split by potency: high-potency (haloperidol, marketed as Serenace) with more extrapyramidal effects and prolactin, low-potency (chlorpromazine) with more sedation, anticholinergic and metabolic effects. Effective against positive symptoms, cheap, but a higher extrapyramidal and tardive burden.
ATYPICAL AND NEWER AGENTS	Second-generation agents (risperidone as Sizodon, olanzapine as Oleanz, quetiapine as Qutipin, amisulpride) trade a lower extrapyramidal burden for a metabolic one. Partial agonists (aripiprazole as Arip, cariprazine, brexpiprazole) are metabolically light. Lurasidone is metabolically favourable, taken with food; asenapine is sublingual; zotepine carries seizure risk. Xanomeline-trospium acts by muscarinic M1 and M4 agonism, not D2 blockade.
CHOOSING THE DRUG	Apart from clozapine, CATIE and CUtLASS found no large efficacy gap between the generations, so choice is driven by the adverse-effect fit for the patient (metabolic vs extrapyramidal vs prolactin vs sedation vs cardiac), not by a claimed superiority.
FIRST EPISODE AND MAINTENANCE	Treat the first episode early at the lowest effective dose (these patients are dose-sensitive); a long duration of untreated psychosis worsens outcome, the rationale for early-intervention services. Maintenance at the lowest effective dose is relapse prevention: relapse is far higher off medication, and intermittent or targeted dosing raises relapse and is not recommended.
DEPOT AND LONG-ACTING INJECTABLES	Assured-adherence maintenance that cuts relapse and rehospitalisation by roughly 20 to 30 percent versus the same oral drug; offer early. Risperidone microspheres need about 3 weeks of oral cover; paliperidone palmitate is 1-monthly and 3-monthly; the olanzapine injectable (Tolaz in India) needs a 3-hour post-injection observation for the post-injection syndrome.

The whole subject in one table	
TREATMENT RESISTANCE	Treatment-resistant schizophrenia is a failure of two adequate antipsychotic trials, each of adequate dose and duration with confirmed adherence. Exclude pseudo-resistance (non-adherence, inadequate trial, substance use, wrong diagnosis) first, then move to clozapine, not a third me-too switch.
CLOZAPINE	The only agent proven superior in true resistance (Kane 1988). Start 12.5 mg, build to 300 to 450 mg/day (up to 900). Neutrophils weekly for 18 weeks, then fortnightly to a year, then 4-weekly: continue at an absolute neutrophil count of 2.0 or above, recheck at 1.5 to 2.0, stop below 1.5, agranulocytosis below 0.5. Watch for myocarditis in the first month and a constipation that can be fatal.
AUGMENTATION AND POLYPHARMACY	For the ultra-resistant patient after an optimised clozapine trial: add a second antipsychotic (amisulpride, aripiprazole), lamotrigine, or electroconvulsive therapy (the ECT and neurostimulation notes). Rational polypharmacy needs a defined target, a defined trial and a plan to stop; long-term two-antipsychotic use without benefit is avoided.
NEGATIVE SYMPTOMS	Separate secondary negatives (from positive symptoms, depression, extrapyramidal effects, understimulation, all reversible) from primary; treat the secondary cause first. No drug reliably treats primary negatives; consider an agent with a better negative signal (amisulpride, cariprazine) and the psychosocial and cognitive approaches.
PSYCHOSOCIAL REHABILITATION	Medication controls symptoms but rehabilitation delivers function and recovery, so it is core, not optional. Its components are psychoeducation and family work, social skills and vocational training, the psychological therapies and community support.
FAMILY AND SKILLS INTERVENTIONS	Family intervention in high-expressed-emotion households is one of the best-evidenced relapse-prevention tools. Supported employment (place then train, the Individual Placement and Support model) beats prevocational train-then-place for competitive work.
PSYCHOLOGICAL THERAPIES	CBT for psychosis is an evidence-based adjunct for persistent distressing symptoms; cognitive remediation improves cognition with a small-to-moderate effect that transfers to function best when paired with rehabilitation.
COMMUNITY MODELS	Assertive community treatment and case management target the most disabled, frequently-admitted patients. The Indian models are the District Mental Health Programme, day care and halfway homes, within the National Mental Health Programme.
EXTRAPYRAMIDAL EFFECTS	By onset: acute dystonia in hours (a parenteral anticholinergic), akathisia in days (reduce or switch, propranolol, never raise the dose), parkinsonism in weeks (reduce or switch, or an anticholinergic).

The whole subject in one table	
	Akathisia mistaken for agitation and treated with more antipsychotic is the classic error.
TARDIVE DYSKINESIA	Late choreoathetoid movements after months to years, screened with the AIMS; risk with older age, first-generation agents and longer exposure. Prevent with the lowest effective dose and second-generation agents; treat established disease with a VMAT2 inhibitor (valbenazine, deutetrabenazine); anticholinergics worsen it.
NEUROLEPTIC MALIGNANT SYNDROME	Lead-pipe rigidity, hyperthermia, autonomic instability and altered mental state over one to three days, with a markedly raised creatine kinase. Stop the antipsychotic, give supportive care, and use dantrolene or bromocriptine. Fever with rigidity in a treated patient is NMS until proven otherwise.
METABOLIC AND CARDIAC EFFECTS	Olanzapine and clozapine carry the highest metabolic risk. Monitor weight at baseline, 6 and 12 weeks then annually, and glucose or HbA1c, lipids and blood pressure at baseline, 12 weeks and annually. Hyperprolactinaemia is worst with risperidone, paliperidone and amisulpride; watch QTc (worst with thioridazine, pimozide, high-dose intravenous haloperidol) and do not stack QT-prolonging drugs.
THE EMERGENCY DIFFERENTIAL	Rigidity with hyporeflexia and a very high creatine kinase is NMS; clonus and hyperreflexia after a serotonergic drug is serotonin syndrome; catatonic signs that precede the picture point to malignant catatonia; hot, dry, flushed skin with absent bowel sounds is anticholinergic toxicity. The discriminator, not the shared fever, makes the call.
APPLY AND CONSOLIDATE	Four worked cases: a first-episode drug choice by adverse-effect fit, a treatment-resistant case reasoned to clozapine, an acute rigidity-and-fever case worked as the NMS differential, and an adverse-effect monitoring case. Then the master mnemonic, answer-free retrieval prompts, and the four-branch synthesis map to redraw from memory.

References

The management content is grounded in the standard prescribing and clinical texts (the source hierarchy below), which anchor the settled facts on antipsychotic pharmacology, dosing, adverse effects and their management; the treatment-algorithm and monitoring detail follows the Maudsley Prescribing Guidelines, Stahl and the schizophrenia treatment guidance of NICE, the American Psychiatric Association and the Indian Psychiatric Society. Every landmark trial, dose, therapeutic range and monitoring threshold has been checked against these sources, and every named clinical trial carries a PubMed-verified journal citation. Each PMID here was checked against PubMed this build, matched on title, first author and year; any identifier that did not resolve to the cited paper was dropped rather than guessed. A few citations that support a claim but have no stable PubMed record (society guidelines, the expressed-emotion classics of Brown

and of Butzlaff and Hooley, and the Individual Placement and Support and recovery literature) are cited by author, title and year in the text, and the same claims are also covered by the verified references retained here.

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PART III

III

Other Psychotic Disorders, Delusional Syndromes and Catatonia

The psychoses beyond schizophrenia: the delusional and brief syndromes, shared and organic psychosis, and catatonia.

01 Other primary psychotic disorders

02 Delusional misidentification and named delusional syndromes

03 Catatonia

04 Apply and consolidate

PAPER II

Other psychotic disorders, delusional syndromes and catatonia

Four sections · one complete notes document

This material closes the schizophrenia-spectrum block, gathering into one document the psychotic disorders that are not schizophrenia, the delusional syndromes, and catatonia. The first band is **other primary psychotic disorders**: the schizophrenia-spectrum decision tree that separates them by duration and mood-loading, then schizoaffective disorder, delusional disorder, the life-cycle of a delusion from its formation to its dissolution, the acute and transient psychotic disorders, brief psychotic disorder, the induced and shared delusional disorders, postpartum psychosis and the late-onset psychoses, the attenuated psychosis syndrome, and the interleaved differential that tells them apart. The second band is **delusional misidentification and named delusional syndromes**: Capgras, Fregoli, intermetamorphosis and the subjective doubles, and the named monothematic syndromes of De Clerambault, Othello, Cotard and Ekbom, each keyed on its core delusional content. The third band is **catatonia**: the classical and modern signs and the examination, the psychiatric, neurological and medical causes and the transdiagnostic placement, the lorazepam challenge and benzodiazepine management, malignant catatonia and its differential from neuroleptic malignant syndrome, and the place of electroconvulsive therapy. The examinable skill is discrimination: to place a psychotic presentation on the spectrum by its duration, mood-loading and delusion-type, to name a syndrome by its core content, and to recognise catatonia and its malignant form and act.

HOW TO USE THESE NOTES

Read the three bands as one exercise in telling psychotic presentations apart. The **other primary psychotic disorders** band opens with the spectrum decision tree, then teaches each disorder against schizophrenia and against each other, and closes on the interleaved differential; each named entity ends with a **Good to remember** box giving what it is, the core criteria or the one discriminating feature, and the one number or eponym to hold. The **delusional misidentification and named syndromes** band draws the eponymous syndromes as grids keyed on the core delusional content, distinguishing which are the content of a delusion from which are named disorders. The **catatonia** band runs from the signs and their examination, through the causes and the transdiagnostic placement, to the lorazepam challenge and the malignant-catatonia emergency. Figures declare one axis and code it in colour: **petrol** marks structure and the neutral case, **coral** marks the trap or the danger, and **marigold** highlights the number or eponym to hold. Several boundaries are worth stating up front: the phenomenology, aetiology, criteria and course of schizophrenia itself are taught in the Schizophrenia: aetiology, phenomenology, classification and course notes and are not repeated here; the antipsychotic drugs and neuroleptic malignant syndrome as an entity belong to the Schizophrenia: management, antipsychotics and adverse effects notes, needed here only inside the malignant-catatonia differential; the technique of electroconvulsive therapy lives in the ECT and neurostimulation notes; the mood-episode criteria for schizoaffective disorder live in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes; and the raw descriptive definitions of the individual delusions and misidentification phenomena live in the Psychometry, Assessment and Descriptive Psychopathology notes, applied here rather than re-derived. This is doctor-facing revision, so the full technical vocabulary is used, and every criterion, eponym and number is verified against a source.

Other primary psychotic disorders

1 · Orientation: the schizophrenia-spectrum decision tree

Why this matters. Schizophrenia does not stand alone. It sits at the centre of a **schizophrenia-spectrum** family of related psychotic disorders that share the same positive symptoms but are told apart by three things the examiner returns to again and again: how long the illness has lasted, whether a full mood episode is riding on top of it, and what kind of delusion is present. Get those three axes straight and the whole block resolves into a clean **decision tree**. This orienting topic builds that tree, seeds the master mnemonic that chains the chapter, and hands the reader a map to the delusional syndromes and to catatonia that follow. The illness schizophrenia itself is not re-taught here: its phenomenology, aetiology, criteria and course are owned by the Schizophrenia: aetiology, phenomenology, classification and course notes and are cross-referenced, not re-derived.

The governing idea: everything in this family is a positive-symptom psychosis, so you never separate them by "is there psychosis" but by the three discriminators. The **criteria map** below is worth memorising as a single object, because in the exam a stem rarely asks "define

schizophreniform"; it hands you a duration and a mood picture and asks you to place the patient. Nosology here is given ICD-11 primary (the current CDDR grouping, "schizophrenia and other primary psychotic disorders") with the DSM-5-TR labels cross-mapped, because the two systems draw the duration lines differently and the difference is itself examinable.

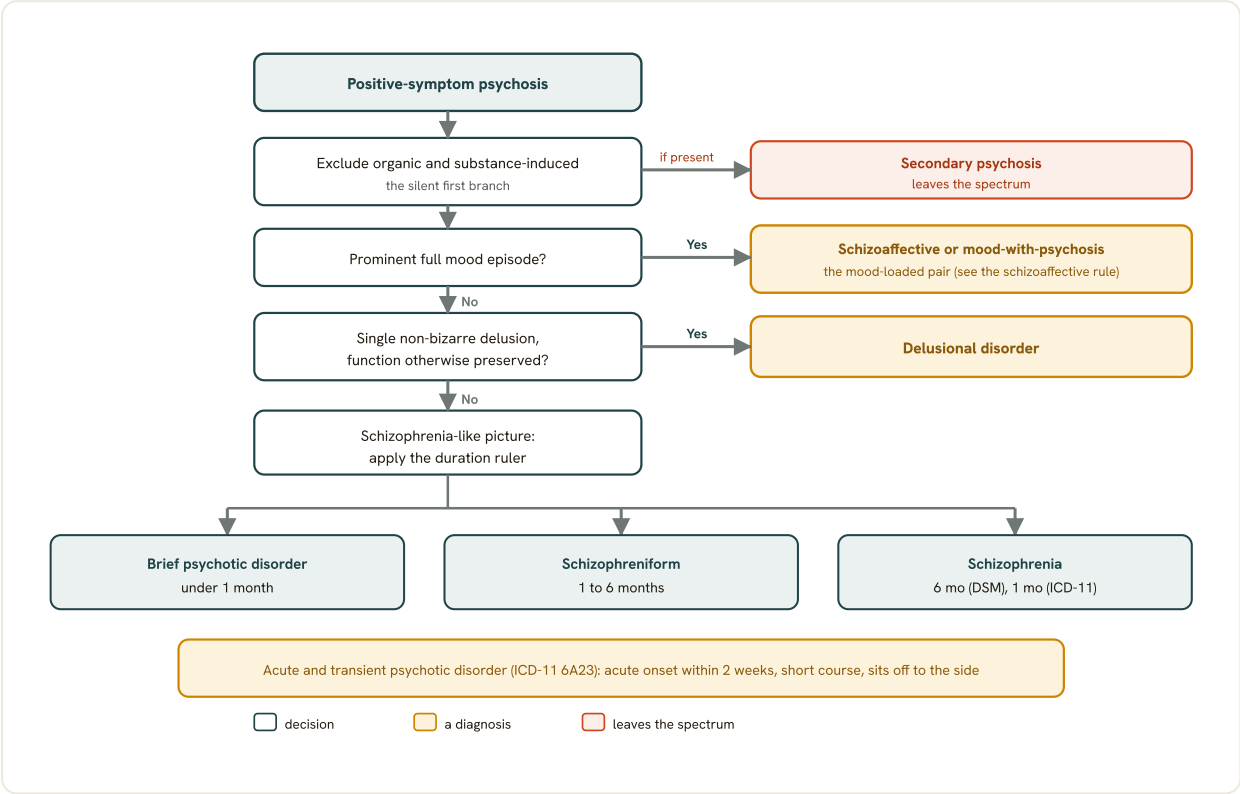


Fig 10.1 The schizophrenia-spectrum decision tree. Exclude the organic and substance-induced first (the silent branch), then walk three axes in order: mood-loading (a prominent mood episode pulls out schizoaffective disorder and mood-with-psychotic-features), delusion-type (a single non-bizarre delusion with preserved function is delusional disorder), and finally, for the remaining schizophrenia-like pictures, the duration ruler (under one month, one to six months, six months or more), with the acute and transient psychotic disorder sitting off to the side.

1.1 The spectrum as one object: what belongs, what does not

The schizophrenia-spectrum and other primary psychotic disorders, in the ICD-11 grouping, comprises schizophrenia, **schizoaffective disorder**, schizotypal disorder, the acute and transient psychotic disorders, and delusional disorder (ICD-11 CDDR). The DSM-5-TR chapter, "Schizophrenia Spectrum and Other Psychotic Disorders", covers the same ground plus brief psychotic disorder and schizophreniform disorder as separate short-duration entities, and organises itself explicitly along a gradient: sub-threshold conditions first, then single-domain conditions (delusional disorder, catatonia), then the time-limited psychoses, then schizophrenia (Kaplan & Sadock 2024). Two members earn their place here for reasons worth naming: **catatonia**, which the chapter carries because it is a psychomotor syndrome that cuts across the whole grouping, and **postpartum (puerperal) psychosis**, owned here as a psychotic presentation while the wider obstetric frame belongs to the Perinatal/women's mental health and emergency psychiatry notes.

What does not belong: a psychosis that is a direct physiological consequence of a substance, medication or medical condition is a secondary psychosis and is excluded before any spectrum

label is applied. That exclusion is the silent first branch of the whole tree, and forgetting it is the classic beginner error.

RULE **Exclude the organic and the substance-induced first, then place on the spectrum.** A secondary psychosis is not a point on this decision tree; it is what you rule out before you enter it.

1.2 Axis one, duration: the timeline that separates the short psychoses from schizophrenia

The first and most heavily tested axis is **duration**. Holding the same positive-symptom picture constant, DSM-5-TR splits the family purely by how long it has run. Brief psychotic disorder lasts at least one day and remits within one month, with full return to premorbid function; below one month is its signature (Kaplan & Sadock 2024). Schizophreniform disorder occupies the middle band, at least one month but less than six, and, crucially, does not require a decline in functioning. Schizophrenia is diagnosed once the illness has run six months or more (including at least one month of active-phase symptoms). Alongside these sit the acute and transient psychotic disorders (ATPD, ICD-11 6A23), defined not by a fixed ceiling but by an acute onset, psychotic symptoms emerging without a prodrome and reaching the full picture within two weeks, and a characteristically short, fluctuating course.

A trap the examiner sets deliberately: the two systems do not agree on where schizophrenia begins. ICD-11 requires symptoms for one month or more, so many cases that DSM-5-TR would call schizophreniform (one to six months) are already schizophrenia in ICD-11 (Kaplan & Sadock 2024). Read the stem for which system it is using.

under 1 mo	1 to 6 mo	6 mo or more	within 2 wk
BRIEF PSYCHOTIC DISORDER	SCHIZOPHRENIFORM (DSM-5-TR)	SCHIZOPHRENIA (DSM-5-TR)	ATPD ACUTE ONSET (ICD-11)

TRAP **Do not swap the duration thresholds between systems.** DSM-5-TR schizophrenia needs six months; ICD-11 needs one month, so DSM schizophreniform maps largely onto ICD-11 schizophrenia.

1.3 Axis two, mood-loading: does a full mood episode ride on the psychosis

The second axis, **mood-loading**, asks whether a prominent, full mood episode (depressive or manic) is part of the picture, and if so, how it sits in time against the psychosis. Two members of the family carry a prominent mood episode by definition: schizoaffective disorder and mood disorder with psychotic features. Two members carry none: delusional disorder and schizophrenia (where any mood symptoms are, by rule, a minority of the total course). The whole discrimination turns on a single temporal criterion. In DSM-5-TR schizoaffective disorder, a major mood episode is present for the majority of the total duration of the illness (Criterion C), and there must have been at least two weeks of delusions or hallucinations in the absence of a major mood episode at some point in the lifetime course (Criterion B) (Kaplan & Sadock 2024). If instead the delusions occur exclusively during mood episodes, the diagnosis is mood disorder with psychotic features. The mood-episode criteria themselves are cross-referenced to the Mood

disorders: classification, depressive and bipolar syndromes, neurobiology notes and not re-derived here.

TRAP **Never diagnose schizoaffective without the at-least-two-weeks-of-psychosis-without-prominent-mood rule.** Psychosis only ever during mood episodes is mood disorder with psychotic features, not schizoaffective disorder.

1.4 Axis three, delusion-type and bizarreness: where delusional disorder splits off

The third axis reads the **content and bizarreness** of the delusion and the state of the rest of the person. Delusional disorder is the anchor case: at least one month of one or more delusions, classically **non-bizarre** (though DSM-5-TR now allows a "with bizarre content" specifier), with no other active-phase symptom of schizophrenia and, strikingly, apart from the direct impact of the delusion itself, function and behaviour are not obviously bizarre and psychosocial functioning is largely preserved (Kaplan & Sadock 2024). This is the discriminator to hold: a well-systematised, encapsulated, often plausible-sounding delusion in an otherwise intact person points to delusional disorder, whereas the same content embedded in disorganisation, hallucinations and negative symptoms points to schizophrenia. Marneros frames it as a disorder in which the delusion is well-systematised and long-lasting while other mental and personality domains stay comparatively intact (New Oxford Textbook of Psychiatry). The raw descriptive definitions of the delusion types and of the misidentification phenomena are cross-referenced to the Psychometry, Assessment and Descriptive Psychopathology notes.

RULE **Delusional disorder is a single non-bizarre delusion in an otherwise preserved person.** No prominent hallucinations, no disorganisation, no negative symptoms, and no functional collapse beyond what the delusion itself drives.

1.5 The decision tree assembled: reading a stem in order

The three axes chain into an ordered walk, and reading them in this order is the fastest route through any placement stem. First, exclude the organic and substance-induced (the silent branch). Second, ask the mood question: is a full mood episode prominent, and what is its temporal relation to the psychosis, which pulls out mood-with-psychotic-features and schizoaffective disorder. Third, if not mood-loaded, ask the content question: is this a single non-bizarre delusion in an otherwise intact person, which pulls out delusional disorder. Fourth, for the remaining schizophrenia-like pictures, apply the duration ruler: under one month (brief psychotic), one to six months (schizophreniform), six months or more (schizophrenia), with the ATPD sitting off to the side as an acute-onset, short-course entity. The illness schizophrenia is the tree's endpoint and is fully taught in the Schizophrenia: aetiology, phenomenology, classification and course notes; here it is only the destination the other branches are defined against. This ordered tree is the concept figure for the block.

WORKED EXAMPLE

A 24-year-old man, well until three weeks ago, is brought with florid persecutory delusions and auditory hallucinations of abrupt onset; no drugs on screen, no mood episode, no prior episodes. Walk the tree: organic and substance-induced excluded; no prominent mood episode (not schizoaffective, not mood-with-psychosis); the picture is not a single encapsulated delusion in an intact person (not delusional disorder); on duration it is under one month with acute onset. The answer is brief psychotic disorder (DSM-5-TR), and given the acute, prodrome-free onset within two weeks, an acute and transient psychotic disorder (ICD-11). Only if it runs past one month, then past six, does it climb to schizophreniform and then schizophrenia.

1.6 The criteria map in one table

The single table below is the object to memorise: each row is a spectrum member, and the columns are the three discriminating axes. The highlighted cell in each row is the one feature that clinches that diagnosis against its neighbours.

DISORDER (DSM-5-TR / ICD-11)	DURATION AXIS	MOOD-LOADING AXIS	DELUSION / DISCRIMINATOR
Brief psychotic disorder (F23)	**at least 1 day, under 1 month, full recovery**	none required	any positive symptom; often stress-triggered
Schizophreniform disorder (F20.81)	**1 to 6 months**	none required	schizophrenia picture, no functional-decline requirement
Schizophrenia (F20.9 / 6A20)	6 months or more (DSM); 1 month or more (ICD-11)	mood a minority of total course	**full active-phase picture; taught elsewhere**
Schizoaffective disorder (F25 / 6A21)	concurrent, over the illness course	**mood episode for majority of course, plus at least 2 weeks psychosis without prominent mood**	psychosis and mood interwoven
Mood disorder with psychotic features	within mood episodes	**psychosis only during mood episodes**	mood-congruent or incongruent delusions
Delusional disorder (F22 / 6A24)	1 month or more of delusion	none prominent	**single non-bizarre delusion, function otherwise preserved**
Acute and transient psychotic disorder (6A23)	**acute onset, full picture within 2 weeks, short course**	variable	often polymorphic, rapidly shifting

The schizophrenia-spectrum criteria map: read each row across the three axes; the highlighted cell is the clinching discriminator.

MNEMONIC

"SPECTRUM by Duration, Mood, Delusion; then the DELUSIONAL syndromes; then CATATONIA moves."

The master chain for the whole chapter. First place the psychosis on the SPECTRUM using the three axes, Duration, Mood-loading, Delusion-type. Then work the named DELUSIONAL syndromes (the jealous, erotomanic, somatic and persecutory types, and the misidentification set). Then finish on CATATONIA, the transdiagnostic psychomotor syndrome that "moves" across the whole grouping. Duration, Mood, Delusion is the three-axis core the examiner rewards.

1.7 India and the systems footnote

The acute and transient psychoses are of particular Indian relevance: acute-onset, brief, full-recovery non-affective psychoses are seen commonly in Indian practice and carry, on the whole, a favourable outcome, which is why ATPD and its ICD-10 antecedents are heavily represented in Indian teaching and examination (Kaplan & Sadock 2024, on the cycloid-psychosis and ATPD overlap). Delusional disorder, by contrast, typically presents in middle to later adult life and is comparatively uncommon in first-contact samples. This material is largely generic and disorder-defining rather than drug-focused; where any pharmacology is needed it is given as a pointer, and the antipsychotic detail is cross-referenced to the Schizophrenia: management, antipsychotics and adverse effects notes.

INDIA

The acute and transient psychotic disorders are a familiar and clinically important presentation in Indian settings: an abrupt, florid, often polymorphic psychosis in a previously well adult, frequently remitting fully within a short course. Treat the episode, then watch longitudinally, because a minority declare themselves later as schizophrenia or a mood disorder on relapse.

HOLD THIS

Every disorder in this family is a positive-symptom psychosis; you separate them by three axes only, duration, mood-loading and delusion-type, after first excluding the organic and substance-induced.

PEARL

Schizophreniform disorder is often **provisional**: if you make it before six months have elapsed and the illness has not yet remitted, you are labelling a work in progress. About one-third of patients recover within the six-month window and keep the schizophreniform label; the majority of the rest convert to schizophrenia or schizoaffective disorder (Kaplan & Sadock 2024).

GOOD TO REMEMBER

- **Schizophrenia spectrum:** the ICD-11 grouping of primary psychotic disorders (schizophrenia, schizoaffective, schizotypal, ATPD, delusional disorder); told apart by duration, mood-loading and delusion-type after organic/substance causes are excluded.
- **Brief psychotic disorder (F23):** at least one day and under **one month** with full recovery; the shortest member; any positive symptom, often stress-related.
- **Schizophreniform disorder (F20.81):** the same picture lasting **one to six months** with no functional-decline requirement; provisional if diagnosed early; introduced by Langfeldt in 1939.
- **Schizophrenia:** DSM-5-TR **six months or more**, ICD-11 **one month or more**; the endpoint of the duration axis, taught in the Schizophrenia: aetiology, phenomenology, classification and course notes.
- **Schizoaffective disorder (F25 / 6A21):** a mood episode present for the majority of the illness plus **at least two weeks** of psychosis without prominent mood (DSM-5-TR Criteria B and C); the two-week rule is the whole discrimination.
- **Delusional disorder (F22 / 6A24):** at least **one month** of a single non-bizarre delusion with function otherwise preserved and no other active-phase symptom; the one-domain psychosis.
- **Acute and transient psychotic disorder (6A23):** acute onset reaching the full psychotic picture **within two weeks**, short fluctuating course, often polymorphic; favourable outcome, clinically common in India.

2 · Schizoaffective disorder

Why this matters. **Schizoaffective disorder** is the schizophrenia-spectrum diagnosis the examiner uses to test whether you can hold two ideas at once: that a patient can have psychosis meeting the full schizophrenia bar together with a full mood episode, and that this is still not enough to call it schizoaffective unless a precise temporal rule is satisfied. The whole topic turns on one gate and one balance: a period of psychosis without a prominent mood episode, and mood symptoms occupying the majority of the illness. Get those two right and the diagnosis is secure; blur them and you have simply relabelled a mood disorder with psychotic features.

The governing sentence: schizoaffective disorder requires that, over the lifetime of the illness, delusions or hallucinations were present for a period of at least **two weeks** in the *absence* of a prominent mood episode, while mood symptoms meeting full criteria were present for the majority of the total duration of the illness (Kaplan & Sadock 2024, DSM-5-TR 2022). The disorder itself, its phenomenology, aetiology, criteria and course, is owned by the Schizophrenia: aetiology, phenomenology, classification and course notes and is not re-taught here; the raw mood-episode criteria (major depressive, manic, mixed) are cross-referenced to the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes; and the drug detail is cross-referenced to the Schizophrenia: management, antipsychotics and adverse effects notes.

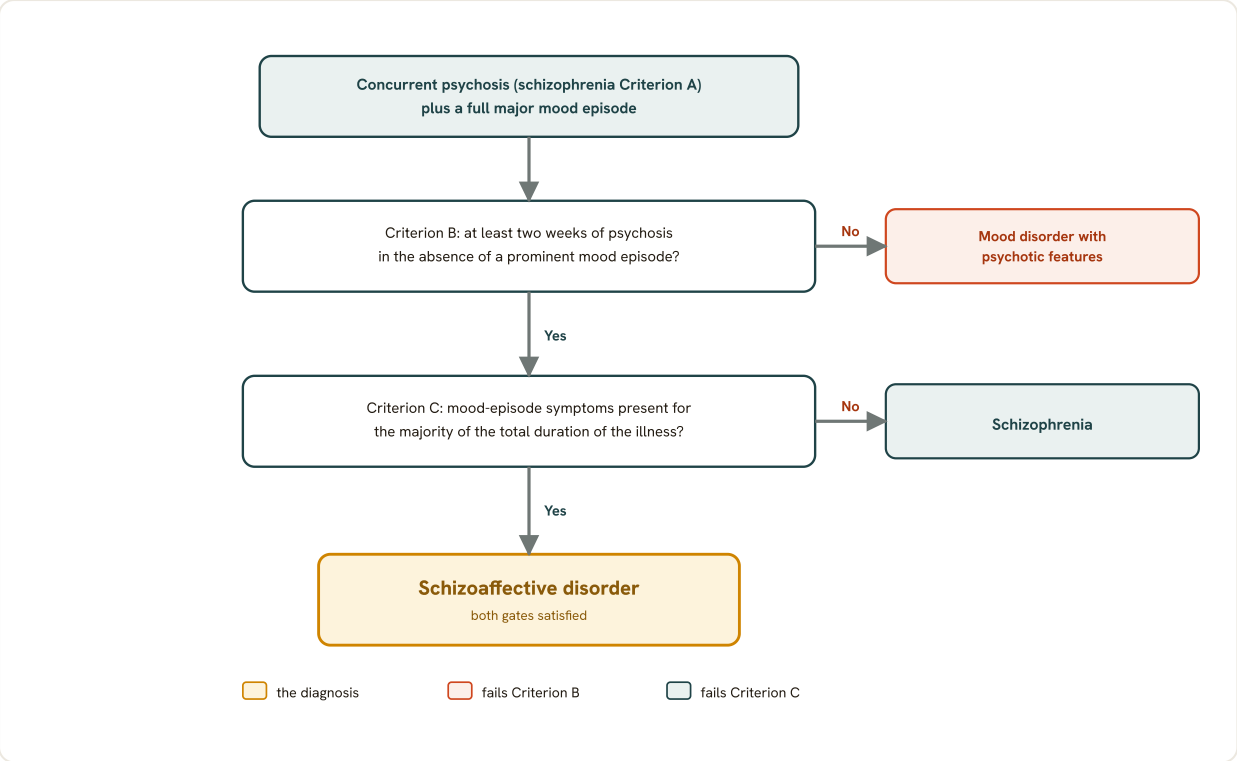


Fig 10.2 The schizoaffective decision rule (DSM-5-TR). Criterion B, at least two weeks of psychosis in the absence of a prominent mood episode, separates it from a mood disorder with psychotic features; Criterion C, mood-episode symptoms for the majority of the total illness, separates it from schizophrenia. Both gates must be satisfied. ICD-11 substitutes onset timing (simultaneous or within a few days, each lasting at least one month) and roughly equal prominence within a single episode.

2.1 The origin: Kasanin and a diagnosis born between two houses

The term schizoaffective psychosis was coined by Jacob Kasanin in a 1933 paper, describing a subgroup of nine young patients with good premorbid functioning, sudden onset of both schizophrenic and mood symptoms, and good outcome (Kasanin 1933, Kaplan & Sadock 2024). Kraepelin had already noticed that his own rich case material included many patients with features of both dementia praecox and manic-depressive illness, and Bleuler held that the co-occurrence of mood and schizophrenic symptoms in the same episode did not change the diagnosis of schizophrenia. Kasanin's category has survived every classification since, but a modern reading of his original case histories finds that all nine could today be diagnosed as a mood disorder with psychotic features, which is a fair emblem of the diagnosis it seeded: real enough to keep, unstable enough to argue about.

2.2 The DSM-5-TR criteria: the two-week gate and the majority rule

DSM-5-TR frames the diagnosis around an uninterrupted period of illness and four criteria (DSM-5-TR 2022). **Criterion A** requires an uninterrupted period during which there is a major mood episode (major depressive or manic) that is a **concurrent mood** episode running alongside psychosis meeting Criterion A of schizophrenia; because anhedonia is common in schizophrenia, a qualifying major depressive episode must include depressed mood itself (Criterion A1), not merely loss of interest. **Criterion B** is the defining rule: delusions or hallucinations for two or more weeks in the *absence* of a major mood episode during the lifetime duration of the illness. **Criterion C** requires that mood-episode symptoms are present for the majority of the total

duration of the active and residual portions of the illness. **Criterion D** excludes substances and another medical condition.

The two criteria that do the diagnostic work point in opposite directions. Criterion B separates schizoaffective disorder from a mood disorder with psychotic features: it demands a stretch of *pure* psychosis, at least two weeks, with no prominent mood episode running. Criterion C separates it from schizophrenia: it demands that mood symptoms dominate the majority of the illness, not a brief slice of it. A presentation can fail either way, and the diagnosis lives only in the narrow band where both hold.

RULE **Two weeks of psychosis without a prominent mood episode, plus mood for the majority of the illness.** Criterion B (the two-week pure-psychosis window) rules out a mood disorder with psychotic features; Criterion C (mood for the majority of the total duration) rules out schizophrenia. Both must hold.

TRAP **Calling any co-occurring psychosis and mood "schizoaffective".** Concurrent psychotic and mood symptoms alone do not make the diagnosis: without the two-week period of psychosis in the absence of a prominent mood episode, this is a mood disorder with psychotic features, where psychosis is confined to the mood episode.

2.3 A worked temporal example

DSM-5-TR gives a canonical pattern worth memorising. An individual has prominent auditory hallucinations and persecutory delusions for two months before a major depressive episode begins; psychosis and the full depressive episode then run together for four months; the depression lifts but the psychosis persists a further one month before it too clears (DSM-5-TR 2022). Total illness about seven months: psychosis alone in the first two months and the last one month (three months of pure psychosis, well over the two-week gate), with depression present for four of the seven, a majority. Both Criterion B and Criterion C are satisfied, so this qualifies as schizoaffective disorder.

WORKED EXAMPLE

Contrast the DSM-5-TR counter-case: a patient with a four-year history of active and residual schizophrenia develops depressive and manic episodes that, taken together, occupy less than one year of those four years. Criterion C fails, mood does not reach the majority of the illness, so the diagnosis is schizophrenia, not schizoaffective disorder, even though full mood episodes did occur.

2.4 Bipolar type and depressive type

DSM-5-TR requires a subtype specifier. The bipolar type (F25.0) applies if a manic episode is part of the presentation, whether or not depressive episodes also occur; the depressive type (F25.1) applies if only major depressive episodes are part of the presentation (DSM-5-TR 2022). The split is not cosmetic: bipolar type tends to present in younger adults, depressive type in older adults, and the bipolar/unipolar division maps onto the split running through the mood disorders themselves, whose full episode criteria are set out in the Mood disorders: classification,

depressive and bipolar syndromes, neurobiology notes. A **with catatonia** specifier is available and coded separately.

2.5 DSM-5 versus ICD-11: two framings of the same problem

The two systems agree on the spirit but differ in the letter, and the examiner likes the contrast. DSM-5-TR builds the diagnosis on the lifetime-course architecture above: a **concurrent mood** episode alongside schizophrenia-criterion psychosis, plus the two-week rule (Criterion B) and the majority rule (Criterion C). ICD-11 collapses the frame onto the current episode: its essential feature is that all the diagnostic requirements for schizophrenia are met concurrently with mood symptoms meeting the requirements of a moderate or severe depressive episode, a manic episode or a mixed episode, with the two symptom sets roughly equally prominent within the same episode (ICD-11 CDDR). The ICD-11 boundary text is exact: the onsets of the psychotic and mood symptoms are either simultaneous or occur within a few days of one another, and both must last at least one month; if the psychotic symptoms without mood symptoms end up much longer than the concurrent phase, the episode is better called schizophrenia. ICD-11 diagnoses episode by episode, so a previous schizoaffective episode does not preclude a later diagnosis of schizophrenia, and vice versa.

FEATURE	DSM-5-TR	ICD-11 CDDR
Unit of diagnosis	Lifetime, uninterrupted period of illness	**Current or most recent episode**
Core requirement	Mood episode concurrent with schizophrenia Criterion A	Schizophrenia requirements met concurrently with a full mood episode, roughly equally prominent
Pure-psychosis rule	**Delusions or hallucinations for at least two weeks in the absence of a prominent mood episode (Criterion B)**	No two-week rule; uses onset timing (simultaneous or within a few days) and duration
Mood-burden rule	**Mood symptoms for the majority of the total duration (Criterion C)**	Psychotic and mood symptoms concurrent and each lasting at least one month
Subtypes	Bipolar type (F25.0), depressive type (F25.1)	Course specifiers (first/multiple episode); type read from the mood episode

The two-week gate and the majority rule are DSM-5-TR devices; ICD-11 substitutes onset-timing and equal-prominence within a single episode.

2.6 The validity controversy: a diagnosis that will not sit still

Schizoaffective disorder is the classic example of a category of debated reliability and validity that sits between the mood and the psychotic disorders, and whose membership shifts with the criteria used (Kaplan & Sadock 2024). The instability is documented, not rhetorical. In a series of roughly 700 first-admission patients with psychotic features, 6% received a diagnosis of schizoaffective disorder at discharge, but only half of these (about 3% of the total) met DSM-III-R research criteria on review; two years later, only one-third of those originally diagnosed were still

called schizoaffective, one-third had become schizophrenia, and one-third an affective disorder (Kaplan & Sadock 2024). Family, twin and adoption studies find raised risks of both schizophrenia and affective disorder in relatives, marking it as a heterogeneous condition, and recent phenomenological work has failed to support the validity of the very two-week cutoff on which the DSM diagnosis rests. In practice the diagnosis is made more often than a strict application of the criteria would justify.

COMMON TRAP

Do not treat the schizoaffective label as a stable, once-and-for-all diagnosis. Because the relative proportion of mood to psychotic symptoms changes over time, DSM-5-TR itself expects the diagnosis to migrate: a severe four-month depressive episode in the first six months of a chronic psychosis may qualify as schizoaffective, then be revised to schizophrenia if psychosis persists for years without a further mood episode. The diagnosis is provisional by design.

at least 2 weeks PSYCHOSIS WITHOUT A PROMINENT MOOD EPISODE (CRITERION B)	**about one-third as common** AS SCHIZOPHRENIA	**0.3%** LIFETIME PREVALENCE, FINNISH SAMPLE (DSM-5-TR)

2.7 Course, prognosis and where it sits on the spectrum

Prognostically the disorder behaves as its name suggests, intermediate: outcome is better than schizophrenia but worse than a pure mood disorder (Kaplan & Sadock 2024, DSM-5-TR 2022). Negative symptoms and cognitive deficits occur but tend to be less severe and less persistent than in schizophrenia, and insight, though often impaired (anosognosia is common), may be less globally lost. Prevalence is about one-third that of schizophrenia, with a lifetime figure of **0.3%** in a Finnish sample and a female preponderance under DSM-IV criteria; the DSM-5 Criterion C (mood for the majority of the illness) is more stringent than the DSM-IV requirement of a merely substantial portion, so measured rates are expected to fall. This intermediate position, better than schizophrenia and worse than mood disorder, is exactly what makes its place on the schizophrenia spectrum contested.

2.8 Management pointers

This is a diagnosis topic, not a treatment topic, so the management is given as pointers only. The principle is combination: an **antipsychotic** to treat the psychotic dimension plus **mood-targeted treatment** for the affective dimension (a mood stabiliser or lithium for bipolar type, an antidepressant added with the usual caution for depressive type), the two chosen to match the subtype (Kaplan & Sadock 2024). Several second-generation antipsychotics carry mood benefit that suits this population, and the full drug detail, mechanisms, dosing and adverse effects, is cross-referenced to the Schizophrenia: management, antipsychotics and adverse effects notes; the mood-episode criteria that determine which affective arm to treat are set out in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes. Paliperidone is the one antipsychotic with a specific schizoaffective licence, but treat brand and licensing detail as belonging to the management notes.

INDIA

In Indian practice the diagnosis is used but, as elsewhere, applied loosely, and the same instability applies: an initial schizoaffective label frequently resolves to schizophrenia or to a mood disorder with psychotic features on longitudinal follow-up. Management follows the same combination logic (antipsychotic plus mood-targeted agent); brand-level detail belongs to the Schizophrenia: management, antipsychotics and adverse effects notes.

MNEMONIC

2 WEEKS PURE, MOOD FOR MOST

Two weeks of pure psychosis (no prominent mood episode) is the gate that excludes a mood disorder with psychotic features (Criterion B); mood for most of the illness is the balance that excludes schizophrenia (Criterion C). Hold both halves and the DSM-5-TR diagnosis is complete.

HOLD THIS

Schizoaffective disorder = at least two weeks of psychosis in the absence of a prominent mood episode (Criterion B), with mood symptoms present for the majority of the total duration of the illness (Criterion C); miss the two-week rule and it is only a mood disorder with psychotic features.

GOOD TO REMEMBER

- **Schizoaffective disorder:** a chronic psychosis with a full mood episode concurrent with schizophrenia-criterion psychosis; the discriminating rule is delusions or hallucinations for at least **two weeks** in the absence of a prominent mood episode (DSM-5-TR Criterion B); coined by Kasanin (1933).
- **Criterion B (the two-week gate):** at least two weeks of psychosis without a prominent mood episode over the lifetime of the illness; separates it from a mood disorder with psychotic features; the exam number is **two weeks**.
- **Criterion C (the majority rule):** mood-episode symptoms present for the majority of the total duration of the active and residual illness; separates it from schizophrenia; the phrase to hold is "majority of the total duration".
- **Bipolar type (F25.0) vs depressive type (F25.1):** bipolar type if a manic episode is part of the presentation (younger adults); depressive type if only major depressive episodes (older adults); the distinguishing feature is the presence or absence of a manic episode.
- **ICD-11 framing:** schizophrenia requirements met concurrently with a full mood episode, roughly equally prominent within the same episode, onsets simultaneous or within a few days, each lasting at least 1 month; no two-week rule, the number to hold is 1 month.
- **Validity controversy:** debated reliability and validity, sitting between mood and psychotic disorders, membership shifting with criteria; the demonstrative figure is that at 2-year follow-up only about one-third of those first diagnosed retain the label (Kaplan & Sadock 2024).

3 · Delusional disorder

Delusional disorder is the diagnostic home for the patient who holds one or more fixed false beliefs yet is, in every other respect, unremarkable: the personality is intact, the affect fits the belief, work and relationships hold up outside the delusional zone, and there are none of the hallucinations, thought disorder or negative symptoms that would push the diagnosis toward

schizophrenia. The examiner loves it precisely because it is a disorder defined by what is *absent* as much as by what is present, and because the classic error, calling it schizophrenia the moment a delusion appears, is so easy to make. This is a clinical-disorder topic: the schizophrenia symptoms it is contrasted against are owned by the Schizophrenia: aetiology, phenomenology, classification and course notes, and the raw descriptive definitions of each delusion type (persecutory, grandiose, jealous, erotomanic, somatic) are cross-referenced to the Psychometry, Assessment and Descriptive Psychopathology notes rather than re-derived here.



Fig 10.3 Delusional disorder commonly preserves much everyday functioning outside a circumscribed fixed belief. Major themes include persecutory, jealous, grandiose, erotomanic and somatic presentations.

How to use this page. Fix the core first (a **non-bizarre** delusion for at least a month, function otherwise preserved, no prominent hallucinations or other schizophrenia symptoms), then the **subtypes** by delusional theme, then Kendler's **dimensions of delusional** severity as a rating frame that cuts across the subtypes, and finally the epidemiology and the management pointers. The duration threshold is the single fact most often swapped in a viva: DSM-5-TR asks for one month, ICD-11 for three.

3.1 The core: a non-bizarre delusion with preserved function

What defines it. Delusional disorder is the presence of one or more persistent delusions, classically **non-bizarre** (plausible in principle, drawn from ordinary life: being followed, deceived by a spouse, loved from afar, infested), in the *absence* of the other features that would make the diagnosis schizophrenia (Kaplan & Sadock 2024, ICD-11 CDDR). There are no prominent or persistent hallucinations, no formal thought disorder, no passivity or first-rank phenomena, and no negative symptoms; apart from the actions and attitudes flowing directly from the delusional system, affect, speech and behaviour are typically unaffected. Personality is relatively preserved, and social and occupational functioning show much less deterioration than in schizophrenia (ICD-11 CDDR). The one nuance introduced by DSM-5 is that the *non-bizarre requirement was removed* from the core criterion and replaced by a "with bizarre content" specifier, so a bizarre delusion no longer excludes the diagnosis in DSM; the non-bizarre character remains the prototype and is retained in the ICD tradition (Kaplan & Sadock 2024).

RULE **A non-bizarre delusion with otherwise preserved functioning.** The whole diagnosis is one or more circumscribed delusions with the personality, affect and function outside the delusional zone essentially intact, and none of the hallucinations, thought disorder or negative symptoms of schizophrenia.

TRAP **Calling it delusional disorder when function is broadly impaired or other psychotic features dominate.** If there is global deterioration, persistent hallucinations, formal thought disorder or negative symptoms, the diagnosis is schizophrenia (or a mood-with-psychosis disorder), not delusional disorder.

3.2 Duration and the diagnostic boundaries

The duration threshold, the fact most often swapped. The delusion must persist for a minimum period: DSM-5-TR requires the delusion(s) for **at least 1 month**, whereas ICD-11 (6A24) requires it **typically for at least 3 months** and often much longer (DSM-5-TR 2022, ICD-11 CDDR). Both systems permit hallucinations only if they are non-prominent, non-persistent and thematically tied to the delusion, the classic example being tactile hallucinations in delusional infestation. The differential is drawn against three neighbours and one exclusion, and holding the discriminator for each is the exam-yield here.

CONTRAST	SHARED FEATURE	DISCRIMINATOR (WHAT MAKES IT DELUSIONAL DISORDER)
Schizophrenia	Persistent delusions	**No prominent hallucinations, thought disorder, passivity or negative symptoms; personality and function preserved; later onset**
Mood disorder with psychotic features	Persecutory, grandiose or somatic delusions	**Delusions occur at times *without* any mood episode; a full manic/depressive syndrome is absent or brief relative to the delusion (mood criteria in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes)**
Paranoid personality disorder	Suspiciousness, guardedness, litigiousness	**A frank, held delusion is present, not merely a pervasive distrustful trait; may be diagnosed alongside the personality disorder**
Illness anxiety / OCD / body dysmorphic disorder	Somatic or contamination preoccupations	**Belief is held with delusional conviction and insight is absent; if only an overvalued idea, code the primary disorder with the "absent insight / delusional beliefs" specifier**
Organic / substance cause	Delusions (often persecutory)	**Excluded first: delirium, dementia, basal-ganglia and limbic disease, amphetamine/cocaine; if present, code psychotic disorder due to another condition**

The differential is drawn by absence: delusional disorder is what remains once schizophrenia, a mood syndrome, a personality trait, an overvalued idea and an organic cause are each excluded (Kaplan & Sadock 2024, ICD-11 CDDR).

3.3 The subtypes by delusional theme

Named by content, not by severity. Both DSM-5-TR and ICD-11 classify delusional disorder into **subtypes** according to the predominant delusional theme (DSM-5-TR 2022). The raw descriptive definition of each delusion is owned by the Psychometry, Assessment and Descriptive Psychopathology notes; here the subtype is defined operationally by its central theme.

Persecutory type

The central theme is being conspired against, cheated, spied on, followed, poisoned, maligned or obstructed; the commonest subtype.

Grandiose type

The central theme is a great unrecognised talent, insight or discovery, or a special identity or relationship.

Jealous type

The central theme is that a spouse or partner is unfaithful (delusional jealousy, the Othello theme); the one subtype more common in men.

Erotomanic type

The central theme is that another person, usually of higher status, is in love with the patient (De Clerambault syndrome, psychose passionelle).

Somatic type

The central theme is bodily: infestation, malfunction, deformity or odour (older term monosymptomatic hypochondriacal psychosis); presents to dermatology, surgery or dentistry, rarely to psychiatry.

Mixed type

No single theme predominates; more than one of the above coexists. (An unspecified type covers themes that fit none of the above.)

MNEMONIC

PG-JES-M

The subtypes in one string: **P**ersecutory, **G**randiose, **J**ealous, **E**rotomanic, **S**omatic, **M**ixed. Persecutory is the commonest; jealous is the one that skews male; erotomanic is the one with the eponym (De Clerambault).

3.4 The named eponyms attached to the subtypes

Three eponyms travel with the themes. The examiner expects the eponyms, but also expects you to know they are *presentations*, not diagnoses in their own right: each can arise in delusional disorder, in schizophrenia, in a mood disorder or organically. De Clerambault syndrome is the erotomanic theme (a person of higher status is secretly in love with the patient, who reads rejection as concealed courtship). Othello syndrome is the delusional-jealousy theme (the conviction of a partner's infidelity, with checking behaviour and a real risk of violence). Ekbom syndrome is delusional infestation or delusional parasitosis, the prototypical somatic-type presentation, often with linked tactile hallucinations of things crawling on or under the skin.

TRAP **Calling any morbid jealousy Othello syndrome.** Othello syndrome is *delusional* jealousy; obsessional or overvalued jealousy, or jealousy secondary to alcohol or a mood state, is not, and the same theme can be a symptom of schizophrenia or a mood disorder rather than delusional disorder.

3.5 Kendler's dimensions of delusional severity

A rating frame, not a subtype scheme. Where the subtypes classify a delusion by *content*, Kendler's **dimensions of delusional** experience classify it by *form and severity*: a set of largely independent axes along which any single delusion can be rated, and along which two patients with the "same" persecutory belief may differ enormously (Kendler 1983). The point for the exam is that **delusional severity** is multidimensional, so a delusion is not simply "present or absent" but strong or weak on several separable measures, and these dimensions do not correlate tightly with each other.

Conviction
The degree of certainty with which the belief is held, from partial doubt to absolute incorrigibility.

Extension
How far the delusion reaches into other areas of the person's life and world (a single encapsulated idea versus a pervasive delusional system).

Bizarreness
How implausible or impossible the belief is by ordinary cultural standards.

Disorganisation
How internally consistent and systematised the belief is, versus fragmented and contradictory.

Pressure
The degree of preoccupation, the amount of mental space and time the delusion occupies.

Affective response (a commonly-taught later addition, not in Kendler's original five)
The intensity of emotion attached to the belief.

Deviant (acting-out) behaviour (a commonly-taught later addition, not in Kendler's original five)
The extent to which the person acts on the delusion (stalking, litigation, assault), the dimension of greatest forensic weight.

Because these are independent, they are useful for *rating* and tracking a delusion (and for understanding why an encapsulated, low-pressure, non-acted-on delusion is compatible with preserved function) rather than for assigning a subtype. This dimensional view sits alongside the standard classifications and is worth naming when a question asks how a delusion is characterised beyond its theme (Kendler 1983).

> **PEARL**
> Content and form answer different questions. If asked to *classify* a patient's delusion, give the subtype (persecutory, jealous and so on); if asked to *characterise or rate* the delusion, reach for the dimensional frame: Kendler's original five (conviction, extension, bizarreness, disorganisation, pressure), with affective response and acting-out commonly added. The "acting-out" dimension is the one that drives risk and admission, whatever the theme.

3.6 Epidemiology and course

Uncommon, and later than schizophrenia. Delusional disorder is relatively uncommon: a general-population study from Finland found a lifetime prevalence of DSM-IV delusional disorder of **0.18%**, and in clinical series it accounts for roughly **1% to 4%** of psychiatric admissions (Kaplan & Sadock 2024). The **age of onset** is characteristically later than in schizophrenia, generally in the **mid- to late-30s**, usually insidious, and the delusions once formed tend to be stable and fixed (Kaplan & Sadock 2024, ICD-11 CDDR). The persecutory subtype is the most common; other than the jealous type, which is more common in men, the disorder is roughly equally distributed between the sexes, with males tending to a younger onset. Functioning is generally preserved, with adverse outcomes arising mainly when the person acts on the belief; a minority progress to schizophrenia over time, and a premorbid personality disorder (classically paranoid) is over-represented.

0.18%	mid to late 30s	1 mo / 3 mo
LIFETIME PREVALENCE (FINLAND, DSM-IV)	TYPICAL AGE OF ONSET	MINIMUM DELUSION DURATION (DSM-5-TR / ICD-11)

3.7 Management pointers

Engagement first, then cautious pharmacology. The management of delusional disorder is dominated by one problem: these patients rarely see themselves as ill, so they present late, reluctantly, and often to a non-psychiatrist. The first task is therefore *engagement and the therapeutic alliance*, working with the distress and the functional consequences rather than confronting the belief head-on, since a frontal challenge to a fixed delusion tends to entrench it and end the consultation. Pharmacologically, antipsychotics are used but the *evidence base is limited* and largely uncontrolled: response is generally more modest and less reliable than in schizophrenia, and the drug detail (agent choice, dosing, adverse effects) is cross-referenced to the Schizophrenia: management, antipsychotics and adverse effects notes rather than re-taught. Comorbid *depression* is common (sometimes an understandable response to the delusional predicament) and should be identified and treated, as it worsens course. Risk assessment is integral, particularly in the jealous and erotomanic subtypes where acting-out (violence, stalking) is the main danger.

WORKED EXAMPLE

A 42-year-old, employed and socially intact, presents only because his wife insists, convinced over eight months that a neighbour is conducting an affair with her; he checks her phone and clothing and has confronted the neighbour once. There are no hallucinations, no thought disorder, no negative symptoms, and no mood episode; outside this belief he functions normally. This is delusional disorder, jealous subtype (Othello theme): non-bizarre delusion, over the duration threshold, preserved function, no other schizophrenia features. The clinical priority is risk (delusional jealousy carries a real risk of violence), then engagement, then a cautious antipsychotic trial and screening for comorbid depression, with the belief itself worked around rather than argued against.

INDIA

In Indian practice, delusional disorder classically presents to non-psychiatric specialists first: the somatic type (delusional infestation, Ekbom syndrome, and delusional parasitosis) reaches dermatology and general physicians, and the jealous type surfaces in the context of marital and family conflict, so much of the early clinical experience is of engaging a patient who does not accept a psychiatric frame. Diagnosis follows the ICD-11 (and long-familiar ICD-10) three-month non-bizarre-delusion template that Indian teaching texts use. The system-wide rule that no diagnosis is named to the patient sits comfortably here: management is framed around the distress and its consequences rather than the label, which also aids engagement. Generic antipsychotics dominate and are affordable; verify the local brand before naming one.

HOLD THIS

Delusional disorder is one or more non-bizarre delusions for at least a month (DSM-5-TR; three months in ICD-11), with personality, affect and function preserved outside the delusion and none of the hallucinations, thought disorder or negative symptoms of schizophrenia; classified by theme into persecutory (commonest), grandiose, jealous (male-predominant, Othello), erotomanic (De Clerambault), somatic (Ekbom) and mixed subtypes, onset in the mid- to late-30s.

GOOD TO REMEMBER

- **Delusional disorder (the diagnosis):** one or more persistent non-bizarre delusions with function otherwise preserved and no other schizophrenia symptoms; the discriminator from schizophrenia is preserved personality/function plus absence of prominent hallucinations, thought disorder and negative symptoms; the number to hold is the duration, at least 1 month (DSM-5-TR) or 3 months (ICD-11 6A24).
- **Subtypes (by theme):** persecutory, grandiose, jealous, erotomanic, somatic, mixed; the discriminator is the predominant delusional content; persecutory is the commonest and jealous the one more common in men.
- **De Clerambault syndrome (erotomanic type):** the delusion that a higher-status person secretly loves the patient; the discriminator is the reading of rejection as concealed courtship; the eponym to hold is De Clerambault (psychose passionelle).
- **Othello syndrome (jealous type):** the delusion of a partner's infidelity; the discriminator from ordinary or obsessional jealousy is delusional conviction; the fact to hold is its association with violence risk.
- **Ekbom syndrome (somatic type):** delusional infestation / delusional parasitosis, often with tactile hallucinations; the discriminator is the fixed conviction of infestation despite normal examination; presents to dermatology, not psychiatry.
- **Kendler's dimensions of delusional severity (the rating frame):** the original five are conviction, extension, bizarreness, disorganisation and pressure (Kendler 1983), with affective response and acting-out commonly added in later descriptive-psychopathology teaching; the discriminator from the subtypes is that these rate form and severity, not content.
- **Epidemiology and management (the pointers):** lifetime prevalence about 0.18%, onset mid- to late-30s, function preserved; engagement and alliance first, antipsychotics with limited evidence, treat comorbid depression; drug detail cross-referenced to the Schizophrenia: management, antipsychotics and adverse effects notes.

Figure. A concept figure contrasting delusional disorder with schizophrenia along two axes (breadth of impairment and presence of non-delusional psychotic features), with the delusional disorder region marked as narrow-impairment, delusion-only, is flagged for central drawing.

4 · The life-cycle of a delusion: formation and dissolution

A delusion is not a static false belief that a patient simply "has"; phenomenologists describe it as a process with a beginning, a crystallisation and, in recovery, a dissolution. Two German-tradition observers frame the two ends of that arc. **Klaus Conrad** traced the *formation* of an evolving psychosis as a staged transformation of the whole field of experience, and **Karl Jaspers** named the discrete primary *forms* in which a true (schizophrenic) delusion first appears. At the far end, Eugen Bleuler's clinical observations of how a settled delusion coexists with, or is sealed off from, ordinary reality describe the ways a psychosis is contained or worked through.

Why it matters. This topic supplies the descriptive spine for the delusion viva: it lets you narrate *how* a persecutory system came into being, distinguish a primary delusion (heavily weighted in the diagnosis of schizophrenia) from a secondary one, and explain why a chronically deluded patient can hold a bizarre belief and a mundane life side by side without felt contradiction. The raw definitions of each delusional form are cross-referenced to the Psychometry, Assessment and Descriptive Psychopathology notes rather than re-derived here; the disorder schizophrenia itself (its phenomenology, criteria and course) is owned by the Schizophrenia: aetiology, phenomenology, classification and course notes.

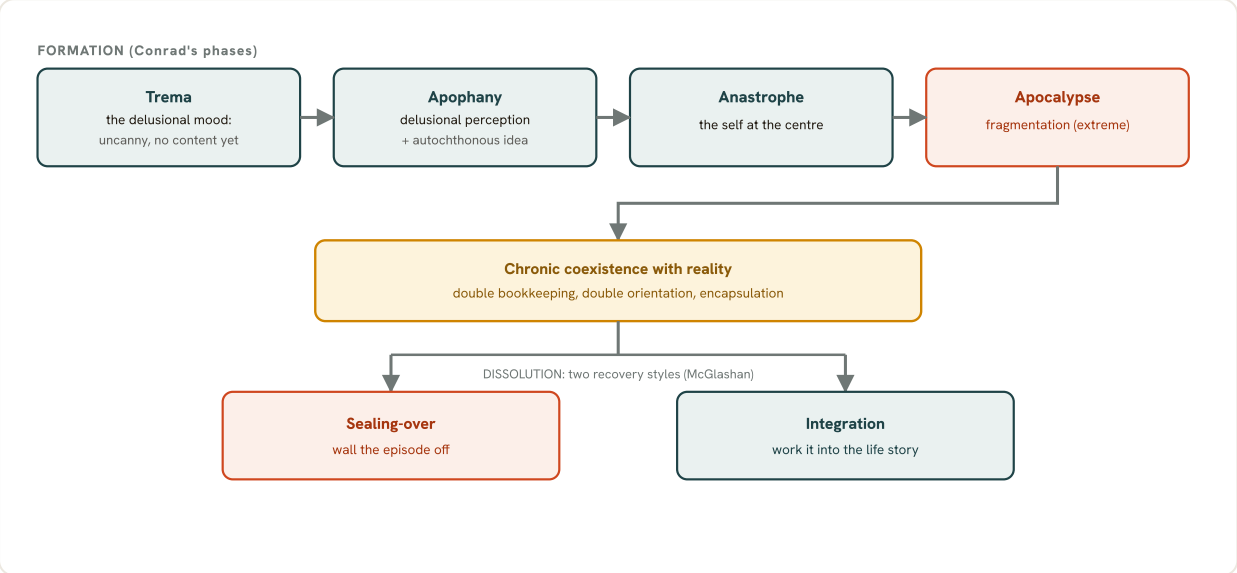


Fig 10.4 The life-cycle of a delusion. Formation runs through Conrad's phases, the trema (delusional mood, an uncanny atmosphere) preceding the apophany (the crystallised delusional perception), then anastrophe and, at the extreme, apocalypse. Once formed, a delusion coexists with reality (Bleuler's double bookkeeping and double orientation, and encapsulation), and at recovery is either sealed over or integrated into the life story.

4.1 Formation: Conrad's phases of an evolving psychosis

Klaus Conrad (1958), studying young soldiers with acute schizophrenia, described the beginning of psychosis as a sequence of gestalt transformations rather than a single event (Conrad 1958; reviewed by Mishara 2010). The sequence is a favourite viva scaffold because it maps the subjective experience onto Jaspers' forms.

Trema

The opening delusional mood (Conrad's word, borrowed from the German for pre-performance stage-fright): a tense, uncanny atmosphere that something momentous is impending, a total change in the perception of the world with no explicit content yet (Mishara 2010).

Apophany

The apophanous phase: the sudden crystallisation of a specific meaning where the patient finds new significance for events. This is the moment of the delusional perception and the autochthonous delusional idea, when "now it all makes sense" (Mishara 2010).

Anastrophe

The world comes to revolve around the self; the patient is placed at the centre of the reorganised field of meaning, heightening the psychosis.

Apocalypse

At the extreme, the disintegration or fragmentation of experience, with dissolution of the coherent world into perplexity and terror.

Conrad's fuller German scheme runs to six phases in all, the four acute phases above followed by *consolidation* (a new psychological world is built on the new meanings) and *residuum* (an eventual defect or autistic end-state); the AIIMS Clinical Methods summary gives a five-stage version (trema, apophany, anastrophe, consolidation, residuum) that folds away the apocalyptic phase (Conrad 1958; AIIMS Clinical Methods 2024, citing Mishara 2010). For the exam the load-bearing point is the ordering of the early phases: the **trema** (delusional mood) is the *prodromal atmosphere* that precedes the **apophany** (the crystallised delusional perception).

RULE **Mood before meaning.** Conrad's trema, the delusional mood, precedes the apophanous delusional perception: the uncanny atmosphere comes first, the specific "now it all makes sense" crystallisation comes second.

4.2 Jaspers' primary delusional forms, applied to this arc

Karl Jaspers separated **primary** delusions (arising *de novo*, ununderstandable, un-derivable from any preceding mental event, and given considerable diagnostic weight in schizophrenia) from **secondary** delusions (psychologically understandable from mood, culture or other symptoms). Four primary forms are recognised; each is a moment on Conrad's formation arc. The crisp descriptive definitions live in the Psychometry, Assessment and Descriptive Psychopathology notes and are only cross-referenced here (Sims 2015; Shorter Oxford 2018).

PRIMARY FORM	ONE-LINE CHARACTER	POINT ON THE ARC
Delusional mood (delusional atmosphere)	**A state of perplexity: something uncanny is going on that involves the patient in unspecified ways, content not yet fixed**	Conrad's *trema* (prodromal)
Delusional perception	**A real, normal percept is invested with a new, self-referential delusional meaning not derivable from mood; Schneider's "two-memberedness"**	Conrad's *apophany*
Sudden delusional idea (autochthonous delusion / delusional intuition)	**A fully formed conviction appearing in an instant "like a bolt from the blue", a single-stage event (no antecedent percept)**	Conrad's *apophany*
Delusional memory (retrospective delusion)	A past memory (real or false) is reinterpreted delusionally, often to explain the illness	Later elaboration

Jaspers' four primary delusional forms mapped onto Conrad's phases. Note the discriminator between delusional perception (two stages: normal perception, then delusional meaning) and the autochthonous sudden idea (one stage: the idea simply arrives), verified against AIIMS Clinical Methods 2024 and Kaplan & Sadock 2024.

WORKED EXAMPLE

A 25-year-old man saw the yellow leaves of the tree outside his house falling and, in that instant, knew this was a signal from God that he was "the chosen one", the sole person able to intercept it. The *percept* (yellowing leaves) is entirely normal; the delusion is the immediate, self-referential meaning attached to it, with no pre-existing delusional system to derive it from. That is a **delusional perception** and its "two-memberedness" (percept, then meaning) is Schneider's diagnostic hallmark (AIIMS Clinical Methods 2024).

4.3 Dissolution: how a delusion is held, contained and given up

Once formed, a delusion may persist, encapsulate, or dissolve. The descriptive vocabulary for the *persistence-alongside-reality* end is Bleulerian; the vocabulary for *recovery* comes from the schizophrenia outcome literature.

Double bookkeeping

Bleuler's observation that the delusion and everyday reality are held in parallel *without felt contradiction*: the patient who insists their food is poisoned will nevertheless eat it, and the espoused belief is not consistently acted upon (Bleuler; Kaplan & Sadock 2024).

Double orientation

The delusion is held with conviction yet has little influence on feelings and actions: a patient may believe himself a member of the royal family while living contentedly in a group home; this separation usually occurs in chronic schizophrenia (Shorter Oxford 2018).

Delusional encapsulation

An *encapsulated delusion* is walled off so that it has limited impact on the person's overall behaviour, the belief coexisting with otherwise intact functioning (AIIMS Clinical Methods 2024).

At recovery, two contrasting *recovery styles* are described (McGlashan, Levy and Carpenter 1975). In sealing-over, the patient walls the psychotic episode off, minimising and encapsulating it as alien and best not examined ("sealing over"). In **integration**, the patient works the experience into the life story, remaining curious about it and weaving it into a continuous sense of self. Integration is generally associated with better insight and engagement; sealing-over with more guarded, defended recovery.

TRAP **Coexistence is not insight.** Do not read double bookkeeping (delusion and reality coexisting, the belief not acted upon) as regained insight: the conviction is intact, only the behavioural consequence is muted.

PEARL

Double bookkeeping, double orientation and encapsulation all describe a delusion that *survives* alongside reality; sealing-over and integration describe two ways the episode is *metabolised* in recovery. Keep the two axes separate in an answer: the first is about how the belief coexists with reality during illness, the second about the stance the patient takes toward the episode afterwards.

4.4 India note and the figure to hold

India. In much Indian public-sector practice the delusional-formation vocabulary is examined from the descriptive-psychopathology tradition (Fish, Sims, and the AIIMS Clinical Methods text), and delusional perception and the autochthonous sudden idea are high-yield viva points precisely because they are the primary forms carrying the greatest diagnostic weight for schizophrenia. Candidates are expected to name the eponyms (Conrad, Jaspers, Schneider, Bleuler) and to distinguish the one-stage sudden idea from the two-stage delusional perception; misattributing these, or swapping the order of trema and apophany, is a classic error.

HOLD THIS

Trema (delusional mood) precedes apophany (delusional perception): mood first, crystallised meaning second, world-around-self (anastrophe) next, fragmentation (apocalypse) at the extreme.

GOOD TO REMEMBER

- **Conrad's phases:** the staged formation of an evolving psychosis; core sequence trema (delusional mood) to apophany (delusional perception) to anastrophe (self at centre) to apocalypse (fragmentation); eponym Conrad 1958.
- **Trema:** the opening delusional mood, a tense uncanny "something is impending" atmosphere with no fixed content; discriminator = prodromal, precedes any specific delusion.
- **Apophany:** the apophanous crystallisation where a specific meaning appears and "now it all makes sense"; discriminator = the moment of the delusional perception and autochthonous idea.
- **Delusional perception:** a normal percept given new self-referential delusional meaning; discriminator = Schneider's "two-memberedness" (two stages), eponym Schneider 1959.
- **Sudden (autochthonous) delusional idea:** a fully formed delusion arriving in one step "like a bolt from the blue"; discriminator = single-stage, no antecedent percept.
- **Delusional memory:** a past memory reinterpreted delusionally (retrospective delusion); discriminator = the falsification lies in the recall, not a current percept.
- **Double bookkeeping:** delusion and reality held in parallel without felt contradiction, belief not consistently acted on; eponym Bleuler.
- **Double orientation:** delusion held with conviction but little effect on feeling or action, typical of chronic schizophrenia; discriminator = conviction intact, behaviour unaffected.
- **Delusional encapsulation:** the belief walled off with limited impact on overall behaviour; discriminator = preserved functioning around a contained delusion.
- **Sealing-over vs integration:** two recovery styles, walling the psychosis off (sealing-over) versus working it into the life story (integration); eponym McGlashan 1975.

5 · Acute and transient psychotic disorders

The **acute and transient psychotic disorders** are the schizophrenia-spectrum group defined by their *tempo* rather than their content: an abrupt onset from a well state into full psychosis, a rapidly shifting clinical picture, and a short, self-limiting course with a characteristically **good outcome**. They are the nosological home of a family of historical syndromes, the French bouffee delirante among them, that European and non-European psychiatrists kept re-describing under different names because the phenomenon is real and recurrent (Kaplan & Sadock 2024). The exam wants three things: the **icd-11** category structure, the abrupt-onset short-course rule with its good prognosis, and the follow-up caveat that a minority re-diagnose over time.

This is a discrimination topic. Master the boundary against schizophrenia (duration and symptom stability) and against mood disorder (whether an affective episode is sustained), and hold the one management pointer: treat the episode, but *follow up*. The raw descriptive definitions of the delusions, hallucinations and perplexity referenced below sit in the Psychometry, Assessment and Descriptive Psychopathology notes; the disorder schizophrenia itself is owned by the Schizophrenia: aetiology, phenomenology, classification and course notes and is not re-taught here.

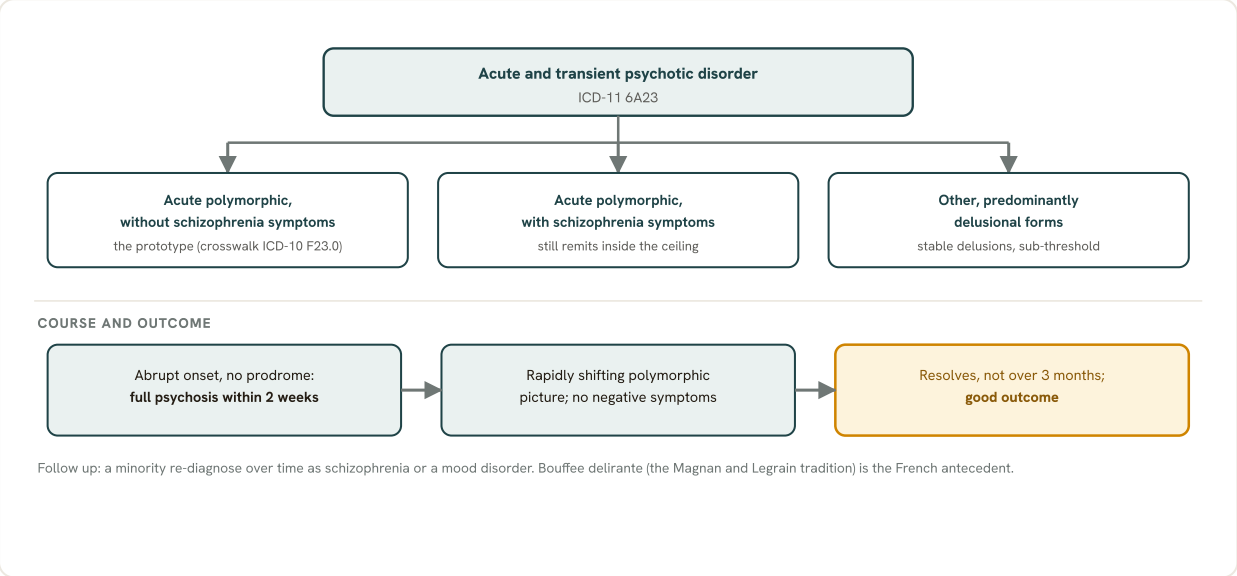


Fig 10.5 The ICD-11 acute and transient psychotic disorders, category and course. The single 6A23 category holds the acute polymorphic form (with or without symptoms of schizophrenia) and the other predominantly-delusional forms. The tempo defines it: abrupt onset to full psychosis within two weeks, a rapidly shifting polymorphic picture with no negative symptoms, and resolution within three months with a characteristically good outcome, though a minority re-diagnose on follow-up.

5.1 The icd-11 category and its essential features

One code, one gestalt. The **icd-11** collapses the older subtypes into a single category, acute and transient psychotic disorder (6A23), whose essential features are: acute onset of psychotic symptoms (delusions, hallucinations, disorganised thinking, or experiences of influence, passivity or control) *without a prodrome*, progressing from a non-psychotic to a clearly psychotic state within **2 weeks**; symptoms that *change rapidly* in nature and intensity, sometimes over the course of hours; *absence of negative symptoms*; and a duration that does not exceed **3 months**, most often lasting from a few days to 1 month (ICD-11 CDDR). Psychomotor disturbance including catatonia may be present. The picture must not be organic, substance-induced, or better explained by schizophrenia or another primary psychotic disorder.

RULE **Tempo defines it.** Acute onset (within 2 weeks) plus a rapidly shifting picture plus a short duration (not over 3 months) with a good outcome is **atpd**, but follow up because some become schizophrenia.

5.2 The acute polymorphic ("kaleidoscopic") picture

Symptoms that will not sit still. The prototype is the acute polymorphic psychotic disorder: an abruptly onset, rapidly shifting, "kaleidoscopic" picture of changing delusions, hallucinations and

affect, with the type and intensity of symptoms fluctuating in relatively rapid succession, and marked emotional turmoil, perplexity or confusion superimposed (ICD-11 CDDR). The polymorphic form comes in two flavours, *with or without symptoms of schizophrenia*: if schizophrenia-type symptoms are present but the whole episode still remits inside the duration ceiling, it remains within this group rather than becoming schizophrenia. The other forms are the *other acute, predominantly-delusional* presentations, in which comparatively stable delusions or hallucinations dominate but do not meet the schizophrenia threshold. In the icd-11, this fluctuating polymorphic quality is the *defining* feature of the single 6A23 category (ICD-11 CDDR).

TRAP **Do not fix schizophrenia on a first brief episode.** A first, brief, polymorphic episode with rapidly shifting content and full remission is **atpd**, not schizophrenia, even if the cross-section technically shows schizophrenia-type symptoms.

5.3 Course, good outcome and the follow-up imperative

Mostly remits, a minority declares itself later. The natural history is a rapid deterioration in social and occupational functioning, then full remission with return to the premorbid level. Favourable outcomes are associated with acute onset, short duration, good premorbid functioning and female gender (ICD-11 CDDR). A proportion of patients, however, re-diagnose over time as schizophrenia, another primary psychotic disorder, or a mood disorder, so the diagnosis is always provisional and follow-up is mandatory. Male gender and younger age of onset carry the greater risk of subsequent schizophrenia. Episodes are often stress-precipitated (an acute stressor is commonly reported but is not required), and the disorder is commoner in women and in developing countries (Kaplan & Sadock 2024).

WORKED EXAMPLE

A 24-year-old woman is brought in three days after a family bereavement: over hours her talk swings between grandiose religious certainty and terrified persecutory fear, voices come and go, and her affect lurches from ecstasy to dread. She is fully alert and oriented. Ten days later she is symptom-free. This is an acute polymorphic presentation of **atpd** (6A23.0, first episode): acute onset under 2 weeks, kaleidoscopic shifting picture, no negative symptoms, full remission. You still book follow-up, because a first episode does not exclude later schizophrenia or a mood disorder.

within 2 weeks	3 months	1 day to under 1 month
ONSET TO FULL PSYCHOSIS (ICD-11)	MAXIMUM DURATION; USUALLY DAYS TO 1 MONTH	DSM-5-TR BRIEF PSYCHOTIC DISORDER

5.4 Bouffee delirante and its nosological place

The French antecedent. Descriptions of acute-onset, remitting psychoses recur across traditions: Meynert's *amentia*, Kleist and Leonhard's cycloid psychosis, the Scandinavian *reactive (psychogenic) psychosis*, and the French bouffee delirant of the late 19th century (Kaplan & Sadock 2024). The nosological place of the bouffee delirante is precisely as the historical antecedent of the acute polymorphic category: an abrupt "delusional flash" out of a clear sky, richly

polymorphic, with rapid full recovery, later distilled (with the cycloid and reactive concepts) into ICD-10's acute and transient category and then ICD-11's 6A23 (Kaplan & Sadock 2024). The classic attribution is to the French degeneration-school tradition of Magnan and his pupil Legrain (Kaplan & Sadock 2024 dates the joint concept to 1895), so name the tradition rather than betting on a single author or year.

PEARL

The recurring theme across all these historical labels is identical: acute onset, polymorphic content, rapid full recovery. That the same syndrome was independently described across cultural and linguistic boundaries is exactly why a unified acute and transient category was worth creating.

5.5 The icd-10 to icd-11 shift, and DSM-5

From subtypes to a single tempo-defined code. ICD-10 split the group into acute polymorphic psychotic disorder (with or without symptoms of schizophrenia) and an acute schizophrenia-like psychotic disorder, each further specified for the presence or absence of an associated acute stressor. The **icd-11** unified all of this into one category, 6A23, in which the rapidly fluctuating polymorphic picture is the essential feature; the official crosswalk maps 6A23 back to ICD-10 F23.0, acute polymorphic psychotic disorder without symptoms of schizophrenia (ICD-11 CDDR). Course is then coded by specifiers only: first episode (6A23.0) or multiple episodes (6A23.1), each further as currently symptomatic, in partial remission, or in full remission.

DSM-5 has no exact equivalent. The DSM-5-TR has no dedicated acute-and-transient section; its nearest match is brief psychotic disorder, defined by a duration of **at least 1 day but less than 1 month** with full return to premorbid functioning (Kaplan & Sadock 2024). Most patients meeting icd-11 **atpd** criteria map onto DSM-5-TR brief psychotic disorder, but a substantial minority fall instead into schizophreniform or other specified schizophrenia-spectrum categories, so the fit is inexact.

INDIA

The acute, benign-course psychoses that this category captures were reported with high frequency in India, Africa and the Caribbean, and the diagnosis is used heavily in Indian practice. Many psychiatrists, especially from developing countries such as India, drove recognition of the acute polymorphic picture as a distinct, good-prognosis entity rather than early schizophrenia.

FEATURE	ACUTE AND TRANSIENT (ICD-11 6A23)	SCHIZOPHRENIA	MOOD DISORDER WITH PSYCHOSIS
Onset	**Abrupt, no prodrome, within 2 weeks**	Often insidious, poor premorbid adjustment	Follows onset of the mood episode
Symptom stability	**Rapidly shifting, polymorphic, over hours to days**	Stable, fixed (same delusion for months)	Mood-congruent, tied to the episode
Negative symptoms	**Absent during the episode**	Often present	Not the defining feature
Duration	Does not exceed 3 months (usually days to 1 month)	At least 1 month florid; typically much longer	Mood episode persists days and usually much longer
Outcome	**Good; full remission to premorbid level**	Variable, often chronic	Episodic, defined by mood recovery

The three-way discrimination: tempo and symptom instability separate **atpd** from schizophrenia; a sustained affective episode separates it from a mood disorder. The mood-episode criteria themselves are in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes.

MNEMONIC

ABRUPT

Acute onset (within 2 weeks), **B**rief (not over 3 months), **R**apidly shifting polymorphic picture, **U**nremarkable premorbid state, **P**rognosis good, **T**rack them (follow up: some become schizophrenia or a mood disorder).

GOOD TO REMEMBER

- **Acute and transient psychotic disorder (icd-11 6A23):** abrupt-onset, short-course psychosis with a good outcome; discriminator is the rapidly shifting polymorphic picture with no negative symptoms; the number to hold is onset within 2 weeks, duration not over 3 months.
- **Acute polymorphic psychotic disorder:** the prototype and the icd-11 crosswalk to ICD-10 F23.0; discriminator is kaleidoscopic changing delusions, hallucinations and affect, with or without symptoms of schizophrenia; the point to hold is that it is the defining form of 6A23.
- **Bouffee delirante:** the French late-19th-century acute polymorphic psychosis, a "delusional flash" with rapid recovery; discriminator is its historical role as the antecedent of the acute polymorphic category; eponym to hold is the Magnan and Legrain tradition (Kaplan & Sadock 2024).
- **Cycloid psychosis:** Kleist and Leonhard's acute-onset, good-prognosis, frequently-recurring psychosis; discriminator is the same acute-remitting theme in a different tradition; hold Leonhard as the name attached to the concept.
- **DSM-5-TR brief psychotic disorder:** the nearest DSM match, with no dedicated acute-and-transient section; discriminator is the duration window; the number to hold is at least 1 day but less than 1 month with full remission.

HOLD THIS

Acute onset within 2 weeks, a rapidly shifting polymorphic picture with no negative symptoms, and full remission within 3 months is acute and transient psychotic disorder (icd-11 6A23), good outcome expected, but follow up because a minority declare as schizophrenia or a mood disorder.

6 · Brief psychotic disorder

The **brief psychotic disorder** of DSM-5-TR is the shortest-lived of the schizophrenia-spectrum entities: a storm of positive psychotic symptoms that erupts suddenly, burns out inside a month, and leaves the person back at their premorbid baseline. It is the diagnosis you reach for when a previously well patient presents floridly delusional or hallucinated after, say, a bereavement or a delivery, and then clears rapidly. For the exam it is a duration problem first and a differential problem second: get the **less than a month** boundary right, name the specifiers, and know that the good prognosis is real but conditional on follow-up.

Why it earns a place. It anchors the short end of the psychosis duration ladder (brief psychotic, then schizophreniform, then schizophrenia), it carries the historical concepts examiners love (brief reactive psychosis, bouffee delirante), and it forces you to weigh a benign transient episode against the first presentation of a lifelong illness. The raw descriptive definitions of the delusions and hallucinations themselves are cross-referenced to the Psychometry, Assessment and Descriptive Psychopathology notes; the disorder schizophrenia itself is owned by the Schizophrenia: aetiology, phenomenology, classification and course notes and is not re-taught here.

6.1 The DSM-5-TR entity: sudden onset, days to weeks, full recovery

Core criterion. Brief psychotic disorder (DSM-5-TR, coded **F23**, page 108) requires the sudden onset of at least one positive psychotic symptom, and one of them must be delusions, hallucinations or disorganised speech (grossly disorganised or catatonic behaviour alone does not qualify). The episode lasts **at least a day but less than a month**, with an eventual full return to the premorbid level of functioning (APA 2022; Kaplan & Sadock 2024). Tasman frames it crisply as a transient psychotic state, not caused by a medical condition or a substance, lasting at least one day and up to the one month upper bound (Tasman 2015).

The bracketing. The one month upper bound is the hinge. Cross the one month line and, if criterion A for schizophrenia is met, the diagnosis becomes schizophreniform disorder (at least one month but less than six months); cross six months and it becomes schizophrenia. The whole point of the entity is that the psychosis is over inside a month and the person is restored.

RULE **Under a month, full recovery.** Brief psychotic disorder resolves within one month with a full return to premorbid functioning; if it runs past a month it is no longer brief psychotic disorder.

HOLD THIS

Brief psychotic disorder = sudden positive psychosis lasting at least a day but less than a month, with full return to premorbid functioning; the post-stressor form is the old brief reactive psychosis.

6.2 The three specifiers: stressor, post-stressor, peripartum

The stressor axis. DSM-5-TR tags the episode *with marked stressor(s)* or *without marked stressor(s)*. The **post-stressor** form, coded when florid psychosis follows an event that would be markedly stressful to almost anyone in that culture, is the modern home of the historical brief

reactive psychosis of DSM-III and DSM-III-R, whose criteria explicitly required a severe precipitant such as a major loss or a combat-type trauma (Kaplan & Sadock 2024). The without-stressor form has no identifiable precipitant.

The peripartum axis. The third specifier is *with peripartum onset*, applied when onset is during pregnancy or within four weeks postpartum. This is the DSM-5-TR route by which a postpartum psychotic episode that clears inside a month is captured; the wider perinatal frame for postpartum psychosis as a psychiatric emergency is developed in the Perinatal/women's mental health and emergency psychiatry notes.

SPECIFIER	WHEN APPLIED	HISTORICAL / LINKED CONCEPT
With marked stressor(s)	**Onset shortly after an event markedly stressful to almost anyone**	Old brief reactive psychosis (DSM-III/III-R); the post-stressor form
Without marked stressor(s)	No identifiable precipitant	Distinguishes reactive from non-reactive episodes
With peripartum onset	**Onset in pregnancy or within four weeks postpartum**	Captures brief postpartum psychotic episodes

The three DSM-5-TR specifiers for brief psychotic disorder; the marked-stressor form is the direct descendant of brief reactive psychosis.

6.3 The ICD-11 near-equivalent: acute and transient psychotic disorder

The counterpart. The ICD-11 acute and transient psychotic disorder (ATPD) is the near-equivalent of brief psychotic disorder: an acute onset of psychotic symptoms that fluctuate rapidly, characteristically with a polymorphic, shifting picture, resolving within a short period. Kaplan & Sadock explicitly link the two, noting that both overlap with the older concept of cycloid psychosis (Kaplan & Sadock 2024). ATPD in turn absorbs the historical European syndromes: the French bouffee delirante and the Scandinavian reactive psychosis tradition (Shorter Oxford 2018).

Where they diverge. The ICD lineage is more elaborate than the single DSM criteria set. ICD-10 split acute and transient psychotic disorders into several types by symptom picture and course, with the maximum duration varying by type: roughly one month for schizophrenia-like symptoms and up to three months for the predominantly delusional form (Tasman 2015). DSM-5, by contrast, uses one criteria set and a single maximum of one month. When mapping in an exam, note that ICD-11 places catatonia transdiagnostically as a separate cross-cutting entity rather than tucking it inside these categories.

TRAP **Do not swap the durations.** Brief psychotic disorder tops out at one month; the predominantly delusional acute and transient psychotic disorder in the ICD lineage may run longer, and schizophreniform runs one to six months. Mismatching these loses the mark.

6.4 Differential from early schizophrenia, and why follow-up is the whole game

The problem of the first episode. The single hardest discrimination is between a true brief psychotic disorder and the opening act of schizophrenia (or a mood disorder with psychotic

features). At presentation they can look identical; only duration and outcome separate them. This is why the diagnosis is provisional in spirit: it is confirmed only in retrospect, once the episode has fully resolved inside a month and the person has been observed to hold their recovery.

Diagnostic instability. The prognosis is genuinely good, but the label is unstable on follow-up: in one clinical series only **23%** of patients given a discharge diagnosis of brief psychotic disorder still held that diagnosis a year later, a proportion having declared a chronic psychotic or mood illness on longer observation (Kaplan & Sadock 2024). The New Oxford Textbook makes the same operational point: individuals who have shown a brief psychotic episode must be monitored to assess the stability of function and the possible emergence of further brief or chronic disorders (New Oxford 2020). Disorder-specific management is short-course antipsychotic cover for the acute episode plus structured follow-up; the antipsychotic drug detail is cross-referenced to the Schizophrenia: management, antipsychotics and adverse effects notes.

TRAP **Not following up.** Treating a resolved brief psychotic episode as closed and discharging without review misses the substantial minority who convert to a chronic psychotic or mood illness; the good prognosis is contingent on surveillance.

under 1 mo	1 to 6 mo	23%
BRIEF PSYCHOTIC DISORDER DURATION	SCHIZOPHRENIFORM DISORDER	RETAINED THE DIAGNOSIS AT 1 YEAR (REST RECLASSIFIED)

WORKED EXAMPLE

A 26-year-old woman, previously well, becomes floridly paranoid and hears accusatory voices ten days after her father's sudden death. She is perplexed, sleepless and frightened; there is no drug use and the physical workup is clean. She is given brief antipsychotic cover and settles completely over three weeks, back to her baseline job and relationships. The provisional formulation is brief psychotic disorder, with marked stressor(s), the post-stressor form. Because a minority declare schizophrenia or a mood illness later, she is not discharged outright but reviewed; if a fresh episode or persistent symptoms emerge, the diagnosis is revised.

INDIA

Acute, short-lived, remitting psychoses after a stressor are a familiar Indian clinical picture and map onto the ICD acute and transient psychotic disorder category used in routine practice; the classic non-affective acute remitting psychosis studied in Indian and other low-and-middle-income-country cohorts sits close to this construct. Treat the episode, then follow up, since a proportion evolve into a chronic illness.

PEARL

Think of brief psychotic disorder as the psychosis that ends before schizophreniform can even begin: same florid positive symptoms, but the clock stops before one month and the person walks out whole. The diagnosis is a promise the follow-up must keep.

GOOD TO REMEMBER

- **Brief psychotic disorder:** sudden onset of one or more positive psychotic symptoms lasting at least a day but less than a month, with full return to premorbid functioning; hold the number: DSM-5-TR F23, one month upper bound.
- **Post-stressor form (with marked stressor(s)):** the psychosis follows an event stressful to almost anyone; the one discriminator is the marked precipitant; the eponymic history is brief reactive psychosis (DSM-III/III-R).
- **With peripartum onset:** onset in pregnancy or within four weeks postpartum; the one number to hold is the four-week postpartum window.
- **Acute and transient psychotic disorder (ICD-11):** the near-equivalent, acute polymorphic rapidly-shifting psychosis; the discriminating feature is the fluctuating polymorphic picture; it subsumes bouffee delirante and cycloid psychosis.
- **Follow-up rule:** good prognosis but diagnostically unstable; the one number is 23% retaining the diagnosis at one year in one series, the rest reclassified to a chronic psychotic or mood illness.

7 · Induced and shared delusional disorder (folie a deux)

A delusion is usually the most private of symptoms, arising and staying inside one mind. The exam-relevant curiosity here is a delusion that **crosses between two people**: a genuinely psychotic, dominant primary transmits a belief to a passive, suggestible secondary who comes to hold it as their own. The entity has collected many names across a century and a half of nosology, and the examiner's favourite hook is precisely that thicket of eponyms and the one management principle that follows from the mechanism.

Why it matters. This is a small, high-yield topic where marks are won on three things: naming the entity correctly across ICD and DSM, attributing the classical folie a deux eponyms without swapping them, and stating the treatment rule (separate the pair) with its diagnostic corollary. The raw descriptive account of delusion as a symptom belongs to the Psychometry, Assessment and Descriptive Psychopathology notes; here the task is the disorder and its discrimination.

7.1 The entity and its many names

One belief, two carriers. The core phenomenon is the transfer of a delusion from a primary, dominant, genuinely psychotic person to a passive, suggestible, usually closely bound and socially isolated secondary who comes to share it (Tasman). Across editions and traditions the same entity is called the **induced delusional** disorder (ICD-10 term), the **shared psychotic** disorder (DSM-IV term), the **shared delusional** disorder, and, in the classical French, the folie a deux (Kaplan & Sadock 2024). Older synonyms include shared paranoid disorder, induced psychosis and double insanity (Kaplan & Sadock 2024).

RULE **Two people, one genuine psychosis.** Only the dominant primary has an authentic, independently generated delusion; the secondary's belief is borrowed and rests on the relationship.

7.2 Nosological placement: ICD-11, DSM-5-TR, ICD-10

Where the codebooks put it. The nosology has drifted, and knowing the current placement is the discriminator. In **ICD-11** the condition no longer has a standalone code: it is folded into

delusional disorder (6A24) as an additional clinical feature, described as "shared or induced delusional disorder", in which one person adopts the delusional belief of another where the two have a strong emotional or situational link (ICD-11 CDDR). In **DSM-5-TR** the discrete category was deleted; the presentation is captured as "delusional symptoms in partner of individual with delusional disorder", coded under other specified schizophrenia spectrum and other psychotic disorder (Kaplan & Sadock 2024). **ICD-10** retained a separate rubric, F24 induced delusional disorder (Shorter Oxford). The wider diagnostic frame for delusional disorder itself is cross-referenced to that topic; the raw phenomenology of the shared delusion is in the Psychometry, Assessment and Descriptive Psychopathology notes.

TRAP **Do not call it a DSM-5 disorder.** DSM-5 and DSM-5-TR deleted the standalone category; ICD-11 also demoted it to a feature of delusional disorder. Only ICD-10 keeps it as a named F24 diagnosis.

7.3 The primary, the secondary and the relationship

An asymmetric pair. The primary (inducer) is typically the older, more intelligent, better educated, dominant partner who carries a genuine psychotic illness, most often schizophrenia or delusional disorder (Tasman). The secondary (induced) is usually more suggestible, more dependent, often less intelligent, more passive or more lacking in self-esteem, and frequently predisposed by personality traits or social circumstance (Tasman). The two are closely associated over a long period, live together, and are relatively or completely isolated from outside social and cultural correction, which removes the reality-testing a wider circle would supply (Tasman). Almost all cases occur within a single family, the commonest dyads being sister-sister, husband-wife and mother-child (Tasman). The content is usually persecutory or hypochondriacal and, being borrowed, tends to stay within the realm of possibility rather than becoming as bizarre as delusions in schizophrenia (Tasman).

7.4 The classical variants

Four named forms, one entity. The historical literature subdivides the syndrome by how the shared belief arose. Hold the two the sources anchor firmly, and recognise the full quartet: **folie imposee**, **folie communiquee**, **folie induite** and **folie simultanee**.

folie imposee

The common, prototypical form: the dominant primary imposes the delusion on a healthy, suggestible secondary, whose belief typically fades on separation (Tasman).

folie communiquee

The delusion is communicated to the secondary after a period of resistance, and the secondary then holds it independently, so that it may persist even after separation (Baillarger's original 1860 description, Tasman).

folie induite

An already-psychotic secondary adds new delusions induced by the dominant partner to their own pre-existing ones.

folie simultanee

Similar delusional systems develop independently and at the same time in two closely associated, often already predisposed people, rather than one being transferred from the other (Tasman).

When the shared system extends beyond a dyad the count is named directly: folie a trois, folie a quatre, folie a cinq, and folie a famille when a whole family is involved; these are rare (Tasman).

MNEMONIC

I C I S: Imposed, Communicated, Induced, Simultaneous

The four classical variants in one string. IMPOSED = healthy secondary, resolves on separation (the exam default); COMMUNICATED = accepted after resistance, may persist; INDUCED = added onto an already psychotic secondary; SIMULTANEOUS = two predisposed people, no true transfer.

7.5 Management: separation, then treat the primary

The pivot is the pair. The single therapeutic and diagnostic manoeuvre is **separation** of the pair. On separating the two, the secondary's delusion frequently resolves, and this resolution both treats the secondary and retrospectively confirms the diagnosis (ICD-11 CDDR; Tasman). The primary does not remit on separation and needs treatment in the usual way for their underlying psychotic illness, the antipsychotic detail of which is cross-referenced to the Schizophrenia: management, antipsychotics and adverse effects notes. Resolution in the secondary on separation is frequent but not invariable, and is least reliable in the communiquee and induite forms where the belief has become independently rooted (Tasman). Supportive work with the secondary during separation, aimed at rebuilding self-esteem and reality contact, supports the recovery.

RULE **Separation is both diagnostic and therapeutic for the secondary.** The delusion that lifts when the pair is parted was never independently generated; the manoeuvre proves and treats the induced case in one move.

TRAP **Do not treat both members as independently and equally psychotic.** Loading the passive secondary with the same long-term antipsychotic plan as the primary misreads a borrowed belief as an autonomous psychosis; separate first, then treat the primary in the usual way.

HOLD THIS

Separate the pair: the secondary's borrowed delusion usually lifts on separation (which both diagnoses and treats them), while the dominant, genuinely psychotic primary is treated in the usual way and does not remit on separation.

INDIA

In Indian family psychiatry the closely bound, co-resident, relatively isolated multigenerational household is exactly the substrate in which induced delusional disorder is described, and the commonest reported dyads, mother-child and husband-wife, map onto that structure. Separation is harder to arrange where the pair share a single home and depend on each other economically, so admission of the secondary, or of the primary, is often the practical route to the therapeutic separation.

PEARL

The bizarreness of the belief is a quiet clue: an induced delusion tends to stay within the realm of the possible (a persecution, an infidelity, a hypochondriacal fear), because a suggestible mind borrows a plausible story more readily than a bizarre one. A frankly bizarre, incoherent delusion in the secondary should push you back toward an independent primary psychosis rather than a shared one.

FEATURE	PRIMARY (INDUCER)	SECONDARY (INDUCED)
Delusion origin	**Authentic, independently generated**	**Borrowed from the primary**
Underlying illness	Genuine psychosis, often schizophrenia or delusional disorder	Usually none; often personality vulnerability
Role in the dyad	Dominant, older, more able	Passive, suggestible, dependent
Effect of separation	Delusion persists; needs treatment	**Delusion frequently resolves**
Management	Treat the underlying psychosis in the usual way	Separate first; support; medicate only if it fails to resolve

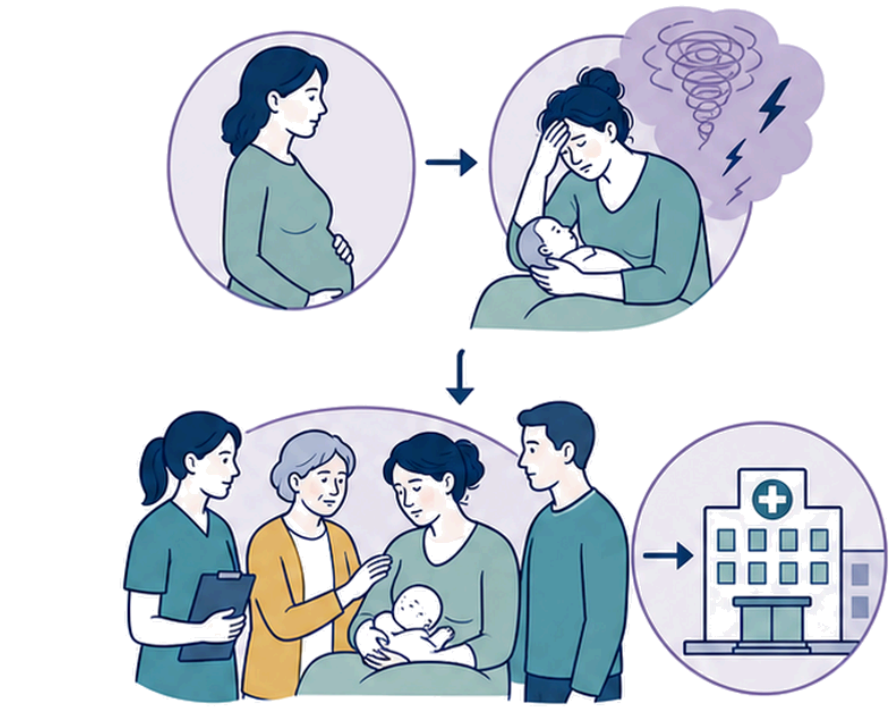
The asymmetry of the pair drives the whole management: the discriminator is what happens on separation.

GOOD TO REMEMBER

- **Folie a deux / shared psychotic disorder / induced delusional disorder:** transfer of a delusion from a dominant, genuinely psychotic primary to a passive, suggestible, closely bound and socially isolated secondary. Discriminator: only the primary has an authentic psychosis. Number/eponym to hold: Lasegue and Falret, 1877.
- **folie communiquee:** the delusion is communicated to the secondary after resistance and then held independently, so it may persist after separation. Eponym: Jules Baillarger, 1860.
- **folie imposee:** the common form, a healthy secondary onto whom the belief is imposed; resolves on separation. Hold: this is the exam default variant.
- **folie simultanee:** similar delusions arise independently and simultaneously in two predisposed, closely associated people; no true transfer. Hold: not a genuine induction.
- **folie induite:** an already-psychotic secondary acquires additional delusions induced by the dominant partner. Hold: the secondary is not delusion-free at baseline.
- **Nosology:** ICD-10 F24 induced delusional disorder (standalone); ICD-11 a feature of delusional disorder (no separate code); DSM-5-TR deleted, coded as delusional symptoms in partner of individual with delusional disorder. Hold: only ICD-10 keeps it as a named diagnosis.
- **Management:** separation of the pair is both diagnostic and therapeutic for the secondary; treat the primary's psychosis in the usual way. Hold: the secondary's delusion frequently, though not invariably, resolves on separation.

8 · Postpartum psychosis and the late-onset psychoses

Two psychotic presentations are bound to a life stage rather than to a diagnosis. **Postpartum psychosis** erupts in the days after a delivery and is one of the true psychiatric emergencies of the discipline; the **late-onset** and **very-late-onset** schizophrenia-like psychoses declare themselves in middle and old age, carry the historical burden of paraphrenia, and hide a neurodegenerative or organic cause behind an apparently functional picture. For the exam they are a pair of high-yield edge cases at either end of adult life, each with its own numbers, its own one discriminator, and its own classic trap.



Abrupt postpartum onset
Mood symptoms
Psychosis
Mother–infant safety
Urgent specialist care

Fig 10.6 Postpartum psychosis is an abrupt, severe perinatal mood-psychosis presentation requiring urgent specialist assessment, coordinated family support and protection of both mother and infant.

Why they earn a place. Postpartum psychosis is where a psychotic-disorders answer meets emergency psychiatry: get the two-week onset window, the bipolar link, and the protect-mother-and-baby imperative right. The late-onset psychoses are where a psychosis answer meets old-age psychiatry: get the international-consensus split at 40 and 60, the paraphrenia lineage, and the duty to exclude a dementing or organic process. The raw descriptive definitions of the delusions themselves are cross-referenced to the Psychometry, Assessment and Descriptive Psychopathology notes; the disorder schizophrenia itself is owned by the Schizophrenia: aetiology, phenomenology, classification and course notes and is not re-taught here.

8.1 Postpartum psychosis: the acute, delirium-like, often affective psychosis of the early puerperium

The entity. Postpartum psychosis, historically puerperal psychosis, is a new onset of a severe psychotic episode in the immediate puerperium. In around **90%** of cases the onset is within the first **two weeks** of delivery (New Oxford 2020). The picture is characteristically affective, most often a manic or mixed episode with psychotic features, and it is strongly associated with bipolar

I disorder (APA 2022; Kaplan & Sadock 2024). Kaplan & Sadock treat postpartum psychosis as, in effect, a subtype of bipolar disorder.

The delirium-like quality. What sets it apart from an ordinary manic relapse is its fluctuating, delirium-like texture: confusion, perplexity and a rapidly shifting, kaleidoscopic symptom picture that can escalate within hours (New Oxford 2020). The Companion notes that perplexity is seen par excellence in puerperal psychosis (Companion 2010). This is why the classic bedside advice is to exclude an organic cause and treat the presentation as an emergency, not to assume a benign course. The raw phenomenology of the perplexity and the delusions is cross-referenced to the Psychometry, Assessment and Descriptive Psychopathology notes.

RULE **Postpartum psychosis is a psychiatric emergency: protect mother and baby, and admit.** Because of the risk of suicide and of infanticide, urgent assessment and, in the majority of cases, admission (ideally to a mother-and-baby unit) are the default.

HOLD THIS

Postpartum psychosis is an acute, fluctuating, delirium-like, usually bipolar-spectrum psychosis with onset within the first two weeks in 90% of cases; it is a psychiatric emergency because of suicide and infanticide risk, so admit and safeguard the infant.

8.2 Why it is a psychiatric emergency: suicide and infanticide

The danger. Postpartum psychosis is a **psychiatric emergency** because it carries an increased risk of both suicide and infanticide (New Oxford 2020). Suicide is a leading cause of maternal death in the perinatal period, and infanticide is more commonly associated with postpartum psychosis than with postpartum depression (Kaplan & Sadock 2024). Roughly **half** of episodes are the woman's first contact with psychiatric services and so could not have been predicted, which is exactly why prompt assessment matters (New Oxford 2020). The wider perinatal frame (maternity blues, postnatal depression, the perinatal service model) is developed in the Perinatal/women's mental health and emergency psychiatry notes; postpartum psychosis is owned here as a psychotic disorder.

TRAP **Treating it as postnatal blues.** Reassuring a confused, perplexed, psychotic new mother and sending her home misreads a psychiatric emergency; the suicide and infanticide risk demands urgent assessment and usually admission.

8.3 Risk factors: bipolar disorder, a previous postpartum psychosis, primiparity, sleep loss

The high-risk profile. The dominant risk factor is a personal history of a **bipolar disorder**: a woman with bipolar disorder has about a **1 in 5** chance of postpartum psychosis with each delivery, and a previous episode of postpartum psychosis confers a risk in excess of **1 in 2** for the next (New Oxford 2020). A family history of postpartum psychosis roughly doubles the risk in women who already have bipolar disorder. **Primiparity** is the most robust obstetric risk factor identified, and sleep loss around the delivery is a recognised precipitant (Sharma 2003; New Oxford 2020). The risk of a manic episode in the first four weeks postpartum is dramatically raised (New Oxford 2020).

within 2 wk	1 in 5	over 1 in 2	1 to 2 / 1000
ONSET IN 90% OF POSTPARTUM PSYCHOSIS	RISK PER DELIVERY WITH BIPOLAR DISORDER	RISK AFTER A PREVIOUS POSTPARTUM PSYCHOSIS	INCIDENCE PER DELIVERIES

8.4 Management principles: urgent assessment, admission, and safeguarding the infant

The disorder-specific pointers. Management rests on urgent assessment and, in the majority, admission, ideally to a mother-and-baby unit so that mother and infant are kept together and the baby is safeguarded (New Oxford 2020). Pharmacological treatment is the mainstay: antipsychotics and mood stabilisers, with a stepped approach of a benzodiazepine, then a dopamine antagonist or partial agonist, then lithium, achieving remission in the large majority; lithium outperforms an antipsychotic alone for maintenance (New Oxford 2020). Electroconvulsive therapy is used, and can be strikingly rapid, in severe, treatment-resistant or life-threatening episodes; the ECT technique itself is cross-referenced to the ECT and neurostimulation notes, and the antipsychotic and mood-stabiliser drug detail to the Schizophrenia: management, antipsychotics and adverse effects notes. Safeguarding the infant runs in parallel with treating the mother.

WORKED EXAMPLE

A 28-year-old primiparous woman with a prior diagnosis of bipolar I disorder becomes elated, overactive and sleepless four days after delivery, then over 48 hours becomes perplexed, disoriented and convinced the baby has been swapped. The picture fluctuates hour to hour. She is treated as a psychiatric emergency: urgent assessment, exclusion of an organic cause, admission to a mother-and-baby unit with the infant safeguarded, and antipsychotic plus mood-stabiliser cover, with ECT held in reserve for a severe non-response. This is postpartum psychosis on a bipolar substrate, not the maternity blues.

INDIA

Acute, fluctuating postpartum psychoses are a familiar Indian clinical picture and are commonly managed on general psychiatry wards, since dedicated mother-and-baby units are scarce in Indian practice; keeping the mother and infant together and safeguarding the baby therefore has to be arranged within general adult inpatient care. ECT is available and used in Indian psychiatry for severe or treatment-resistant postpartum psychosis where a rapid response is needed.

GOOD TO REMEMBER

- **Postpartum psychosis (puerperal psychosis):** an acute, fluctuating, delirium-like, usually affective (bipolar-spectrum) psychosis of the early puerperium; the one discriminator is the confused, perplexed, rapidly shifting picture; hold the number, onset within two weeks in 90% of cases.
- **Emergency status:** a psychiatric emergency because of suicide and infanticide risk; the one imperative is admit and safeguard the infant; hold that infanticide is more linked to postpartum psychosis than to postpartum depression.
- **Risk factors:** bipolar disorder, a previous postpartum psychosis, primiparity, sleep loss; the biggest single number is a 1 in 5 risk per delivery with bipolar disorder, rising above 1 in 2 after a prior postpartum psychosis.

8.5 The late-onset psychoses: the international-consensus split at 40 and 60

The nosology. An international consensus (Howard, Rabins, Seeman & Jeste 2000) recommended that schizophrenia with onset between ages **40 and 60** be termed late-onset schizophrenia, and psychosis with onset after age **60** be termed very-late-onset schizophrenia-like psychosis, that is, a very late onset variant (Kaplan & Sadock 2024). The **late-onset schizophrenia-like** label thus spans the middle-aged and elderly cases that older classifications handled poorly. The very-late-onset group is the modern home of the old concept of paraphrenia, Kraepelin's term for a paranoid psychosis of middle and later life that was separated from dementia praecox because it lacked the emotional and volitional deterioration, later revived by Roth as late paraphrenia (Shorter Oxford 2018; Companion 2010). ICD-11 keeps a single schizophrenia category rather than a separate age-defined disorder; note that ICD-11 additionally places catatonia transdiagnostically as a cross-cutting entity, a high-yield nosology point developed with the catatonia material.

Epidemiology and the female preponderance. Late-onset schizophrenia is commoner in women, who are affected between **2 and 10** times more often than men, a robust finding often linked to the loss of estrogen-mediated dopaminergic protection at menopause (Kaplan & Sadock 2024). The International Late-Onset Schizophrenia Group judged late-onset schizophrenia to be broadly a neurodevelopmental disorder differing from early-onset disease more in degree than in kind, whereas very-late-onset schizophrenia-like psychosis showed features (more brain abnormalities and neuropsychological deficits) suggesting a neurodegenerative component (Kaplan & Sadock 2024).

RULE **Split by the two ages.** Onset 40 to 60 is late-onset schizophrenia; onset after 60 is very-late-onset schizophrenia-like psychosis (the old paraphrenia); both are commoner in women.

8.6 The clinical picture: persecutory and partition delusions, preserved affect and cognition

The phenomenology. The late-onset picture is dominated by prominent, well-organised **persecutory** delusions and by partition delusions, the conviction that people, objects or radiation can pass through impermeable structures such as walls, ceilings, doors or windows (Kaplan & Sadock 2024). Hallucinations are common and may be multimodal (auditory, visual, tactile, olfactory). By contrast, formal thought disorder and negative symptoms are infrequent, and affect and cognition are relatively preserved, which is precisely why some doubt whether very-late-onset psychosis belongs under schizophrenia at all (Kaplan & Sadock 2024; Tasman 2015). The raw descriptive definition of the partition delusion is cross-referenced to the Psychometry, Assessment and Descriptive Psychopathology notes.

The predisposing background. The late-onset psychoses are classically associated with **sensory impairment** (especially deafness and visual loss), social isolation, and premorbid schizoid or paranoid personality traits; marriage and fertility rates are lower and social isolation greater than in the general population (Kaplan & Sadock 2024). Cognitive dysfunction, where present, affects frontal-subcortical domains, and, importantly, retention of information is usually preserved, in

contrast to the retention (storage) deficit of a cortical dementia like Alzheimer's disease (Kaplan & Sadock 2024).

FEATURE	LATE-ONSET SCHIZOPHRENIA (40 TO 60)	VERY-LATE-ONSET SCHIZOPHRENIA-LIKE PSYCHOSIS (AFTER 60)
Historical label	Late-onset schizophrenia	**Paraphrenia / late paraphrenia**
Sex	Female preponderance	**Female preponderance, more marked**
Delusions	Prominent persecutory	**Persecutory plus partition delusions**
Thought disorder / negative symptoms	Relatively infrequent	**Infrequent (fuels doubt about the diagnosis)**
Affect and cognition	Relatively preserved	Preserved, but organic cause must be excluded
Postulated mechanism	Largely neurodevelopmental (de-gree, not kind)	**Possible neurodegenerative component**

The international-consensus split: late-onset schizophrenia versus the very-late-onset schizophrenia-like psychosis that inherits the paraphrenia concept.

8.7 The imperative: exclude a neurodegenerative or organic cause

The discriminator that matters most. Late-life psychotic symptoms can arise de novo or be driven by dementia, delirium, medical illness, polypharmacy, substance misuse or sensory deficit; secondary psychosis (attributable to another medical or neurological disorder) accounts for a large share of late-life cases (Kaplan & Sadock 2024). A very-late-onset presentation in particular must be worked up as potentially the herald of a dementing process: a proportion convert to dementia on follow-up, so a confident diagnosis of very-late-onset schizophrenia-like psychosis can be made only after a sufficient observation period (Kaplan & Sadock 2024). Disorder-specific treatment is low-dose antipsychotic cover (the starting dose is a fraction of the usual adult dose, with careful attention to older-age adverse effects), plus correcting sensory deficits and social isolation; the antipsychotic drug detail is cross-referenced to the Schizophrenia: management, antipsychotics and adverse effects notes.

TRAP **Missing an emerging dementia.** Labelling a first psychosis after 60 as very-late-onset schizophrenia-like psychosis without a neurocognitive workup and follow-up misses the organic or neurodegenerative cause hiding behind it.

PEARL

Preserved retention is the tell: in very-late-onset psychosis the patient can still lay down and hold new memories, so a rapidly failing memory should push you towards a dementia, not towards paraphrenia. Deafness, isolation and a suspicious premorbid personality complete the classic late-onset triad.

GOOD TO REMEMBER

- **Late-onset schizophrenia:** schizophrenia with onset between 40 and 60; the discriminator is the age band with prominent persecutory delusions and relatively preserved affect and cognition; hold the international-consensus split at 40 (Howard et al. 2000).
- **Very-late-onset schizophrenia-like psychosis:** psychosis with onset after 60, the old paraphrenia; the discriminator is partition delusions with a possible neurodegenerative component; hold the number, onset after 60.
- **Paraphrenia:** Kraepelin's paranoid psychosis of later life spared the emotional and volitional decline of dementia praecox, revived by Roth as late paraphrenia; the one feature is well-organised persecutory delusions with preserved personality.
- **Partition delusion:** the belief that people, objects or radiation pass through walls, doors or windows; the discriminating context is very-late-onset schizophrenia-like psychosis; the one association is late-life onset.
- **Associations:** female sex (2 to 10 times commoner), sensory impairment, social isolation, paranoid or schizoid premorbid traits; the imperative is to exclude a neurodegenerative or organic cause.

9 · Attenuated psychosis syndrome

The **attenuated psychosis syndrome** is DSM-5-TR's attempt to give the clinical high-risk state a name inside the manual: sub-threshold positive symptoms, present often enough and distressing enough to bring a young person to attention, but with reality testing still relatively intact and the person still able to doubt the experience. It is not a full psychotic disorder and, importantly, it is not a formal diagnosis: it sits in Section III among the conditions for further study. For the exam it is a small, high-yield item precisely because it is the point where the **at-risk mental state** becomes a candidate category, and where the false-positive problem is the reason it stops short of the main manual.

Why it earns a place. It formalises the prodrome or at-risk mental state that the schizophrenia course chapter describes, and it forces the discrimination examiners want: an at-risk state named for study is not established schizophrenia. The prodrome and the wider at-risk-mental-state material, along with the schizophrenia course it belongs to, are owned by the Schizophrenia: aetiology, phenomenology, classification and course notes and are not re-derived here; this section is deliberately short.

9.1 The DSM-5-TR condition for further study: attenuated, sub-threshold, insight relatively intact

Core definition. Attenuated psychosis syndrome is a DSM-5-TR **condition for further study** (Section III), characterised by **attenuated psychosis**: delusion-like ideas, unusual perceptual experiences or disorganised speech that are psychosis-like but below the threshold of a full psychotic symptom, with reality testing still relatively intact and the person generally still able to appreciate that the perceptions are altered (APA 2022). The symptoms are less severe and more transient than in a psychotic disorder, and skepticism about them can be induced. In effect it is the at-risk mental state formalised into a candidate category (Kaplan & Sadock 2024).

The operational criteria. Criterion A requires at least one of three attenuated symptoms in relatively intact reality testing: attenuated delusions, attenuated hallucinations, or attenuated disorganized speech. The symptom must have been present **at least once per week for the past**

month (Criterion B) and must have **begun or worsened in the past year** (Criterion C). It must be sufficiently distressing or disabling to warrant clinical attention (Criterion D), not better explained by another mental disorder or a substance or medical cause (Criterion E), and the criteria for any psychotic disorder must never have been met (Criterion F) (APA 2022).

RULE **It names the at-risk mental state, but it is not a formal diagnosis.** Attenuated psychosis syndrome is a DSM-5-TR condition for further study, a candidate label for the clinical high-risk state, not an established Section II diagnosis.

HOLD THIS

Attenuated psychosis syndrome = sub-threshold delusion-like ideas, unusual perceptions or disorganised speech with reality testing relatively intact, at least once a week for the past month and worsening in the past year, distressing enough to warrant clinical attention; it is the at-risk mental state as a DSM-5-TR condition for further study, not a formal diagnosis.

9.2 Why it stays "for further study": only a minority transition, so false-positive and stigma risks dominate

The transition problem. The syndrome remains a condition for further study rather than a formal diagnosis because only a minority of those identified go on to a full psychotic disorder. Modern meta-analytic clinical-high-risk data put transition to a full psychotic disorder at roughly **11% at 6 months**, **15% at 1 year** and **20% at 2 years**, with the older ultra-high-risk cohorts reporting higher rates of around a third at one year; across all of them most people meeting criteria never convert, the non-converting group generally improving in symptoms over time (Kaplan & Sadock 2024, citing Fusar-Poli et al.). The at-risk mental state is detected with structured measures: the Comprehensive Assessment of At-Risk Mental State (CAARMS) and the Structured Interview for Psychosis-Risk Syndromes (SIPS) (New Oxford 2020; Kaplan & Sadock 2024).

The cost of a false positive. Because most identified individuals will not become psychotic, formalising the label risks over-diagnosis: labelling large numbers of help-seeking adolescents as pre-psychotic, exposing them to stigma and to potentially unnecessary antipsychotic treatment. That false-positive and stigma calculus is exactly why DSM-5-TR held the syndrome back in Section III for study rather than promoting it to a full diagnosis. Management is therefore watchful clinical attention and monitoring, not routine antipsychotic prescription; where drug treatment is considered, the antipsychotic detail is cross-referenced to the Schizophrenia: management, antipsychotics and adverse effects notes.

TRAP **Labelling an at-risk state as established schizophrenia.** Calling a person with attenuated, sub-threshold symptoms "schizophrenic" mislabels a candidate at-risk state as a lifelong illness that most of them will never develop.

~15% at 1 yr	Section III	most
TRANSITION TO PSYCHOSIS (ABOUT 20% AT 2 YEARS)	DSM-5-TR CONDITION FOR FURTHER STUDY, NOT A FORMAL DIAGNOSIS	DO NOT CONVERT; NON-CONVERTERS GENERALLY IMPROVE

WORKED EXAMPLE

A distressed 17-year-old is brought in with a few months of intermittent suspiciousness that people are talking about him, fleeting shadow-like visual experiences, and speech that his teachers find vague and off-track. He can, when gently challenged, entertain that there might be another explanation and does not act on the ideas. Symptoms are present several times a week, began this year, and are impairing his schooling. Reality testing is relatively intact and full psychotic-disorder criteria have never been met. This fits attenuated psychosis syndrome as a condition for further study: he is monitored and supported, not diagnosed with schizophrenia and not started on an antipsychotic by reflex.

INDIA

Dedicated clinical-high-risk and early-intervention services are still uncommon in routine Indian practice, so young people with attenuated, sub-threshold symptoms are usually seen once frankly psychotic rather than in a formal at-risk clinic. The practical lesson is the same as the syndrome's own caution: hold the at-risk label lightly, monitor over time, and avoid committing an adolescent to a schizophrenia diagnosis, and to long-term antipsychotics, on sub-threshold symptoms alone.

GOOD TO REMEMBER

- **Attenuated psychosis syndrome:** sub-threshold delusion-like ideas, unusual perceptual experiences or disorganised speech with reality testing relatively intact, distressing enough to warrant clinical attention; the one discriminator is preserved insight with symptoms below full psychotic threshold; hold the number: DSM-5-TR Section III condition for further study, symptoms at least once a week for the past month.
- **At-risk mental state / clinical high-risk:** the construct the syndrome formalises; the discriminating feature is help-seeking with sub-threshold symptoms not yet meeting psychotic-disorder criteria; the number to hold is a minority transition (about 15% at one year, 20% at two years), with most never converting.
- **Why "for further study":** only a minority transition, so the false-positive and stigma risks of formalising the label keep it out of the main diagnostic manual; the one point is that it is not a formal diagnosis.

10 · Differentiate: the schizophrenia-spectrum differential

Why this matters. This is the payoff of the whole primary-psychosis band: the examiner does not hand you a label, they hand you a presentation and ask which spectrum diagnosis it is. Every one of these disorders can look identical on a single afternoon of cross-section, a patient who is deluded, hallucinating and functioning poorly. What separates them is almost never the snapshot; it is the **longitudinal architecture**, chiefly two axes: how long the psychosis has run, and how much mood has been loaded onto it. Hold those two axes and the spectrum falls into an orderly grid; forget them and you will misclassify on the strength of a single interview.

This topic does not re-teach any of these disorders. Schizophrenia itself, its phenomenology, aetiology, criteria and course, is owned by the Schizophrenia: aetiology, phenomenology, classification and course notes; the raw descriptive definitions of the delusions live in the Psychometry, Assessment and Descriptive Psychopathology notes; the mood-episode criteria that

schizoaffective leans on are cross-referenced to the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes; and the drug detail belongs to the Schizophrenia: management, antipsychotics and adverse effects notes. Here we do one thing: we **distinguish** the members of the spectrum from one another, keyed on the single discriminator for each pairing.

10.1 The two master axes: duration and mood-loading

Almost the entire spectrum resolves onto two continuous variables. The first is **duration of psychosis**: the DSM-5 ladder runs less than **one month** (brief psychotic disorder), **one to six months** (schizophreniform disorder), and more than **six months** (schizophrenia), with the ICD-11 threshold for schizophrenia set at **one month** or longer (Kaplan & Sadock 2024, DSM-5-TR 2022, ICD-11 CDDR). The second is **mood-loading**: how much of the illness is occupied by a full mood episode, and whether any psychosis ever runs in the absence of a prominent mood episode. Schizoaffective disorder, mood-with-psychosis and schizophrenia are separated almost entirely on this second axis. Learn to place a case on both axes before you reach for a name.

RULE **Duration and mood-loading are the master discriminators across the spectrum.** Duration sorts the short-course psychoses (brief, schizophreniform, schizophrenia); mood-loading sorts schizoaffective from mood-with-psychosis and from schizophrenia. Place the case on both axes first, then name it.

TRAP **Letting a cross-sectional snapshot of psychosis override the longitudinal criteria.** A single florid interview cannot distinguish brief psychotic disorder, schizophreniform disorder, schizophrenia or an acute mood episode with psychosis; only the course over time can. Diagnosing from the snapshot is the classic spectrum error.

10.2 Schizoaffective vs mood-with-psychosis vs schizophrenia: the mood-loading axis

This is the three-way discrimination that turns entirely on mood-loading, and it is the single highest-yield pairing on the spectrum. Two rules do the work (DSM-5-TR 2022, Kaplan & Sadock 2024). First, schizoaffective disorder requires a period of at least **two weeks** of delusions or hallucinations in the absence of a prominent mood episode over the lifetime of the illness (Criterion B): this is the two-weeks-of-psychosis-without-a-prominent-mood-episode rule, and it is what separates schizoaffective disorder from mood-with-psychosis, where psychosis is confined to the mood episode and never runs alone. Second, schizoaffective disorder requires that mood symptoms are present for the majority of the total duration of the active and residual illness (Criterion C): this mood-for-the-majority requirement is what separates it from schizophrenia, which carries no prominent mood for the majority of its course.

So the logic is a fork. If psychosis *only ever* appears inside a mood episode, it is **mood-with-psychosis** (a mood disorder with psychotic features), and its mood-episode criteria are set out in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes. If psychosis runs for at least two weeks *without* a prominent mood episode, and mood nonetheless occupies the majority of the illness, it is schizoaffective disorder. If psychosis dominates and mood is a minor, non-majority accompaniment, it is schizophrenia. The two-week gate excludes

mood-with-psychosis below; the majority rule excludes schizophrenia above; schizoaffective disorder lives only in the narrow band where both hold.

10.3 Delusional disorder vs paranoid schizophrenia: the breadth axis

Here duration is not the discriminator (both are chronic); breadth of the psychosis is. Delusional disorder is defined by one or more well-systematised, long-lasting delusions on a single circumscribed theme, classically *non-bizarre*, with the rest of mental life and personality relatively intact and social and occupational functioning largely preserved (New Oxford Textbook 2020, Kaplan & Sadock 2024, ICD-11 CDDR). What is *absent* is what makes the diagnosis: no persistent prominent hallucinations, no formal thought disorder or disorganisation, no negative symptoms, no experiences of influence or passivity, no general functional decline. The contrast with **paranoid schizophrenia** is exactly this breadth. Schizophrenia brings the wider syndrome, prominent hallucinations, disorganised thinking and behaviour, negative symptoms and functional deterioration, on top of the delusions; if those broader features are present, the ICD-11 boundary text is explicit that a diagnosis of schizophrenia is made instead of delusional disorder (ICD-11 CDDR). Two further pointers: delusional disorder comes to attention at a later age (onset generally in the mid- to late-30s) and shows far less deterioration over time than schizophrenia (Kaplan & Sadock 2024). Hallucinations may occur in delusional disorder if they are congruent with the delusional theme and not persistent; persistent, prominent hallucinations push the diagnosis over into schizophrenia.

RULE **One theme, preserved function equals delusional disorder; the wider syndrome equals schizophrenia.** A single-theme non-bizarre delusion with otherwise intact personality and function is delusional disorder; add prominent hallucinations, disorganisation, negative symptoms or functional decline and it becomes paranoid schizophrenia.

10.4 ATPD vs brief psychotic disorder vs schizophreniform: the duration ladder

These three are the short-course psychoses, and the discrimination is chiefly the duration ladder plus, for ATPD, a distinctive onset and course. In DSM-5-TR the ladder is clean: brief psychotic disorder lasts at least one day but less than **one month** with eventual full return to premorbid functioning; schizophreniform disorder lasts at least **one month but less than six months** and is otherwise identical to schizophrenia (a diagnosis of exclusion in time, made provisional if recovery has not yet occurred); and beyond six months with functional impairment the diagnosis becomes schizophrenia (DSM-5-TR 2022, Kaplan & Sadock 2024). The ICD-11 counterpart to the acute end is acute and transient psychotic disorder (ATPD, 6A23), and its signature is not merely brevity but the *quality* of the episode: an abrupt onset progressing from a non-psychotic to a clearly psychotic state within **two weeks**, with symptoms that fluctuate rapidly in intensity and type (the content of delusions and hallucinations shifting even on a daily basis), an absence of negative symptoms, a duration that does not exceed **three months** (most often lasting from a few days to one month), and a characteristically good outcome with full recovery (ICD-11 CDDR). This rapidly-shifting, abrupt-onset, short-and-remitting picture is the ATPD fingerprint; the older Scandinavian reactive-psychosis and cycloid-psychosis concepts feed into it.

Two boundary points the examiner likes. A case that meets all schizophrenia requirements but has lasted less than the one-month threshold, with no previous history of schizophrenia, is *not* ATPD in ICD-11: it is assigned to other specified primary psychotic disorder, because ATPD is defined by its fluctuating acute quality, not merely by being schizophrenia-cut-short (ICD-11 CDDR). And because ICD-11 sets the schizophrenia duration at one month, many cases that DSM-5 would call schizophreniform disorder are simply classified as schizophrenia in ICD-11; there is no schizophreniform category in ICD-11 (Kaplan & Sadock 2024).

under 1 mo	1 to 6 mo	up to 3 mo	within 2 wk
BRIEF PSYCHOTIC DISORDER (DSM-5-TR)	SCHIZOPHRENIFORM DISORDER (DSM-5-TR)	ATPD, DOES NOT EXCEED THREE MONTHS (ICD-11)	ATPD ONSET, NON-PSYCHOTIC TO PSYCHOTIC (ICD-11)

10.5 The interleaved spectrum differential

The grid below interleaves all the spectrum members onto the two master axes and names, for each, the one discriminator that settles the pairing. Read it as a single decision tool: place the case by presentation, duration and mood-loading, then read off the discriminator column.

DISORDER	PRESENTATION	DURATION	MOOD-LOADING	THE ONE DISCRIMINATOR
Brief psychotic disorder	Acute florid psychosis, often with a stressor; full return to premorbid function	1 day to under 1 month	None required	**Resolves in under one month with full recovery**
ATPD (ICD-11 6A23)	Abrupt onset, rapidly fluctuating delusions or hallucinations shifting even daily; no negative symptoms; good outcome	Onset within 2 weeks; does not exceed 3 months (often days to 1 month)	Variable, mood may colour the picture but is not the axis	**Abrupt onset plus rapidly shifting content plus short remitting course**
Schizophreniform disorder	Identical to schizophrenia in symptoms; functional decline not required	1 to 6 months	Mood-with-psychosis and schizoaffective ruled out	**Duration one to six months (provisional if recovery not yet occurred)**
Schizophrenia	Full syndrome: delusions, hallucinations, disorganisation, negative symptoms, functional decline	6 months or more (ICD-11: 1 month or more)	No prominent mood for the majority of the illness	**Duration over 6 months (owned by the schizophrenia notes)**

DISORDER	PRESENTATION	DURATION	MOOD-LOADING	THE ONE DISCRIMINATOR
Schizoaffective disorder	Full mood episode concurrent with schizophrenia-criterion psychosis	Chronic	Mood for the majority; at least 2 weeks of psychosis without a prominent mood episode	**Two weeks of psychosis without a prominent mood episode, and mood for the majority**
Mood-with-psychosis	Delusions or hallucinations occurring only within a mood episode	Duration of the mood episode	Maximal, psychosis is confined to the mood episode	**Psychosis only within mood episodes, never for two weeks alone**
Delusional disorder	Single-theme, well-systematised, non-bizarre delusion; personality and function preserved	Chronic, at least 3 months (ICD-11); later onset (mid to late 30s)	Low, mood not the axis	**One non-bizarre theme with preserved function and no wider syndrome**
Paranoid schizophrenia	Persecutory delusions plus prominent hallucinations, disorganisation, negative symptoms, decline	6 months or more	No prominent mood for the majority	**The wider syndrome and functional decline on top of the delusions**

The spectrum keyed on two axes: duration sorts the short-course psychoses; mood-loading sorts schizoaffective from mood-with-psychosis and schizophrenia; breadth sorts delusional disorder from paranoid schizophrenia.

10.6 Working the differential in practice

The examiner rewards a method, not a lucky guess. Take any psychotic presentation and ask, in order: has an organic or substance cause been excluded (a detailed history, examination and, where indicated, toxicology and imaging, since a rapid onset in someone with a substance history should raise substance-induced psychosis)? How long has the psychosis run in its full form (the duration ladder)? Does any psychosis run in the absence of a prominent mood episode, and does mood occupy the majority of the illness (the mood-loading fork)? Is the psychosis a single circumscribed non-bizarre theme with preserved function, or the wider syndrome with decline (the breadth axis)? Is the onset abrupt with rapidly shifting content and a short remitting course (the ATPD fingerprint)? Answer those five in sequence and the spectrum diagnosis is usually forced. The one thing that must never drive the answer is the cross-sectional snapshot alone.

COMMON TRAP

Do not diagnose schizoaffective disorder simply because psychosis and a mood episode co-occur. Concurrent psychotic and mood symptoms are equally compatible with a mood disorder with psychotic features; the diagnosis turns on the two-weeks-of-psychosis-without-a-prominent-mood-episode rule (Criterion B) and the mood-for-the-majority rule (Criterion C). Without the two-week window this is mood-with-psychosis, not schizoaffective disorder.

INDIA

Acute, abrupt-onset, short-course psychoses of the ATPD type are a well-recognised and relatively common presentation in Indian practice, frequently precipitated by an acute stressor and carrying a good outcome, which fits the classic acute-and-transient picture; longitudinal follow-up remains essential because a proportion later declare themselves as schizophrenia or a mood disorder. Delusional disorder is similarly encountered as a late-onset, single-theme, function-preserving condition. Verify any local prevalence claim against a primary source before quoting a figure.

MNEMONIC

DURATION, MOOD, BREADTH

Three questions settle almost the whole spectrum. DURATION sorts the short-course psychoses (under one month brief, one to six months schizophreniform, over six months schizophrenia). MOOD-loading sorts schizoaffective (two weeks of psychosis without a prominent mood episode, plus mood for the majority) from mood-with-psychosis (psychosis only within mood episodes) and schizophrenia (no prominent mood for the majority). BREADTH sorts delusional disorder (one theme, preserved function) from paranoid schizophrenia (the wider syndrome, decline).

HOLD THIS

Never diagnose the spectrum from a cross-sectional snapshot: duration (the under-one-month / one-to-six-month / over-six-month ladder) and mood-loading (two weeks of psychosis without a prominent mood episode, plus mood for the majority) are the master discriminators, and breadth (one non-bizarre theme with preserved function versus the wider syndrome) settles delusional disorder against paranoid schizophrenia.

GOOD TO REMEMBER

- **Schizoaffective vs mood-with-psychosis vs schizophrenia:** schizoaffective needs at least **two weeks** of psychosis without a prominent mood episode (Criterion B, separates it from mood-with-psychosis) and mood for the majority of the illness (Criterion C, separates it from schizophrenia); mood-with-psychosis has psychosis only within mood episodes; the number to hold is two weeks.
- **Delusional disorder vs paranoid schizophrenia:** a single-theme, non-bizarre delusion with preserved personality and function is delusional disorder; add prominent hallucinations, disorganisation, negative symptoms or decline and it is paranoid schizophrenia; delusional disorder onset is later (mid to late 30s).
- **Brief psychotic disorder:** acute psychosis lasting at least one day but less than **one month** with full recovery; the one number is under one month (DSM-5-TR).
- **Schizophreniform disorder:** schizophrenia-identical symptoms lasting **one to six months**; the one eponym is Langfeldt (1939), who introduced the concept; no equivalent in ICD-11.
- **ATPD (ICD-11 6A23):** abrupt onset from non-psychotic to psychotic within **two weeks**, rapidly shifting content, no negative symptoms, duration not exceeding **three months** (often days to one month), good outcome; the discriminator is the abrupt-onset, fluctuating, short-remitting quality, not brevity alone.
- **The two master axes:** duration sorts the short-course psychoses; mood-loading sorts schizoaffective from mood-with-psychosis and schizophrenia; the trap is diagnosing from the cross-sectional snapshot instead of the longitudinal course.

Delusional misidentification and named delusional syndromes

11 · Delusional misidentification syndromes

Why this matters. The **delusional misidentification syndromes** are a small keyed grid the examiner loves precisely because the eponyms are so easy to swap: four named beliefs, each turning on *who* is misidentified and in *which direction*. They are not a disorder in their own right but a recurring content pattern that rides on top of schizophrenia, mood disorder with psychosis, dementia and focal brain disease. The whole topic can be held on two axes: the familiar-versus-stranger axis (Capgras is the familiar seen as an impostor; Fregoli is the stranger seen as a familiar-in-disguise), and the appearance-versus-identity axis (whether the physical face changes, the psychological identity changes, or both).

Because these beliefs so often sit on organic pathology, the topic doubles as a trap about aetiology: a striking eponymous delusion is an invitation to look for a right-hemisphere lesion, a dementia or a metabolic cause, not to reflexively call it functional psychosis. The raw descriptive phenomenology of each belief (how it is elicited and graded at the mental-state level) is cross-referenced to the Psychometry, Assessment and Descriptive Psychopathology notes; here the job is the diagnosis and the discrimination. The **misidentification syndromes** are grouped in ICD-11 and DSM-5-TR under other specified schizophrenia-spectrum and other psychotic disorders when they stand alone (Kaplan & Sadock 2024).

Syndrome	The core misidentification	Typical association
Capgras	A familiar person seen as an identical impostor	commonest; up to 40% organic; right hemisphere
Fregoli	One persecutor disguised inside strangers	persecutory psychosis; rarer; Courbon & Fail 1927
Inter-metamorphosis	Appearance AND identity both swapped	total transformation; rare
Subjective doubles	Doubles of the self, acting on their own	not heautoscopy (self seen)
Reduplicative paramnesia	A place or object believed duplicated	right-hemisphere / frontal lesion

Fig 10.7 The delusional misidentification syndromes, keyed on the core misidentification. Capgras and Fregoli are direction-reversed (the familiar seen as an impostor versus one persecutor seen disguised inside strangers); intermetamorphosis changes both appearance and identity; subjective doubles turns the belief on the self; reduplicative paramnesia is the organic marker of the group. A face-processing disconnection and a high rate of right-hemisphere or organic pathology make excluding an organic cause mandatory.

11.1 Capgras syndrome: the familiar seen as an impostor

Capgras syndrome. The belief that a familiar person, to whom the sufferer is emotionally close (typically a spouse or relative, and sometimes a pet or an object), has been replaced by an identical impostor or double who has assumed that person's role and behaves like them (Companion 2010, Kaplan & Sadock 2024). It is the most common of the group. The conviction can be dangerous: some patients threaten, harm or even kill the supposed impostor, so the recognition of Capgras

carries a real risk assessment. It was described by the French psychiatrist Joseph Capgras (Capgras & Reboul-Lachaux 1923), who called it the "illusion of doubles" (Tasman 2015). The core is a paradox the patient rationalises: the person looks exactly the same but does not *feel* the same, and so must be a substitute.

RULE **Capgras is the familiar seen as an impostor; Fregoli is the stranger seen as a familiar-in-disguise.** Fix the direction first (who is real, who is disguised) and the two eponyms stop swapping.

11.2 Fregoli syndrome: the persecutor disguised as everyone

Fregoli syndrome. The belief that a persecutor is present but disguised as different people the patient meets: a single familiar figure (usually the persecutor) is repeatedly identified inside strangers who bear no physical resemblance, so the doctor is "really" the persecutor, then the nurse is, and so on, yet the persecutor is always one and the same (New Oxford 2020, Shorter Oxford 2018). The direction is the mirror-image of Capgras: the outward appearance is a stranger's, but the inner identity is claimed to be a known person. It was originally described by Courbon and Fail in 1927 and is even rarer than the Capgras delusion (Shorter Oxford 2018), named after Leopoldo Fregoli, the Italian stage actor famous for rapid changes of appearance and character.

TRAP **Attributing misidentification to a functional psychosis without excluding neurological or organic disease.** Up to 40% of Capgras cases carry an organic disorder (head injury, dementia); a striking misidentification delusion mandates an organic screen before it is called schizophrenia.

11.3 Intermetamorphosis and the syndrome of subjective doubles

Intermetamorphosis. The belief that others have been swapped in *both* physical appearance and identity, so that people (and sometimes animals or objects) are transformed into one another; unlike Fregoli, where only the hidden identity changes, here the delusion is of a total transformation, psychological as well as physical (New Oxford 2020, AIIMS Clinical Methods 2024). **Syndrome of subjective doubles.** The belief in doubles of oneself: the patient is convinced that exact physical copies of themselves exist and carry out independent actions, each with a separate psychological identity (New Oxford 2020, AIIMS Clinical Methods 2024). It is distinct from heautoscopy, in which the self is *seen* as a visual double rather than believed to exist as an independent agent.

11.4 The proposed mechanism: a face processing disconnection

The influential cognitive account of Capgras, and by extension the group, is the two-route model of face processing (Ellis & Young 1990). It proposes two routes to facial recognition: one for the identification of the face itself and one that gives the face its affective sense of familiarity. Prosopagnosia is a loss of the first route; Capgras is proposed as its "mirror image", an intact primary recognition route with a disconnection of the second, so the face is recognised as identical but is stripped of the emotional feeling that should accompany a loved one (Ellis & Young 1990). Ellis et al (1997) supported this by showing that Capgras patients fail to show the normal autonomic (skin-conductance) discrimination between familiar and unfamiliar faces. This

account is consistent with the high rate of right-hemisphere and organic pathology in these patients (Companion 2010). The patient mistakes a change in themselves (the missing sense of familiarity) for a change in the other person, and rationalises it as substitution.

The imperative to exclude an organic cause. Because delusional misidentification is so strongly associated with right-hemisphere dysfunction and structural or metabolic brain disease, an organic cause must be actively excluded in every case. Capgras has been reported in central nervous system lesions, dementia (especially dementia with Lewy bodies), vitamin B12 deficiency, hepatic encephalopathy, diabetes and hypothyroidism (AIIMS Clinical Methods 2024, Companion 2010). Right-sided cerebral pathology also produces reduplicative paramnesia, the belief that a familiar place, object or body part has been duplicated, which sits alongside the misidentification group and points the same way, toward the right hemisphere.

up to 40%
OF CAPGRAS CASES CARRY AN ORGANIC DISORDER (COMPANION 2010)

1927
COURBON AND FAIL DESCRIBE FREGOLI SYNDROME

right hemisphere
THE PATHOLOGY TO SUSPECT ACROSS THE GROUP

11.5 The differentiation grid

The grid is the deliverable: each syndrome is defined by *who* is misidentified and in *which* direction (familiar to stranger, or the reverse), and by whether appearance, identity, or both are held to have changed. Read down the "core misidentification" column and the eponyms separate cleanly.

SYNDROME	THE CORE MISIDENTIFICATION	TYPICAL ASSOCIATION
Capgras syndrome	**A familiar person (or pet or object) is believed replaced by an identical impostor or double; looks the same, does not feel the same**	Most common of the group; schizophrenia; organic disease in up to 40%; right-hemisphere pathology
Fregoli syndrome	**A persecutor is present but disguised as different strangers the patient meets; one persecutor inside many faces**	Persecutory psychosis; rarer than Capgras; Courbon and Fail 1927
Intermetamorphosis	**Others are swapped in both physical appearance and identity; a total transformation, not merely a disguise**	Psychotic disorders; rare; may include animals and objects
Syndrome of subjective doubles	**Belief in exact doubles of oneself, acting independently with separate identities**	Psychotic disorders; distinguish from heautoscopy (the self seen, not believed independent)
Reduplicative paramnesia	A familiar place, object or body part is believed duplicated (e.g. the real home moved and replaced by an identical one)	Right-hemisphere and frontal lesions; organic marker rather than functional psychosis

The misidentification grid: Capgras and Fregoli are direction-reversed (familiar-as-impostor versus stranger-as-familiar); intermetamorphosis changes both appearance and identity; subjective doubles turns the belief on the self.

HOLD THIS

Capgras = the familiar person seen as an identical impostor (looks the same, does not feel the same); Fregoli = the one persecutor seen disguised inside many strangers; a face processing disconnection between recognition and the affective sense of familiarity, plus right-hemisphere or organic pathology in a large minority, makes excluding an organic cause mandatory.

PEARL

The two-route face-recognition model gives the group a tidy logic: prosopagnosia loses the recognition route but keeps the feeling of familiarity; Capgras is the mirror image, keeping recognition but losing the feeling, so the face is known yet feels wrong and is rationalised as a substitute (Ellis & Young 1990). One model, two opposite clinical pictures.

INDIA

In Indian practice these syndromes are seen most often as content within schizophrenia and, increasingly, within dementia in older patients; the clinical discipline is identical, an organic and metabolic screen (including B12, thyroid and neuroimaging where a focal or right-hemisphere picture is suspected) before the belief is attributed to a functional psychosis. The named beliefs are managed by treating the underlying disorder, not as entities in themselves.

GOOD TO REMEMBER

- **Capgras syndrome:** a familiar person replaced by an identical impostor; the discriminator is "looks the same, does not feel the same"; the number to hold is up to 40% organic, and the eponym is Joseph Capgras (1923).
- **Fregoli syndrome:** a persecutor disguised as different strangers the patient meets; the discriminator is one identity inside many unfamiliar faces (mirror image of Capgras); the eponym and date are Courbon and Fail, 1927.
- **Intermetamorphosis:** others swapped in both physical appearance and identity; the discriminator is a total transformation (not just a disguise); hold that both appearance and identity change.
- **Syndrome of subjective doubles:** the belief in doubles of oneself acting independently; the discriminator is that the double is of the self and is believed to exist as an agent; distinguish it from heautoscopy.
- **The mechanism:** a face processing disconnection between visual recognition and the affective sense of familiarity; the fact to hold is the high rate of right-hemisphere and organic pathology and the imperative to exclude an organic cause (Ellis & Young 1990, Companion 2010).

12 · Named monothematic delusional syndromes

A handful of delusions carry their own eponyms, and the examiner loves them precisely because they are quick to name and easy to misattribute. Each is a **monothematic** delusion: a single, circumscribed belief that dominates the clinical picture while the rest of thought stays comparatively intact (Coltheart, Langdon & McKay 2007; New Oxford Textbook). The trap built into the whole set is a category error, treating the eponym as a diagnosis in its own right, when almost all of these are **delusional content** that can appear across schizophrenia, delusional disorder, a mood episode or an organic state.

Why it matters. Marks here are won on three moves: attaching each eponym to the correct content without swapping them, stating that the content is transdiagnostic rather than a disorder in itself, and, for one of them, recognising a real forensic danger. The raw descriptive definitions of the delusions themselves belong to the Psychometry, Assessment and Descriptive Psychopathology notes; the task here is to name the content precisely and then find the illness underneath it.

Eponym	Core delusional content	Association or risk
De Clerambault (erotomania)	A higher-status person is secretly in love	solitary women; stalking
Othello (delusional jealousy)	A partner is being unfaithful	violence and homicide risk; commoner in men
Cotard (nihilistic)	Being dead, not existing, or the organs lost	severe psychotic depression; severity marker
Ekbom (infestation)	Infested with parasites under the skin	matchbox sign; presents to dermatology

Fig 10.8 The named monothematic delusional syndromes, keyed on the core delusional content. Each is delusional content that can occur across schizophrenia, delusional disorder, a mood episode or an organic state, not a disorder in itself: name the content, then find the illness. Othello syndrome (delusional jealousy) is the one that carries a genuine forensic risk of violence to the partner.

12.1 Content, not disorder: the governing principle

Name the content, then find the illness. These eponymous syndromes are defined by *what* the patient believes, not by any distinct aetiology or course. Each can occur as the somatocentric, erotocentric or securocentric expression of an underlying condition, so the same named delusion is seen in schizophrenia, in delusional disorder as a monothematic somatic or persecutory belief, in a severe mood episode, and in organic and drug-induced states (New Oxford Textbook; Tasman; Kaplan & Sadock 2024). The clinical move is therefore two-step: recognise the content, attach the eponym, then work out the diagnostic bed it sits in. Only where the belief stands alone, monosymptomatic and monothematic with otherwise preserved functioning, does it become a delusional disorder in its own right (New Oxford Textbook).

RULE **Eponym first, diagnosis second.** Erotomania, morbid jealousy, nihilism and infestation are *content* that occurs across schizophrenia, delusional disorder, mood disorder and organic states; name the content, then find the illness that carries it.

12.2 De Clerambault syndrome: erotomania

The delusion of being loved. In de clerambault syndrome, also written **clerambault**'s syndrome and synonymous with erotomania (psychose passionelle), the patient is imperturbably convinced that another person, usually of higher social status and often a celebrity or a distant figure, is secretly in love with them (New Oxford Textbook; Kaplan & Sadock 2024; AIIMS Clinical Methods 2024). The supposed lover is typically unaware, unattainable and out of reach, and the belief persists even when that person ignores or rejects the patient's contacts (Kaplan & Sadock

2024). It is classically described in solitary, withdrawn, dependent women, though it is not confined to them, and it can drive persistent stalking and unwanted approach behaviour (Kaplan & Sadock 2024; New Oxford Textbook). Erotomanic content is not unique to delusional disorder and occurs as a symptom of other psychotic conditions (Tasman).

GOOD TO REMEMBER

- **De Clerambault syndrome (erotomania):** the delusion that another person, usually of higher status, is secretly in love with the patient. Discriminator: the object is typically unaware and unattainable, yet the conviction is unshakeable. Eponym to hold: de Clerambault (psychose passionelle); classically described in women.

12.3 Othello syndrome: delusional jealousy

The dangerous one. In othello syndrome, also called morbid jealousy, conjugal paranoia or delusional jealousy, the patient holds the fixed, false belief that their sexual partner is being unfaithful, pursued with relentless checking, interrogation and demands for confession (New Oxford Textbook). The name is drawn directly from Shakespeare's Othello, who killed his wife on a false belief of infidelity (New Oxford Textbook). This is the syndrome that carries a genuine forensic risk: the jealous delusion is associated with a real danger of violence, including homicide, toward the accused partner, and morbid jealousy is over-represented in spousal violence and killing (New Oxford Textbook; Companion to Psychiatric Studies). It is reported as more common in men, and, like the others, delusional jealousy is transdiagnostic and can be a symptom of schizophrenia, an organic or alcohol-related state, or delusional disorder (Companion to Psychiatric Studies; New Oxford Textbook).

TRAP **Treating Othello syndrome as benign.** Delusional jealousy is not a quirk of a suspicious marriage; it carries a real risk of harm to the partner, up to homicide, and mandates a formal risk assessment and, often, separation for the partner's safety.

GOOD TO REMEMBER

- **Othello syndrome (delusional jealousy):** the delusion that a partner is unfaithful. Discriminator: fixed, false conviction of infidelity, pursued with checking and demands for confession, distinct from ordinary jealousy. Forensic caveat to hold: genuine risk of violence and homicide toward the partner; reported commoner in men.

12.4 Cotard syndrome: the nihilistic delusion

The delusion of non-existence. Cotard syndrome, the delusion of negation, is the nihilistic delusion that the self, others or the world no longer exist, have been destroyed, or have lost their meaning and value (Shorter Oxford Textbook; AIIMS Clinical Methods 2024). In its fuller forms the patient believes they are dead, do not exist, or have lost or rotted away their internal organs, that the bowels are blocked or the blood has stopped, and it may extend to a delusion that the whole world is about to end (Shorter Oxford Textbook). It is classically seen in severe, often psychotic, depression, and also occurs in schizophrenia and in organic states (Shorter Oxford Textbook; Kaplan & Sadock 2024). It is a marker of severity: the nihilistic-somatic core signals a profound depressive or organic illness rather than a benign hypochondriacal worry.

GOOD TO REMEMBER

- **Cotard syndrome (nihilistic delusion):** the delusion of being dead, not existing, or having lost the internal organs. Discriminator: nihilistic-somatic negation, classically bowels or blood, not merely fear of illness. Association to hold: severe, often psychotic, depression (Jules Cotard, delire de negation).

12.5 Ekbom syndrome: delusional infestation

The delusion of parasites under the skin. Ekbom syndrome, or delusional infestation (delusional parasitosis, acarophobia, monosymptomatic hypochondriacal psychosis), is the fixed belief that one is infested with parasites, insects or small organisms crawling on or under the skin (Kaplan & Sadock 2024; Shorter Oxford Textbook). Thibierge first described the condition in the 1890s; it is now widely termed Ekbom syndrome after Karl-Axel Ekbom (Kaplan & Sadock 2024). The hallmark clinical sign is the **matchbox sign**: the patient brings collected specimens, usually skin, hair or lint, in a small container as proof of the infestation (Kaplan & Sadock 2024). These patients present most often to dermatology rather than psychiatry, and self-treat by washing, excoriating and using insecticides (Kaplan & Sadock 2024). It is the commonest presentation of monosymptomatic hypochondriacal psychosis and, again, can be primary (delusional disorder, somatic type) or secondary to schizophrenia, depression, dementia or drug intoxication such as cocaine (Tasman; Kaplan & Sadock 2024).

PEARL

The matchbox sign (the patient arriving with a container of "specimens", now sometimes the "specimen-jar" or smartphone-photo sign) is near-pathognomonic for delusional infestation and a fast bedside pointer. Before settling on Ekbom syndrome, exclude a real infestation, and screen for the organic and drug causes, cocaine and amphetamine "formication", B12 deficiency, hypothyroidism and dementia, that mimic it.

GOOD TO REMEMBER

- **Ekbom syndrome (delusional infestation):** the delusion of being infested with parasites or small organisms. Discriminator: the matchbox sign, specimens brought as proof; presents to dermatology. Eponym to hold: Karl-Axel Ekbom (first described by Thibierge, 1890s); commonest monosymptomatic hypochondriacal psychosis.

12.6 The keyed grid: eponym, content, association

The four in one table. The classic way to hold these is by their arche-theme: erotocentric (erotomania, jealousy), securocentric (persecutory, misidentification) and somatocentric (infestation, nihilistic-somatic) content (New Oxford Textbook). The grid below pins each eponym to its core delusional content and its single most exam-relevant association or risk. Every row is content that can occur across diagnoses; the eponym names the belief, not the illness.

EPONYM	CORE DELUSIONAL CONTENT	CLASSIC ASSOCIATION OR RISK
De Clerambault syndrome	**Another person, often of higher status, is secretly in love with the patient (erotomania)**	Classically solitary women; stalking and unwanted approach
Othello syndrome	**A partner is being unfaithful (delusional jealousy)**	**Real forensic risk of violence and homicide to the partner; commoner in men**
Cotard syndrome	**One is dead, does not exist, or has lost the internal organs (nihilistic delusion)**	Severe, often psychotic, depression; a severity marker
Ekbom syndrome	**One is infested with parasites or small organisms (delusional infestation)**	Matchbox sign; presents to dermatology; exclude cocaine, B12, dementia

Fig 10.8: the named monothematic delusional syndromes, eponym to content to association; each is delusional content that occurs across diagnoses, not a disorder in itself.

MNEMONIC

JELLI: Jealousy, Erotomania, Loss-of-existence, Little-organisms Infest

Othello = Jealousy; de Clerambault = Erotomania; Cotard = Loss of existence (nihilism); Ekbom = Little organisms Infest the skin. Four eponyms, four contents, in one string.

INDIA

In Indian delusional-disorder series the somatic and jealous subtypes are well represented, and delusional infestation and morbid jealousy are recognisable presentations in general and old-age psychiatry practice; the jealous subtype in particular carries the same domestic-violence risk that mandates a routine risk assessment and, where alcohol is the driver, attention to the alcohol-related state underlying the jealousy. The onset in delusional disorder is typically later than in schizophrenia (Companion to Psychiatric Studies), which fits the older, married patient in whom Othello and Ekbom syndromes are so often seen.

HOLD THIS

De Clerambault (loved by another), Othello (partner unfaithful), Cotard (dead or without organs) and Ekbom (infested) are monothematic delusional *contents* that occur across schizophrenia, delusional disorder, mood disorder and organic states; name the content, find the illness, and never call Othello syndrome benign, it can kill the partner.

Catatonia

13 · Catatonia: the signs and their examination

Catatonia is elicited, not merely observed. **Catatonia** is a syndrome of disturbed motility, volition and reactivity that sits *transdiagnostically* across mood, psychotic, autistic, developmental and organic disease. The examiner who only watches a still patient will miss it; the one who

reaches out, resists, mirrors and instructs will find it. This topic teaches the **catatonic signs** in their classical and modern groupings, the bedside **examination** that elicits them, and the Bush-Francis rating scale that standardises the search. The raw descriptive definitions of the movement and volition disorders are cross-referenced to the Psychometry, Assessment and Descriptive Psychopathology notes; here the target is recognition and the discrimination from the mimics that get catatonia missed.

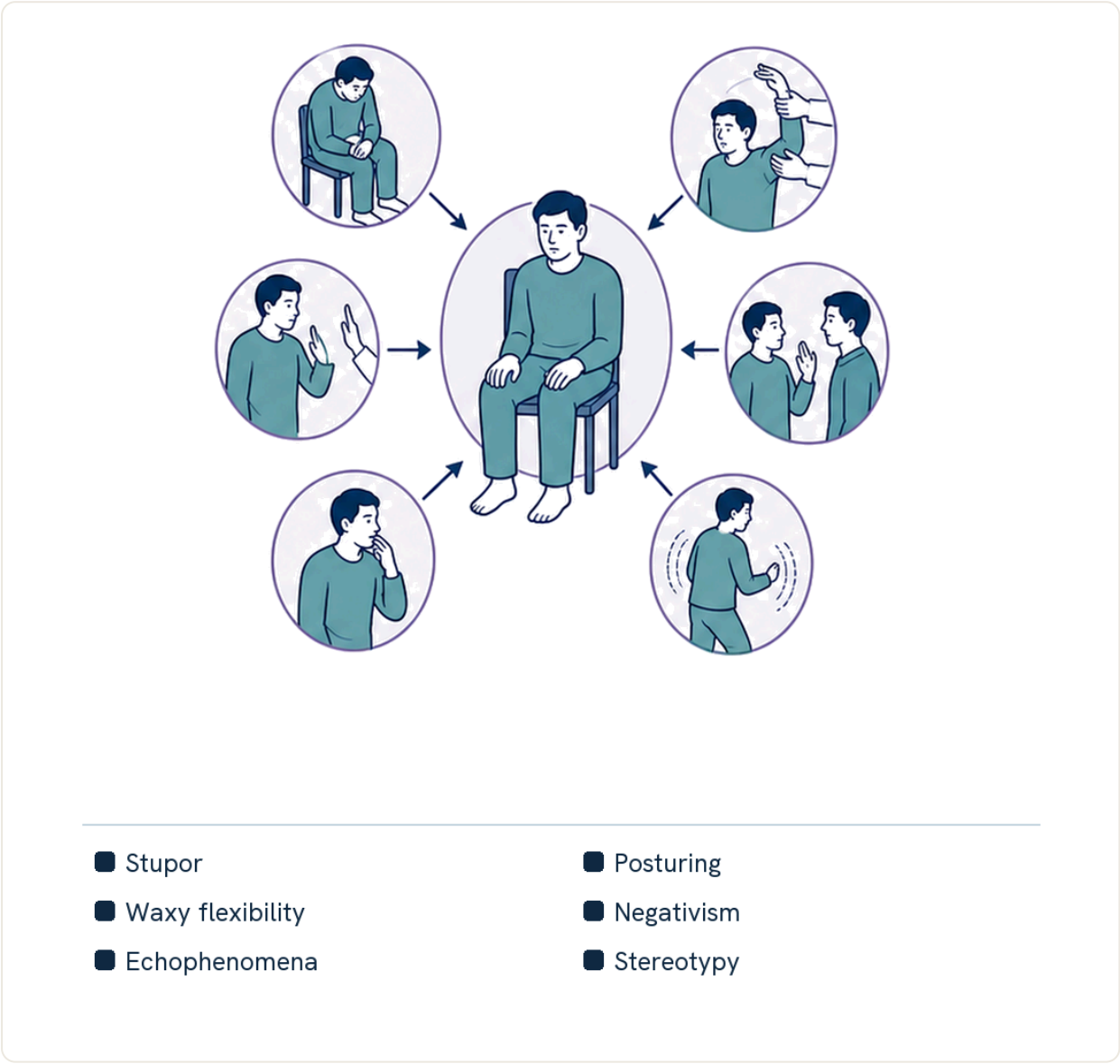


Fig 10.9 A structured examination for catatonia samples reduced movement and interaction, maintained posture, waxy flexibility, resistance or negativism, echophenomena and purposeless repetitive movement.

The high-yield frame for a viva: catatonia is a *clinical* diagnosis made on a defined constellation of signs, most of which must be actively drawn out. Naming the sign, describing how you elicit it, and placing it on the Bush-Francis map is the examiner-pleasing sequence.

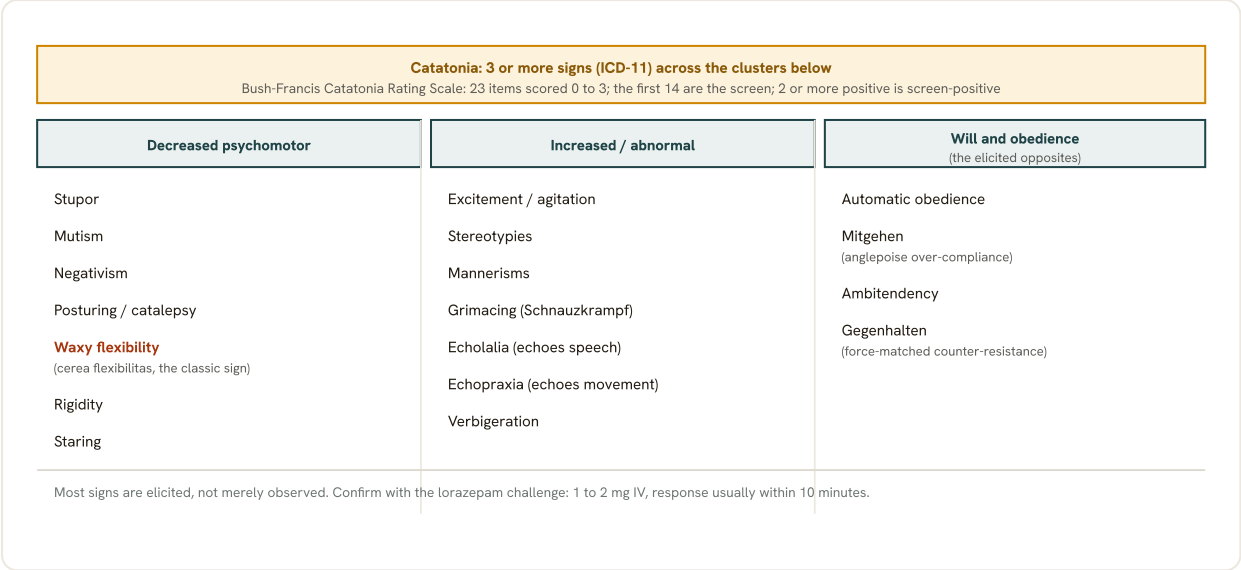


Fig 10.10 The catatonic signs grouped across the three ICD-11 psychomotor clusters, mapped onto the Bush-Francis rating scale. Waxy flexibility (cerea flexibilitas) is the classic elicited sign. Most signs must be actively drawn out at the bedside, which is why stuporous catatonia is so easily missed as depression or non-cooperation; three or more signs meet the ICD-11 threshold, and a lorazepam challenge confirms.

13.1 The Kahlbaum picture and the transdiagnostic modern concept

Origin. Kahlbaum described catatonia (*Die Katatonie oder das Spannungsirresein*, the "tension insanity") in 1874 as a cyclical illness passing through melancholic, manic, stuporous and, ultimately, dementing phases (Kahlbaum 1874). Kraepelin then folded it into dementia praecox as a subtype, and catatonia was for a century treated as a form of schizophrenia. That is the error the modern concept corrects.

The modern reframe. Catatonia is a *transdiagnostic* motor syndrome: in a New York cohort of catatonic inpatients only a small minority met criteria for schizophrenia, while more than two-thirds had affective disorders, usually mania (Kaplan & Sadock 2024). The disorder schizophrenia itself is not re-taught here; its phenomenology and criteria are owned by the Schizophrenia: aetiology, phenomenology, classification and course notes. What matters for catatonia is that a mood episode, an organic or medical illness, autism or substances are each more likely than schizophrenia to be the substrate.

RULE **Catatonia is a syndrome, not a subtype.** Diagnose the sign-constellation first, then hunt the cause; mood and medical illness outrank schizophrenia as the substrate.

13.2 The ICD-11 placement and diagnostic requirement

Nosology (ICD-11 primary). ICD-11 makes catatonia a free-standing, cross-cutting entity with its own grouping: 6A40 Catatonia associated with another mental disorder, 6A41 Catatonia induced by substances or medications, 6E69 Secondary catatonia syndrome, and 6A4Z Catatonia, unspecified (ICD-11 CDDR 2024). This is a genuinely high-yield point: catatonia is coded independently of the underlying disorder.

The threshold. ICD-11 requires **three or more** symptoms of decreased, increased or abnormal psychomotor activity, drawn from any combination of three clusters, typically lasting **at least several hours** (ICD-11 CDDR 2024). DSM-5-TR cross-maps closely, requiring **three or more** of

twelve psychomotor features (DSM-5-TR 2022). ICD-10 flagged the older habit of counting catatonia as a schizophrenia subtype, which both current systems abandon.

three or more	3 clusters	6A40
SIGNS FOR ICD-11 / DSM-5-TR CATATONIA	DECREASED, INCREASED, ABNORMAL PSYCHOMOTOR	ICD-11 CODE, ASSOCIATED WITH ANOTHER DISORDER

13.3 The motor and volitional signs

The core cluster. These are the hypokinetic and postural signs that dominate the classical stuporous picture.

Stupor

Immobility with no or markedly reduced psychomotor activity, minimally responsive to external stimuli, yet the patient is often aware of the surroundings (Fish, in Companion 2010).

Mutism

No or very little verbal response; speech hushed to unintelligibility. Do not count if due to a nervous-system disease or a speech/language disorder (ICD-11 CDDR 2024).

Negativism

Motiveless resistance to instruction; the patient does the reverse of what is asked, holding the breath when told to breathe deeply, resisting being stood up then refusing to lie down (Sims 2015).

Posturing / catalepsy

Posturing: spontaneous active maintenance of a posture against gravity. Catalepsy: passive induction of a posture by the examiner that is then held against gravity (ICD-11 CDDR 2024).

Waxy flexibility (cerea flexibilitas)

Slight, even, plastic resistance to positioning, "like bending a warm candle wax," the limb then held in the new position (ICD-11 CDDR 2024).

Rigidity

Resistance from increased tone, from mild to severe "lead-pipe" rigidity; requires examination (ICD-11 CDDR 2024).

Staring

Fixed gaze with decreased blinking, often with widely opened eyes (ICD-11 CDDR 2024).

Waxy flexibility is the classic teaching sign of catatonia: the examiner moulds the limb and it stays. It is distinct from *catalepsy* (posture held without the plastic resistance) and from lead-pipe *rigidity* (uniform resistance with no "give").

> **HOLD THIS**
> Waxy flexibility (cerea flexibilitas) is the classic catatonic sign: mould the limb like warm wax and it holds the new position against gravity.

13.4 The echo phenomena, and the disorders of will and obedience

Echo phenomena. Echolalia is the automatic mirroring of the examiner's speech; echopraxia is the mirroring of the examiner's movements. ICD-11 groups them as "echophenomena" under abnormal psychomotor activity (ICD-11 CDDR 2024).

Disorders of will and obedience. These paired opposites are the volitional heart of catatonia and are pure elicited signs.

Automatic obedience

Every instruction is carried out regardless of consequence. Kraepelin's demonstration was to ask the patient to put out the tongue and prick it with a pin; the patient kept protruding it despite the repeated prick.

Mitgehen

Extreme cooperation: the limb moves in the direction of the examiner's slightest pressure ("anglepoise-lamp" sign), then returns, despite instruction to resist (Companion 2010).

Ambitendency

The patient appears "motorically stuck," alternating between starting and stopping a movement in indecisive, hesitant fashion (ICD-11 CDDR 2024).

Gegenhalten (opposition)

The opposite of mitgehen: springy resistance to passive movement that increases in proportion to the force the examiner applies (Sims 2015; Companion 2010).

The clinical elegance is the pairing: mitgehen is over-compliance with passive movement, gegenhalten is motiveless counter-resistance to it, and both can appear in the same patient.

13.5 Mannerisms, stereotypies, grimacing and verbigeration

The abnormal-activity cluster. These are the "odd but active" signs.

Mannerisms

Odd, purposeful, goal-directed acts executed in an idiosyncratic, exaggerated-caricature way (e.g. a bizarre style of washing or dressing) (ICD-11 CDDR 2024; Companion 2010).

Stereotypies

Repetitive, non-goal-directed motor activity (finger-play, patting or rubbing the self). The abnormality is not in the action but in its frequency (ICD-11 CDDR 2024).

Grimacing

Odd or distorted facial expressions inappropriate to the situation. The exaggerated forward-thrusting of the lips (Schnauzkrampf, snout spasm) is a related facial sign that the AIIMS Clinical Methods text files as a facial stereotypy (ICD-11 CDDR 2024; AIIMS 2024).

Verbigeration

Continuous, directionless repetition of words, phrases or sentences; the senseless repetition of sounds or words (ICD-11 CDDR 2024; Shorter Oxford 2018).

In practice mannerisms and stereotypies shade into one another; both are motor behaviour rendered abnormal by repetitiveness, purposelessness or stiltedness. Mannerisms retain a goal (a distorted *way* of doing a normal act); stereotypies have no goal at all.

13.6 The bedside examination: catatonia is elicited

Observe, then elicit. A structured examination splits the signs into those you simply observe (staring, mutism, grimacing, stupor, excitement, stereotypy, mannerism, verbigeration, spontaneous echo) and those you must actively draw out (rigidity, negativism, posturing, waxy

flexibility, catalepsy, automatic obedience, mitgehen, mitmachen, ambitendency, echo phenomena) (AIIMS 2024). The whole discipline of the topic is that most catatonic signs live in the second column.

How to elicit the key signs.

- **Posturing and waxy flexibility.** Passively move the neck, jaw, shoulders, elbows, fingers and lower limbs; feel for the even, plastic "candle-wax" resistance and watch whether the induced posture is held against gravity (catalepsy). Look for the "psychological pillow," where the head is held elevated as if on a pillow (AIIMS 2024).
- **Negativism and gegenhalten.** Instruct simple actions and note reversal; then move a limb passively and feel for springy resistance that grows to match your force (AIIMS 2024).
- **Automatic obedience and mitgehen.** Instruct the patient to resist your manipulation; if the limb nonetheless rises with the slightest upward pressure of your finger and returns when released, that is mitgehen. The pin-prick tongue test is the historical automatic-obedience manoeuvre; instructing the patient to "resist" is the humane modern substitute (AIIMS 2024).
- **Echo phenomena.** Perform a gesture or a phrase and watch for spontaneous mirroring (echopraxia, echolalia).

WORKED EXAMPLE

A mute, immobile young man on the ward is written up as "uncooperative." You lift his arm; it offers the even plastic resistance of warm wax and stays raised (waxy flexibility, catalepsy). You press a finger under his forearm having told him to keep still; the arm floats upward and returns when you let go (mitgehen). You now have two elicited signs, staring and mutism observed: four signs, well over the three-sign threshold. This is catatonia, not obstinacy.

13.7 The Bush-Francis rating scale: domains and screen

The standard instrument. The Bush-Francis Catatonia Rating Scale (BFCRS) is the preferred scale for routine use for its validity, reliability and ease of administration (Bush 1996; AIIMS 2024). It has 23 items rated 0 to 3 for severity, and the presence or absence of the first 14 items forms the standardised *screening* examination (the Bush-Francis Catatonia Screening Instrument, BFCSI) (Bush 1996; AIIMS 2024).

The screen. By convention, **two or more** of the first 14 signs identify probable catatonia and warrant the full 23-item rating and a lorazepam challenge (a widely-applied screening cutoff; the standardised instrument is Bush 1996). The 14 screening items span the same clusters covered above: the standardised examination proceeds observe-then-elicit, exactly as in 13.6. FIG 10.7 maps the catatonic signs onto the Bush-Francis domains.

23 items	first 14	two or more
FULL BFCRS, SCORED 0 TO 3	SCREENING INSTRUMENT (BFCSI)	SCREEN-POSITIVE THRESHOLD (BUSH 1996)

Confirmation, cross-referenced. Once catatonia is identified, the intravenous lorazepam challenge helps confirm it and predicts treatment response: 1 to 2 mg IV over two minutes, with reassessment at 5 minutes and a favourable response usually within 10 minutes (AIIMS 2024). The therapeutics of benzodiazepines and ECT are disorder-specific pointers here; ECT technique points to the ECT and neurostimulation notes.

TRAP **Do not read hypokinetic catatonia as "just severe depression."** A mute, staring, immobile, food-refusing patient is easily filed as retarded depression or an "uncooperative" patient; examine for the elicited signs before you settle for either.

COMMON TRAP

Stuporous (hypokinetic) catatonia hides in plain sight. Because the patient looks passively unwell, teams label it depression, negativistic personality, or non-cooperation and never lay hands on the limbs. Several catatonic signs (waxy flexibility, gegenhalten, mitgehen, catalepsy) exist only when elicited, so a purely observational assessment will systematically miss them.

INDIA

Catatonia remains common in Indian inpatient practice and is a mainstay indication for ECT, which is widely available in government and teaching hospitals; the AIIMS Clinical Methods text codifies the observe-and-elicit examination taught in Indian residencies (AIIMS 2024). Benzodiazepine (lorazepam) first-line and ECT for lorazepam-non-response are the standard Indian pathway, with the lorazepam challenge used at the bedside to confirm.

PEARL

Malignant catatonia (hyperthermia, autonomic instability, rigidity, raised creatine phosphokinase) is clinically near-identical to neuroleptic malignant syndrome and shares management logic; NMS as an entity is owned by the Schizophrenia: management, antipsychotics and adverse effects notes and appears here only as this differential. If antipsychotics were recently given, you cannot separate the two on signs alone: stop the antipsychotic, support in intensive care, and treat as malignant catatonia.

MNEMONIC

WRENCHES-M: Waxy flexibility, Rigidity, Echophenomena, Negativism, Catalepsy/posturing, Automatic obedience/Mitgehen, Stupor/mutism, Stereotypy/mannerism

A rough hook for the sign families across the three ICD-11 clusters; the "M" tail flags mitgehen and mannerisms as the easily forgotten elicited/abnormal-activity signs.

GOOD TO REMEMBER

- **Catatonia:** transdiagnostic psychomotor syndrome; ICD-11 needs three or more signs from decreased, increased and abnormal-activity clusters; coded free-standing (6A40 associated with another disorder).
- **Kahlbaum:** first described catatonia (the "tension insanity") in 1874; hold the eponym and the year.
- **Waxy flexibility (cerea flexibilitas):** even plastic "warm-wax" resistance with the limb held in the new position; the classic catatonic sign, an elicited sign.
- **Catalepsy vs rigidity:** catalepsy is a passively induced posture held against gravity; rigidity is uniform increased tone ("lead-pipe"), no plastic give; waxy flexibility sits between as plastic resistance.
- **Negativism:** motiveless doing-the-reverse of instruction; discriminator from apathy is the active opposition.
- **Mitgehen vs gegenhalten:** mitgehen is anglepoise-lamp over-compliance to slight passive pressure; gegenhalten is force-matched springy counter-resistance; the elicited opposites of obedience/opposition.
- **Echophenomena:** echolalia (mirrors speech), echopraxia (mirrors movement); the discriminator is automatic, uninstructed mimicry.
- **Verbigeration:** senseless directionless repetition of words or phrases; a speech-level stereotypy.
- **Bush-Francis (BFCRS):** 23 items scored 0 to 3; first 14 form the screen; two or more screen-positive signs identify probable catatonia (Bush 1996).
- **Lorazepam challenge:** 1 to 2 mg IV over two minutes, reassess at 5 minutes, favourable response usually within 10 minutes; confirms and predicts response (AIIMS 2024).

14 · Aetiology and the transdiagnostic placement of catatonia

Catatonia is the syndrome that most reliably catches the resident out, because its causes are wide and its nosology has just moved under the examiner's feet. The old teaching, that catatonia is a subtype of schizophrenia, is wrong on both counts: the commonest psychiatric cause is a mood disorder, not schizophrenia, and a large minority of cases are driven by a neurological or medical process that will be missed unless it is actively sought. This is a clinical-disorder topic, so it teaches the two things a viva tests: the *causes* (which three groups, and which is commonest), and the *discrimination* (why an organic cause must be excluded, and where ICD-11 now places the syndrome). The descriptive definitions of the individual catatonic signs (stupor, mutism, negativism, waxy flexibility, echophenomena) are owned by the Psychometry, Assessment and Descriptive Psychopathology notes and are not re-derived here; the schizophrenia disorder itself is owned by the Schizophrenia: aetiology, phenomenology, classification and course notes.

How to use this page. Hold three cause groups (**psychiatric**, **neurological**, **medical**), then one principle (**organic catatonia** must always be excluded in new or atypical presentations), then one nosological shift (**ICD-11** codes catatonia as a **transdiagnostic** syndrome that many conditions can share, not a schizophrenia subtype). The single fact most often swapped is which psychiatric disorder is the commonest cause: it is the *mood* disorders, not schizophrenia (DSM-5-TR 2022).

14.1 The aetiology of catatonia in three groups

Causes are widespread and cut across the whole of medicine. The **aetiology of catatonia** is best carried as three groups (Kaplan & Sadock 2024, ICD-11 CDDR). The first is **psychiatric**: the

mood disorders (both depressive and bipolar episodes) and schizophrenia and other primary psychotic disorders, with neurodevelopmental disorders (especially autism spectrum disorder) a third psychiatric home. The crucial exam point is that, taken together, the mood disorders are a *commoner psychiatric cause than schizophrenia*: catatonia occurs in up to **35%** of individuals with schizophrenia, but the majority of catatonia cases arise in depressive or bipolar disorders (DSM-5-TR 2022). The second group is a **neurological cause**: encephalitis, in particular anti-NMDA-receptor encephalitis, seizures and the postictal state, stroke (cerebrovascular disease), and space-occupying lesions (neoplasms), alongside head trauma. The third group is **medical causes**: metabolic and electrolyte derangement (diabetic ketoacidosis, hypercalcaemia, hyponatraemia, hepatic encephalopathy, homocystinuria), infection (typhoid, HIV, infectious mononucleosis), autoimmune disease (systemic lupus erythematosus, Hashimoto/autoimmune encephalopathy, PANDAS), and drug-related or withdrawal states (antipsychotics, benzodiazepines, steroids, disulfiram, ciprofloxacin; and intoxication with or withdrawal from PCP, cannabis, cocaine, MDMA, LSD or opioids) (ICD-11 CDDR).

GROUP	REPRESENTATIVE CAUSES	THE ONE POINT TO HOLD
Psychiatric	Mood disorders (depressive and bipolar); schizophrenia and other primary psychotic disorders; autism spectrum disorder	**The *mood disorders are the commonest psychiatric cause*, not schizophrenia; catatonia in up to 35% of schizophrenia but most cases are mood**
Neurological cause	Encephalitis (esp. anti-NMDA-receptor encephalitis); seizures and the postictal state; stroke; space-occupying lesions; head trauma	**Anti-NMDA-receptor encephalitis is the archetypal treatable neurological cause and classically presents with psychiatric features then catatonia**
Medical causes	Metabolic and electrolyte derangement; infection; autoimmune disease; drug-related or withdrawal states	**Any of these produces catatonia indistinguishable from the psychiatric form; screening bloods, imaging and (if encephalitis is suspected) lumbar puncture are how they are found**

The three cause groups of catatonia; the trap is to stop at the psychiatric group and, within it, to assume schizophrenia rather than a mood disorder (Kaplan & Sadock 2024, DSM-5-TR 2022, ICD-11 CDDR).

RULE **Always exclude a medical or neurological cause of new catatonia, and remember the mood disorders are the commonest psychiatric cause.** New or atypical catatonia is organic until proven otherwise; among psychiatric causes, think mood first, not schizophrenia.

TRAP **Assuming catatonia means schizophrenia.** Catatonic signs are nonspecific: the commonest psychiatric cause is a mood disorder, and a substantial share of cases are neurological or medical; treating catatonia as pathognomonic of schizophrenia misses both the mood disorder and the organic cause.

14.2 The organic catatonia principle

Exclude a physical cause before you land on a psychiatric one. The **organic catatonia** principle is the governing safety rule of the syndrome: a medical or neurological cause must *always* be excluded, especially in new or atypical catatonia, because so many treatable physical illnesses reproduce it exactly and because an untreated organic driver can be lethal (Kaplan & Sadock 2024). Several pointers raise the prior for an organic cause: a first-ever episode, an atypical picture, older age (secondary catatonia syndrome becomes more likely after 40 and rises sharply after 65), very early onset (before 20, which associates with nervous-system disease or a neurodevelopmental disorder), co-occurring delirium or fluctuating consciousness, focal neurological signs, or autonomic instability. Catatonia itself has *no* specific laboratory, imaging or EEG signature, so the workup is aimed at the underlying cause and at complications: complete blood count, a complete metabolic panel, serum creatine kinase (markedly raised in malignant catatonia and NMS, and a warning of rhabdomyolysis), neuroimaging for a lesion, EEG (diffuse slowing points to delirium or encephalitis rather than a primary psychiatric cause), and, where encephalitis is suspected, a lumbar puncture with an autoimmune-encephalitis panel (Kaplan & Sadock 2024). If the entire workup is unremarkable, a psychiatric cause becomes the likely explanation, but only by exclusion.

WORKED EXAMPLE

A previously well 24-year-old woman is admitted with two weeks of mutism, negativism and waxy flexibility, preceded by headache, low-grade fever and a few days of odd, fearful behaviour. She meets the criteria for catatonia. Because this is a *first, atypical* episode in a young person with a prodrome suggesting encephalitis, the organic catatonia principle applies: alongside a lorazepam challenge for the catatonia, she needs neuroimaging and a lumbar puncture with an autoimmune-encephalitis panel. Anti-NMDA-receptor encephalitis is the target diagnosis (it classically opens with psychiatric symptoms and catatonia before seizures and dysautonomia appear), and immunotherapy, not an antipsychotic, is the definitive treatment. Reaching for schizophrenia here would be the cardinal error.

14.3 The ICD-11 transdiagnostic placement

Catatonia is now a syndrome of its own, not a schizophrenia subtype. The important nosological shift is that **ICD-11** treats catatonia as a **transdiagnostic** syndrome of primarily psychomotor disturbance that **catatonia can accompany** many conditions (ICD-11 CDDR). It is given its own grouping with four categories rather than being buried as a form of schizophrenia: 6A40 catatonia associated with another mental disorder (the associated disorder, whether a mood disorder, schizophrenia or another primary psychotic disorder, or autism spectrum disorder, is coded separately), 6A41 catatonia induced by substances or medications, 6E69 secondary catatonia syndrome (the direct pathophysiological consequence of a medical or neurological condition), and 6A4Z catatonia, unspecified. So the syndrome sits above any single diagnosis: it is defined once (three or more psychomotor symptoms from decreased, increased or abnormal activity) and then attributed to whatever underlies it. This is the important shift from the older ICD-10 view, in which catatonic schizophrenia (F20.2) was a named schizophrenia subtype and

the organic form (F06.1, organic catatonic disorder, which maps onto ICD-11's 6E69) sat apart; ICD-11 dissolves the subtype and makes the transdiagnostic syndrome primary (ICD-11 CDDR).

PEARL

The examiner's favourite one-liner is the direction of the shift. ICD-10 had a *catatonic subtype of schizophrenia* (F20.2); ICD-11 abolishes the schizophrenia subtypes and codes catatonia as a standalone transdiagnostic syndrome (6A40 / 6A41 / 6E69 / 6A4Z) that can accompany many disorders. If asked "where does catatonia live in ICD-11?", the answer is "its own grouping, coded to whatever it accompanies", not "under schizophrenia".

14.4 DSM-5-TR: a specifier and an associated syndrome, not a subtype

DSM-5-TR reaches the same destination by a different route. DSM-5 similarly stopped treating catatonia as a subtype of schizophrenia and instead handles it three ways: as a *specifier* ("with catatonia") that can be appended to a neurodevelopmental, psychotic, bipolar or depressive disorder; as **catatonia associated with another mental disorder** (the catatonia specifier, coded F06.1) when it is the focus; and as two standalone entities, *catatonic disorder due to another medical condition* and *unspecified catatonia* (DSM-5-TR 2022). Catatonia is defined by three or more of twelve psychomotor features. DSM-5-TR is explicit that although catatonia has historically been associated with schizophrenia, the symptoms are *nonspecific* and occur across mood, neurodevelopmental and medical conditions, and that "the majority of catatonia cases involve individuals with depressive or bipolar disorders" (DSM-5-TR 2022). So both major systems now converge: catatonia is a transdiagnostic syndrome, commonest in mood disorders, and never assumed to mean schizophrenia.

SYSTEM	HOW CATATONIA IS PLACED	THE DISCRIMINATING POINT
ICD-10 (older view)	Catatonic schizophrenia F20.2 as a named subtype; organic catatonic disorder F06.1 separate	**Catatonia partly owned *within* schizophrenia as a subtype: the view now superseded**
ICD-11	Own grouping: 6A40 associated with another mental disorder, 6A41 substance/medication-induced, 6E69 secondary catatonia syndrome, 6A4Z unspecified	**A transdiagnostic syndrome coded to whatever it accompanies; schizophrenia subtypes abolished**
DSM-5-TR	"With catatonia" specifier; catatonia associated with another mental disorder (F06.1); catatonic disorder due to another medical condition; unspecified catatonia	**A specifier or an associated syndrome, *not* a subtype; 3 of 12 features; explicitly nonspecific**

The nosological placement of catatonia across systems: the shared modern message is transdiagnostic, and the ICD-10 catatonic-schizophrenia subtype is the view being left behind (ICD-11 CDDR, DSM-5-TR 2022).

14.5 Why the placement changed: the aetiological and neurobiological logic

The nosology followed the biology and the epidemiology. Two lines of evidence made the schizophrenia subtype untenable. The first is epidemiological: once catatonia was rated

systematically (with scales such as the Bush-Francis Catatonia Rating Scale, Bush 1996), it was found across mood, neurodevelopmental, medical and neurological conditions, with mood disorders supplying more cases than schizophrenia (a clinical-sample meta-analysis put the pooled prevalence of catatonia at about **9%**) (Bush 1996, DSM-5-TR 2022). The second is neurobiological: catatonic features arise from disruption of cortical-subcortical (basal-ganglia-thalamocortical) circuits regulating cortical function, producing reduced dopaminergic and GABA-A activity and upregulation of NMDA activity, and this final common pathway can be reached from many upstream causes (Kaplan & Sadock 2024). The same model explains the diagnostic-and-therapeutic lorazepam challenge (a GABA-A agonist disinhibits striatal dopamine and reverses the state) and why glutamate antagonists such as amantadine help in refractory cases. A shared circuit-level endpoint entered from many directions is exactly a transdiagnostic syndrome, which is what the classifications now encode.

up to 35%	~9%	3 of 12
OF SCHIZOPHRENIA SHOWS CATATONIA	POOLED PREVALENCE IN CLINICAL SAMPLES	FEATURES REQUIRED (DSM-5-TR)

14.6 The one differential the placement forces: malignant catatonia versus NMS

The organic-exclusion rule has one high-stakes special case. When catatonia is accompanied by autonomic instability and hyperthermia it becomes malignant catatonia, a life-threatening state that carried a **75% to 100%** mortality before modern treatment and around **10%** with benzodiazepines and ECT (Kaplan & Sadock 2024). Its near-twin is neuroleptic malignant syndrome, which shares rigidity, hyperthermia, dysautonomia and a raised creatine kinase; the practical distinction is the drug history (NMS follows dopamine-antagonist exposure or dopamine-agonist withdrawal), and the two are increasingly regarded as variants of the same catatonic spectrum. NMS as an entity is owned by the Schizophrenia: management, antipsychotics and adverse effects notes and is taught in full there; it appears here only as the differential that malignant catatonia forces. The management principle is that antipsychotics can worsen catatonia and precipitate the malignant form, so in a catatonic patient they are used cautiously and covered by lorazepam; the ECT technique itself points to the ECT and neurostimulation notes.

TRAP **Mistaking malignant catatonia for NMS (or giving a catatonic patient an antipsychotic).** The two overlap almost completely; the drug history separates them, and reaching for an antipsychotic in catatonia can tip a patient into the malignant, potentially fatal form.

INDIA

Catatonia is a familiar presentation in Indian practice, where a substantial share is mood-related and organic causes (post-infective, metabolic, autoimmune encephalitis) are actively sought given the local infectious and nutritional burden; the ICD-11 (and long-familiar ICD-10) framework is standard in Indian teaching texts. A practical advantage is that ECT, the definitive treatment for severe and malignant catatonia, is comparatively well established and available across Indian psychiatric units, and lorazepam is cheap and generic, so the diagnostic-therapeutic lorazepam challenge is readily performed at the bedside. The system-wide rule that no diagnosis is named to the patient sits comfortably here: the family is engaged around the psychomotor state and its urgency rather than a label. Where a brand is needed, lead with the Indian generic and verify locally rather than inventing one.

GOOD TO REMEMBER

- **Aetiology of catatonia (three groups):** psychiatric (mood disorders and schizophrenia/primary psychotic disorders, plus autism), neurological (encephalitis including anti-NMDA-receptor encephalitis, seizures/postictal state, stroke, space-occupying lesions) and medical (metabolic/electrolyte, infective, autoimmune, drug/withdrawal); the number to hold is that the mood disorders are the commonest psychiatric cause, with catatonia in up to 35% of schizophrenia but most cases being mood.
- **Organic catatonia principle:** a medical or neurological cause must always be excluded, especially in new or atypical catatonia; the discriminator prompting a physical workup is a first, atypical, older-onset or delirium-associated episode; the workup to hold is CBC, CMP, creatine kinase, neuroimaging, EEG and (if encephalitis suspected) lumbar puncture.
- **Anti-NMDA-receptor encephalitis:** the archetypal treatable neurological cause; the discriminator is a young patient with a psychiatric-then-catatonic prodrome progressing to seizures and dysautonomia; the point to hold is that CSF autoimmune-encephalitis testing and immunotherapy, not an antipsychotic, are definitive.
- **ICD-11 transdiagnostic placement:** catatonia is its own grouping, coded to whatever it accompanies; the discriminator from the old view is that the schizophrenia subtype (ICD-10 F20.2) is abolished; the codes to hold are 6A40 (associated with another mental disorder), 6A41 (substance/medication-induced), 6E69 (secondary catatonia syndrome) and 6A4Z (unspecified).
- **DSM-5-TR placement:** a "with catatonia" specifier, catatonia associated with another mental disorder (F06.1), catatonic disorder due to another medical condition and unspecified catatonia; the discriminator is that it is a specifier or associated syndrome, not a subtype; the number to hold is 3 of 12 psychomotor features.
- **Malignant catatonia:** catatonia plus hyperthermia and autonomic instability; the discriminator from NMS is the drug history (NMS follows dopamine antagonism); the number to hold is the mortality, 75% to 100% untreated, about 10% with benzodiazepines and ECT.

HOLD THIS

Catatonia is a transdiagnostic psychomotor syndrome, not a schizophrenia subtype: its commonest psychiatric cause is a mood disorder (catatonia occurs in up to 35% of schizophrenia but most cases are mood), it is frequently neurological or medical (encephalitis, especially anti-NMDA-receptor encephalitis, seizures, stroke, metabolic, autoimmune, drug or withdrawal), so a medical or neurological cause must always be excluded in new or atypical catatonia; ICD-11 codes it in its own grouping (6A40 / 6A41 / 6E69 / 6A4Z) that catatonia can accompany many conditions, and DSM-5-TR treats it as a specifier or associated syndrome rather than a subtype.

15 · Catatonia management: the lorazepam challenge and benzodiazepines

Why this matters. Catatonia is the one psychiatric syndrome where a single bedside manoeuvre is at once the diagnostic test and the first dose of treatment. The **lorazepam challenge** lets you confirm the syndrome and start reversing it in the same act, and the examiner rewards the resident who states the drug, the route, the dose and the response window, and who knows why a high-potency antipsychotic is the wrong reflex. The raw descriptive signs of catatonia (stupor, mutism, negativism, waxy flexibility, echophenomena) are set out in the Psychometry, Assessment and Descriptive Psychopathology notes and are not re-derived here; this topic teaches what you *do* once the syndrome is recognised.

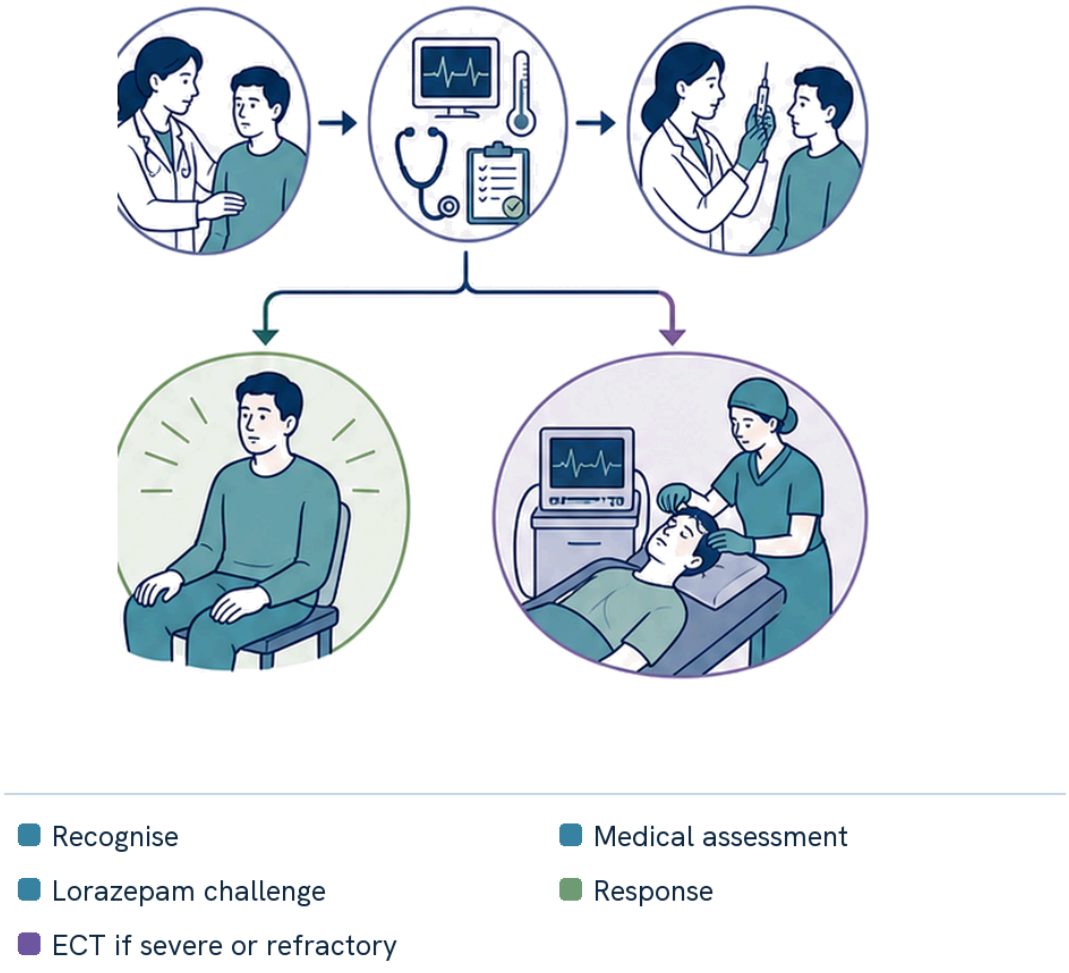


Fig 10.11 Catatonia management begins with recognition and urgent medical assessment, followed by a benzodiazepine challenge; severe, malignant or non-responsive illness requires prompt electroconvulsive therapy.

The governing principle is simple and heavily tested: benzodiazepines, opened by the lorazepam challenge and then titrated, are first-line for catatonia regardless of the underlying cause, and antipsychotics are the classic trap. Two facts anchor the topic: a **benzodiazepine** reduces catatonic symptoms in roughly 70% to 80% of patients (Kaplan & Sadock 2024), and the

antipsychotic reflex can worsen catatonia or tip it into malignant catatonia. Supportive care and treatment of the cause run alongside from the outset; ECT is the definitive treatment where the drug fails or the picture is malignant, with its technique cross-referenced to the ECT and neurostimulation notes.

15.1 The lorazepam challenge: one act, two purposes

The lorazepam challenge is a test dose of **lorazepam** given to a patient with suspected catatonia, watched for a rapid reduction in catatonic features. It is diagnostic and therapeutic in the same stroke: a positive response (increased interaction, reduction of catatonic features) is confirmatory of catatonia and is simultaneously the first therapeutic dose (Kaplan & Sadock 2024). The standard adult dose is **2 mg**, commonly quoted as **1 to 2 mg** given intravenously or intramuscularly; IV is preferred for its quick onset and because a stuporous patient may be unable to swallow the oral formulation, with IM or sublingual used when IV access is unavailable (Kaplan & Sadock 2024). Lower doses suit paediatric and frail older adults, but 2 mg is recommended for most adults to avoid an equivocal result.

The **response** is often dramatic and quick: a robust "Lazarus" response may be seen within 30 minutes of a 2 mg dose, though some patients need up to 120 minutes; the AIIMS bedside protocol gives 1 to 2 mg IV over two minutes and reassesses at 5 to 10 minutes (Kaplan & Sadock 2024, Clinical Methods in Psychiatry AIIMS 2024). Interpretation has a trap of its own: a positive response confirms catatonia, but a negative response (sedation, or no change) does *not* rule it out, so if suspicion stays high a further dose is given and the patient reassessed. Monitor the change with a standardised scale rather than by impression.

RULE **The lorazepam challenge is diagnosis and treatment in one.** A test dose of lorazepam (2 mg, IV preferred) that produces a marked partial or full response both confirms catatonia and begins reversing it.

TRAP **Reading a negative challenge as excluding catatonia.** A positive response confirms the syndrome; sedation or no change does not rule it out. If clinical suspicion remains, repeat the dose rather than abandon the diagnosis.

15.2 Benzodiazepines as first-line: titration after the challenge

Once the challenge is positive, **lorazepam** is the first-line treatment irrespective of aetiology, carrying an efficacy of **70% to 80%** for symptom reduction (Kaplan & Sadock 2024). The drug is then scheduled and titrated upward, often to higher-than-usual doses. A typical regimen schedules lorazepam (for example 2 mg every 6 hours) for at least the first 24 to 48 hours, moving to a titrated total daily dose that controls symptoms without excessive sedation; some patients need a total of 30 mg or more per day (Kaplan & Sadock 2024). Nursing must give scheduled doses even when the patient appears to sleep, because that "sleep" may be stupor returning as the last dose wears off. Once symptoms have clearly improved, taper slowly (a 10% to 25% reduction per day).

Second-line and adjunctive agents exist but are not the answer to hold first: zolpidem 5 to 10 mg, GABA-active antiepileptics (valproate, topiramate, carbamazepine), and NMDA-receptor antagonists (amantadine 100 to 600 mg/day, memantine 10 to 20 mg/day) are used as adjuncts to lorazepam rather than as monotherapy, chiefly in lorazepam-refractory cases (Kaplan & Sadock 2024).

RULE **Benzodiazepines, not antipsychotics, are first-line for catatonia.** Lorazepam challenge, then titration (often to higher-than-usual doses), reverses roughly 70% to 80% of cases whatever the cause.

15.3 Supportive care and treating the cause

Catatonia is a medical emergency of immobility, so supportive care runs in parallel from the outset and is examinable in its own right. The stuporous, immobile patient is at risk of dehydration, malnutrition, aspiration pneumonia, pressure sores, contractures, urinary retention, rhabdomyolysis with renal failure, and venous thromboembolism. Management therefore includes hydration and nutrition (IV fluids, nasogastric or PEG feeding), VTE prophylaxis (anticoagulation), pressure care and mobilisation, aspiration precautions, urinary catheterisation, and monitoring of vitals and fluid balance (Kaplan & Sadock 2024, Clinical Methods AIIMS 2024). In parallel, the underlying cause is investigated and treated: catatonia is transdiagnostic, so a medical, neurological or substance cause must be actively excluded and managed, and treatment must not be delayed merely because the cause has not yet been found. Serum creatine kinase is tracked because marked elevation flags malignant catatonia or neuroleptic malignant syndrome and predicts renal risk.

WORKED EXAMPLE

A young man with schizophrenia is mute, immobile and holds imposed postures; he is not eating or drinking. You give 2 mg lorazepam IV over two minutes and at 8 minutes he begins to speak and move: the challenge is positive, confirming catatonia and starting treatment. You schedule lorazepam 2 mg every 6 hours, start IV fluids, VTE prophylaxis and pressure care, send CK and a metabolic screen, and arrange ECT cover in case of incomplete response. You do *not* reach for haloperidol to treat his psychosis while he is catatonic.

15.4 The antipsychotic caution: precipitating malignant catatonia

Antipsychotics were historically used to treat catatonia, but in many cases this worsened symptoms and increased mortality (Kaplan & Sadock 2024). The mechanistic reason fits the model: catatonia involves reduced GABA-A activity and a resulting hypodopaminergic state, so a dopamine-blocking drug can deepen the very dysfunction that drives the syndrome. The clinical danger is that a high-potency antipsychotic given to a catatonic patient can precipitate malignant catatonia or neuroleptic malignant syndrome (NMS), both life-threatening. Where the underlying psychosis genuinely needs antipsychotic cover, it should be given alongside lorazepam, and a second-generation agent, especially one with partial D2-agonist activity such as aripiprazole, is preferred over a high-potency D2 blocker (Kaplan & Sadock 2024). The drug detail and NMS as

an entity are owned by the Schizophrenia: management, antipsychotics and adverse effects notes; here NMS appears only as the malignant-catatonia differential.

TRAP **Giving a high-potency antipsychotic to a catatonic patient.** It can fail to help, worsen the catatonia, and precipitate malignant catatonia or neuroleptic malignant syndrome. Treat the catatonia with a benzodiazepine first; if antipsychotic cover is needed, add it to lorazepam and prefer a partial D2 agonist.

15.5 Malignant catatonia versus NMS, and where ECT comes in

Malignant catatonia (the older terms lethal catatonia and malignant catatonia are used interchangeably) is catatonic stupor accompanied by hyperthermia and autonomic instability, a potentially fatal state that on presentation may be clinically and biochemically indistinguishable from neuroleptic malignant syndrome, which has led to the view that NMS is best regarded as a drug-induced variant of malignant catatonia (Maudsley Prescribing Guidelines 2021, DSM-5-TR 2022). The practical consequence for management is that antipsychotics must be stopped and benzodiazepines and ECT brought forward urgently. **ECT** is the definitive treatment: it is the gold-standard for catatonia with about 90% efficacy, has no absolute contraindications, and is the treatment of choice when the patient is lorazepam-refractory or has progressed to malignant catatonia (Kaplan & Sadock 2024). Because malignant catatonia can evolve fast, ECT should be considered and consent sought early rather than after the drug has clearly failed. The ECT technique itself is set out in the ECT and neurostimulation notes and is not taught here.

FEATURE	MALIGNANT CATATONIA	NEUROLEPTIC MALIGNANT SYNDROME
Nature	Severe catatonia with hyperthermia and autonomic instability	**Antipsychotic-induced; often viewed as a drug-triggered variant of malignant catatonia**
Trigger	**Any cause of catatonia; may arise without any drug**	Onset after starting or increasing a dopamine antagonist
Core signs	Stupor, rigidity, fever, autonomic instability; raised CK	Fever, "lead-pipe" rigidity, altered mental state, autonomic instability; raised CK
The offending drug	**Antipsychotics can precipitate or worsen it: stop them**	Antipsychotic is the cause: withdraw immediately
Treatment overlap	Benzodiazepines and ECT; stop antipsychotics	**Supportive care, dantrolene/bromocriptine, benzodiazepines; ECT if refractory (see the Schizophrenia: management, antipsychotics and adverse effects notes)**

Malignant catatonia and NMS may be indistinguishable at the bedside; the discriminator is the drug history, and either way antipsychotics come off and benzodiazepines plus ECT go on. NMS as an entity is owned by the Schizophrenia: management, antipsychotics and adverse effects notes.

TRAP **Chasing the malignant-catatonia versus NMS label instead of acting.** The two overlap so closely they may be one spectrum; do not delay stopping the antipsychotic and starting benzodiazepines and ECT while you argue the name.

15.6 ICD-11 and the transdiagnostic frame

The nosology carries a high-yield point that shapes management. ICD-11 treats catatonia as a separate transdiagnostic grouping of primarily psychomotor disturbance that can arise across schizophrenia and other primary psychotic disorders, mood disorders, neurodevelopmental disorders (especially autism), with substances or medications, and with medical conditions (ICD-11 CDDR). The grouping codes are 6A40 catatonia associated with another mental disorder, 6A41 catatonia induced by substances or medications, and 6E69 secondary catatonia syndrome (a medical cause), with 6A4Z unspecified. Because catatonia crosses diagnoses, the management principle is the same whatever the parent: treat the syndrome with a benzodiazepine and, where needed, ECT, while identifying and treating the cause. DSM-5-TR maps the same idea through a "with catatonia" specifier and catatonia due to another medical condition; ICD-10 lacked the clean transdiagnostic grouping and is flagged as the older frame.

INDIA

Indian practice fits the standard picture and adds two local realities. The lorazepam-based approach is the AIIMS bedside standard: 1 to 2 mg IV over two minutes, reassessed at 5 to 10 minutes, with at least 6 mg given over 24 hours if the response is partial, then scheduled IV lorazepam continued (Clinical Methods in Psychiatry AIIMS 2024). Lorazepam is widely available and inexpensive, so benzodiazepine-first is fully practicable. ECT is comparatively accessible and heavily used in Indian tertiary centres, and modified ECT (mECT) is explicitly recommended as an urgent, life-saving intervention in malignant catatonia, with consent sought as early as possible; maintenance mECT is used in some cases (Clinical Methods AIIMS 2024). The 2025 Indian Psychiatric Society schizophrenia Clinical Practice Guideline (IPS 2025, Sahoo et al., Indian J Psychiatry 2026;68:94-121) is concordant: it endorses the lorazepam challenge test as serving both a diagnostic and a therapeutic purpose in catatonia, with benzodiazepines (lorazepam or clonazepam) used short-term and their long-term use avoided because of tolerance and dependence risk. This material is largely generic; lorazepam is prescribed by generic name.

70% to 80%	2 mg	~90%
RESPOND TO A BENZODIAZEPINE (LORAZEPAM), FIRST-LINE	STANDARD ADULT LORAZEPAM CHALLENGE DOSE (1 TO 2 MG IV/IM)	ECT EFFICACY, THE DEFINITIVE TREATMENT

MNEMONIC

CHALLENGE, THEN CLIMB, NEVER BLOCK

CHALLENGE: 2 mg lorazepam confirms and starts treatment. CLIMB: titrate the benzodiazepine up, often to higher-than-usual doses, with supportive care and cause-treatment alongside. NEVER BLOCK: avoid a high-potency antipsychotic, which can precipitate malignant catatonia or NMS; ECT is the definitive step.

HOLD THIS

Catatonia is treated benzodiazepine-first: a 2 mg lorazepam challenge that produces a rapid response both confirms the diagnosis and begins treatment, then lorazepam is titrated up (roughly 70% to 80% respond); antipsychotics are the trap because they can precipitate malignant catatonia or NMS, and ECT is the definitive treatment.

GOOD TO REMEMBER

- **Lorazepam challenge:** a test dose of lorazepam, **2 mg** (1 to 2 mg IV or IM), watched for a rapid partial or full response that both confirms catatonia and starts treatment; a negative response does not exclude catatonia; response often within 30 minutes ("Lazarus" response).
- **Benzodiazepine, first-line:** lorazepam titrated up after a positive challenge, often to higher-than-usual doses (up to 30 mg/day or more); efficacy for symptom reduction is **70% to 80%** (Kaplan & Sadock 2024).
- **Antipsychotic caution:** may not help and can worsen catatonia or precipitate malignant catatonia or NMS; if antipsychotic cover is needed, add it to lorazepam and prefer a partial D2 agonist (aripiprazole).
- **Malignant catatonia:** catatonic stupor with hyperthermia and autonomic instability, potentially fatal; may be indistinguishable from NMS (which is viewed as a drug-induced variant); stop antipsychotics, give benzodiazepines and urgent ECT.
- **ECT:** the definitive, gold-standard treatment, about **90%** efficacy, for lorazepam-refractory or malignant catatonia; technique in the ECT and neurostimulation notes.
- **Bush-Francis Catatonia Rating Scale:** the 23-item scale (Bush 1996) used to identify and monitor catatonic signs and to track response to the challenge and titration.
- **ICD-11 placement:** catatonia is a separate transdiagnostic grouping, 6A40 (with another mental disorder), 6A41 (substance/medication-induced), 6E69 (secondary), so the management principle holds across every parent diagnosis.

16 · Malignant catatonia and the differential from NMS

Why this matters. This is the emergency at the far end of the catatonia spectrum and the closer of the schizophrenia-spectrum block: an untreated catatonia that tips into fever, autonomic storm and rigidity is a life-threatening state with a high mortality if it is missed. The examiner's favourite pivot here is the differential from neuroleptic malignant syndrome, because the two are so alike that many authors treat them as one entity, and the resident who can say what leans the picture one way or the other, and who knows that the first move is the same for both, scores. The raw descriptive catatonic signs (stupor, mutism, negativism, waxy flexibility) are set out in the Psychometry, Assessment and Descriptive Psychopathology notes and are not re-derived here.

Two things carry the topic. First, malignant catatonia is a diagnosis of the whole picture, not of a single sign: it is catatonia complicated by hyperthermia and autonomic instability, and it can grow out of an ordinary catatonia that was not treated in time. Second, the differential from NMS is more a matter of leaning than of a clean line, and the safe reflex is identical whichever way you lean: stop any antipsychotic, give benzodiazepines, and move to ECT early. The neuroleptic malignant syndrome as an entity is owned by the Schizophrenia: management, antipsychotics and adverse effects notes and appears here only for this differential; the ECT technique points to the ECT and neurostimulation notes.

	Malignant catatonia (lethal catatonia, Stauder 1934)	Neuroleptic malignant syndrome (owned by the management notes)
Preceding picture	catatonic signs come first	on recent antipsychotic
Drug trigger	none needed (may follow catatonia)	antipsychotic start or dose rise
Rigidity	rigidity within a catatonic picture	lead-pipe rigidity
Fever, autonomic	present (shared)	present (shared)
Creatine kinase	raised (shared)	raised, often marked (shared)
First move (same)	stop the drug, benzodiazepines, ECT	identical: stop, benzodiazepines, ECT

Almost every cross-sectional feature is shared; the preceding picture and drug history lean the label, and NMS is often held to be a drug-induced malignant catatonia.

Fig 10.12 Malignant catatonia versus neuroleptic malignant syndrome. Fever, rigidity, autonomic instability and a raised creatine kinase are shared, so the discriminators are the preceding picture (catatonic signs first, without a necessary antipsychotic trigger, lean to malignant catatonia; a recent antipsychotic with lead-pipe rigidity leans to NMS). The first management move is the same for both: stop the antipsychotic, give benzodiazepines, and move to ECT early.

16.1 The entity: catatonia plus fever, dysautonomia and rigidity

Malignant catatonia, historically named lethal catatonia, is catatonic stupor accompanied by hyperthermia and autonomic instability, a potentially fatal emergency (Maudsley Prescribing Guidelines 2021). The fatal, hyperpyrexial form of catatonia was described by Karl Heinz Stauder at the Munich University Psychiatric Hospital in 1934 (Kaplan & Sadock 2024), which is why the older literature speaks of Stauder's lethal catatonia. The defining move from ordinary to malignant catatonia is the arrival of autonomic and thermoregulatory failure: on top of the immobility, mutism, posturing and rigidity of catatonia the patient develops fever, labile blood pressure and pulse, tachycardia, sweating, and often a raised serum creatine kinase. It is important that this is not always a fresh presentation: a catatonia that was recognised late or treated inadequately can progress into malignant catatonia, so the state is partly a failure to intervene in time (Kaplan & Sadock 2024).

The **stakes** are what make it examinable as an emergency. Untreated, malignant catatonia carries a high mortality, historically very high before benzodiazepines and ECT, driven by the complications of prolonged immobility and dysautonomia: hyperthermia, dehydration and malnutrition, rhabdomyolysis with acute renal failure, aspiration pneumonia, venous thromboembolism and cardiovascular collapse (Kaplan & Sadock 2024). The practical reading is that malignant catatonia is treated as a medical emergency in parallel with, not after, the diagnostic workup, and that recognising the febrile, rigid, autonomically unstable catatonic patient early is the whole game.

RULE **Fever plus autonomic instability turns catatonia into an emergency.** Malignant catatonia is catatonic stupor complicated by hyperthermia and dysautonomia, it can evolve from an untreated catatonia, and it kills if it is not treated.

16.2 The overlap with NMS: two names, arguably one entity

The heart of the topic is the differential from neuroleptic malignant syndrome, the NMS. The problem is that the two states share almost every feature: fever, rigidity, altered consciousness, autonomic instability and a raised creatine kinase all appear in both, and malignant catatonia may not be distinguishable from NMS either clinically or by laboratory testing (Maudsley Prescribing Guidelines 2021). This near-identity has produced a genuine nosological view rather than a mere resemblance: a symposium at the American Psychiatric Association meeting in 2000 concluded that NMS and malignant catatonia were the same (Kaplan & Sadock 2024), and the widely quoted formulation is that NMS is best regarded as a drug-induced form of malignant catatonia, that is, a malignant catatonia whose trigger happens to be a dopamine antagonist (Maudsley Prescribing Guidelines 2021). DSM-5-TR lists the two together precisely as a differential-diagnostic pair, malignant catatonia versus neuroleptic malignant syndrome (DSM-5-TR 2022).

Because the states overlap, the **discriminating leaning** rests less on the cross-sectional signs than on the preceding picture and the drug history. Catatonic signs that came first, in a patient who has not necessarily had an antipsychotic trigger, favour malignant catatonia: NMS can probably be ruled out in the absence of any prior or recent administration of a dopamine antagonist (Maudsley Prescribing Guidelines 2021). Conversely, a recent antipsychotic start or a dose rise, with lead-pipe rigidity emerging in that context, favours NMS. The leaning is a lean, not a proof, and the examiner wants it framed that way: the drug history tilts the label, the two may in truth be one spectrum, and the management does not wait on the argument.

TRAP **Treating malignant catatonia and NMS as cleanly separable.** They overlap so closely that they may be one entity; the drug history only leans the label, and chasing the name must never delay stopping the antipsychotic and starting benzodiazepines and ECT.

16.3 The differential grid: what leans which way

The discriminators are best held as a grid, because the point is exactly which features overlap (almost all of them) and which few lean the diagnosis. The shared column is large: fever, rigidity, autonomic instability and raised creatine kinase sit in both. The leaning column is small and is dominated by the temporal and pharmacological sequence.

FEATURE	LEANS TO MALIGNANT CATATONIA	LEANS TO NMS
Preceding picture	**Catatonic signs first (stupor, mutism, negativism, posturing), then fever and dysautonomia**	Rigidity and fever emerge on a background of recent antipsychotic exposure
Drug trigger	**No antipsychotic trigger necessary; may arise from an untreated catatonia**	**Recent antipsychotic start or dose rise (a dopamine antagonist)**
Character of the rigidity	Rigidity within a catatonic picture (posturing, waxy flexibility may be present)	**"Lead-pipe" rigidity is the classic descriptor**
Fever and autonomic instability	Present (defining the malignant state)	Present (shared, non-discriminating)
Creatine kinase	Often raised	Often markedly raised (shared, non-discriminating)
Nosological view	The primary entity	**Often regarded as a drug-induced form of malignant catatonia**
First management move	Stop any antipsychotic, benzodiazepines, ECT early	**Identical: stop the antipsychotic, benzodiazepines, ECT early (see the Schizophrenia: management, antipsychotics and adverse effects notes)**

The malignant catatonia versus NMS differential: almost every cross-sectional feature is shared, so the discriminators are the preceding picture and the antipsychotic history, and the first management move is the same either way.

16.4 Management: stop the drug, benzodiazepines, ECT early, intensive care

The management is deliberately the same whichever side of the differential the patient sits, because the states overlap and delay is what kills. The steps are: **stop any antipsychotic** (it can precipitate or worsen the state, and if the diagnosis is NMS the antipsychotic is the cause); **give benzodiazepines**, with lorazepam first-line and the lorazepam challenge as the entry point; **move to ECT early**, which treats both malignant catatonia and NMS and is the definitive step; and run **intensive supportive care** in parallel (hydration and nutrition, cooling, VTE prophylaxis, monitoring of vitals, creatine kinase and renal function, aspiration precautions) (Maudsley Prescribing Guidelines 2021, Kaplan & Sadock 2024). ECT is the gold-standard treatment for catatonia with about **90%** efficacy (Kaplan & Sadock 2024), and because malignant catatonia can evolve fast it should be considered and consent sought early rather than after benzodiazepines have clearly failed. In malignant catatonia every effort is made to maximise the effect of ECT by using liberal stimulus dosing to induce well-generalised seizures (Maudsley Prescribing Guidelines 2021); the technique itself is set out in the ECT and neurostimulation notes and is not taught here.

WORKED EXAMPLE

A woman with a two-week history of progressive mutism, immobility and imposed posturing, never started on an antipsychotic, now spikes a temperature of 39.5 C with labile blood pressure, tachycardia and a creatine kinase of several thousand. The catatonic picture came first and there is no dopamine antagonist in the history, so this leans to malignant catatonia rather than NMS, but the management does not depend on settling the label: no antipsychotic is given, lorazepam is started (2 mg challenge, then scheduled), ECT is arranged urgently, and she is managed with IV fluids, cooling, VTE prophylaxis and renal monitoring on a medical or high-dependency setting. Had she instead deteriorated days after a haloperidol start with lead-pipe rigidity, the lean would be to NMS, and the first moves would be identical.

RULE **Malignant catatonia and NMS overlap, so treat both the same.** Stop the antipsychotic, reach for benzodiazepines, and move to ECT early, with intensive supportive care alongside.

TRAP **Giving more antipsychotic to a febrile, rigid, catatonic patient.** Adding or increasing a dopamine antagonist here can precipitate or deepen malignant catatonia or NMS; the antipsychotic comes off, it does not go up.

~90%	2 mg	1934
ECT EFFICACY IN CATATONIA, THE DEFINITIVE STEP, TREATS BOTH	LORAZEPAM CHALLENGE, BENZODIAZEPINE ENTRY POINT	STAUDER DESCRIBES FATAL HYPERPYREXIAL (LETHAL) CATATONIA

INDIA

Indian tertiary practice fits the standard picture and is well placed for it. Lorazepam is widely available and inexpensive, so a benzodiazepine-first approach is fully practicable, and ECT is comparatively accessible and heavily used in Indian centres. Modified ECT is explicitly recommended as an urgent, life-saving intervention in malignant catatonia, with consent sought as early as possible (Clinical Methods in Psychiatry AIIMS 2024). The message for the Indian resident is that the definitive treatment for this emergency is within reach and should not be delayed while the malignant catatonia versus NMS label is debated.

MNEMONIC

STOP, SEDATE, SHOCK

STOP the antipsychotic (it can precipitate or is the cause). SEDATE with benzodiazepines (lorazepam, the challenge then titration). SHOCK, that is ECT, early, because it treats both malignant catatonia and NMS. All three run with intensive supportive care.

HOLD THIS

Malignant (lethal) catatonia is catatonic stupor plus fever and autonomic instability, and it overlaps so completely with NMS that they may be one entity; the drug history only leans the label (catatonia-first without a drug leans malignant catatonia, a recent antipsychotic with lead-pipe rigidity leans NMS), so for both you stop the antipsychotic, give benzodiazepines, and move to ECT early.

GOOD TO REMEMBER

- **Malignant catatonia (lethal catatonia):** catatonic stupor complicated by hyperthermia and autonomic instability, a life-threatening emergency that can evolve from an untreated catatonia; the fatal hyperpyrexial form was described by Stauder in 1934.
- **The one discriminator from NMS:** the preceding picture and drug history, catatonic signs first without a necessary antipsychotic trigger lean to malignant catatonia, a recent antipsychotic start or dose rise with lead-pipe rigidity leans to NMS; the states otherwise overlap and NMS is often regarded as a drug-induced form of malignant catatonia.
- **The first step, the same for both:** stop any antipsychotic, give benzodiazepines (lorazepam), move to ECT early (which treats both), with intensive supportive care; ECT is the gold-standard with about **90%** efficacy (Kaplan & Sadock 2024).

17 · ECT in catatonia and the Bush-Francis rating scale

Catatonia is treatable, and knowing the ladder is the exam point. Once catatonia is recognised as a syndrome (its signs and the raw descriptive definitions are cross-referenced to **the Psychometry, Assessment and Descriptive Psychopathology notes**, and its transdiagnostic nosology sits under ICD-11 6A40), management runs a short, fixed sequence: withdraw dopamine antagonists, correct the medical substrate, give a lorazepam challenge, and move to **electroconvulsive** therapy where the benzodiazepine fails or the picture turns malignant. This topic covers the place of **ect in catatonia** and the one instrument every resident is asked to name, the Bush-Francis Catatonia Rating Scale.

The examiner will not ask you to re-teach schizophrenia (that is owned by **the Schizophrenia: aetiology, phenomenology, classification and course notes**); the discriminator here is knowing *when not to delay* ECT, and knowing what the scale is for. The technique of ECT (electrode placement, stimulus dosing, the course itself) belongs to **the ECT and neurostimulation notes** and is cross-referenced, not taught here.

17.1 The place of ECT: gold standard, and definitive

Highly effective. Electroconvulsive therapy is the gold standard treatment for catatonia, with an efficacy around **90%** in catatonia (Kaplan & Sadock 2024). It has no absolute contraindications and is well tolerated even in medically ill patients, which matters because catatonia often presents in the acutely unwell. Most patients improve within the first **two to three** treatments (Kaplan & Sadock 2024). Lorazepam is best framed as a temporary bridge to definitive ECT: in many cases the benzodiazepine buys time while ECT is arranged, and some patients need monthly maintenance ECT to prevent relapse into catatonia.

RULE **Do not delay it.** ECT is the treatment for malignant or benzodiazepine-non-responsive catatonia; arrange it early, do not wait out a deteriorating patient.

17.2 When ECT is definitive: malignant and benzodiazepine-non-responsive catatonia

Two clear indications. ECT is specifically the treatment for **benzodiazepine-non-responsive** catatonia and for malignant catatonia. In malignant catatonia (also called lethal or pernicious catatonia, described by Stauder), the syndrome is acute in onset with stupor or excitement,

hyperthermia, autonomic instability, rigidity and altered consciousness; it is potentially fatal and, clinically and by laboratory testing, may be indistinguishable from neuroleptic malignant syndrome (Maudsley 2021). Here ECT can be lifesaving and should not be delayed. The same holds for **benzodiazepine non-responsive** catatonia: once an adequate lorazepam challenge has failed, escalating benzodiazepines or, worse, antipsychotics wastes time. Anticipating this, the clinician arranges ECT while the challenge is still running, so that a non-response or a slide into malignant catatonia does not cost days (Kaplan & Sadock 2024).

TRAP **Persisting with benzodiazepines alone.** In a deteriorating malignant catatonia, staying on lorazepam and hoping is the classic error; the patient needs urgent ECT.

WORKED EXAMPLE

A young man in catatonic stupor, mute and rigid, spikes a fever to 39.5 with labile blood pressure and a rising creatine kinase. He had a partial response to 2 mg lorazepam yesterday but is now worse. This is malignant catatonia (indistinguishable from NMS if he was recently on an antipsychotic). The move is not more lorazepam: it is to stop any dopamine antagonist, support vitals, and arrange urgent ECT the same day.

17.3 The lorazepam challenge: the step before ECT

Diagnostic and therapeutic. The lorazepam challenge is given both to confirm catatonia and to treat it. An initial dose of **2 mg** lorazepam is standard for most adults (lower in frail older adults and children), used for both diagnostic and treatment purposes (Kaplan & Sadock 2024). Indian practice describes an intravenous injection of **1 to 2 mg** lorazepam given over two minutes, with catatonic features reassessed shortly after (AIIMS Clinical Methods 2024). The patient is observed over roughly **30 to 60** minutes to see whether the catatonia dissipates; a positive response supports both diagnosis and the plan, and daily lorazepam then holds the symptoms at bay (Practical Psychopharmacology). A positive challenge is also a signal to arrange ECT, because a good lorazepam response predicts a good ECT response.

2 mg	30 to 60 min	around 90%
INITIAL LORAZEPAM CHALLENGE DOSE	OBSERVATION WINDOW	ECT EFFICACY IN CATATONIA

17.4 The Bush-Francis Catatonia Rating Scale: structure

The standard instrument. The **bush-francis catatonia rating scale** (Bush, Fink, Petrides, Dowling & Francis 1996) is the most used scale to identify catatonia and to grade its severity. It is a 23-item scale with two parts that map onto its two jobs (AIIMS Clinical Methods 2024):

The 14-item screen

The presence or absence of items 1 to 14 (the screening subscale) is scored to flag whether catatonia is present.

The severity scale

All 23 items are then rated 0 to 3 to grade severity, based on behaviour observed during a standardised examination.

Ratings are made on observed behaviour during the examination, with withdrawal and autonomic abnormality drawing on chart and collateral. The scale earns its keep at the bedside because catatonia often goes undetected or is mistaken for psychotic agitation, and it does not respond to escalating antipsychotic dosing (Practical Psychopharmacology).

17.5 Using the scale to monitor response

Serial scoring tracks treatment. Beyond identifying catatonia, the Bush-Francis Catatonia Rating Scale is used to monitor the response to the lorazepam challenge and to ECT: the same 0 to 3 severity ratings, repeated before and after the challenge and across the ECT course, give an objective measure of whether the catatonic burden is falling. This is why the instrument is paired with the challenge and the course rather than used once. It is not diagnostic on its own; the ICD-11 or DSM-5-TR criteria (with the anchoring signs cross-referenced to **the Psychometry, Assessment and Descriptive Psychopathology notes**) make the diagnosis, and the scale quantifies it.

MNEMONIC

SCREEN 14, SCORE 23

Items 1 to 14 are the presence/absence screen; all 23 items rated 0 to 3 give the severity score you track across the lorazepam challenge and ECT.

17.6 Malignant catatonia versus NMS: the differential that decides urgency

The one that changes management. The reason malignant catatonia is worth a row of its own is that it can be indistinguishable from neuroleptic malignant syndrome, and mistaking one for the other is a classic error. Both show hyperthermia, autonomic instability and rigidity; a 2000 American Psychiatric Association meeting concluded the two are the same entity, and NMS is often viewed as a drug-induced (antipsychotic-precipitated) variant of malignant catatonia (Kaplan & Sadock 2024; Maudsley 2021). NMS as a discrete entity is owned by **the Schizophrenia: management, antipsychotics and adverse effects notes**; it appears here only as the mirror of malignant catatonia. The practical convergence is the same: stop the offending dopamine antagonist, support the patient, and both respond to ECT.

FEATURE	MALIGNANT CATATONIA	NMS
Core state	Stupor or excitement, then hyperthermia, autonomic instability, rigidity	Hyperthermia, lead-pipe rigidity, autonomic instability, altered consciousness
Trigger	**May arise primary to the psychiatric illness, without a drug trigger**	**Drug-induced: follows a dopamine antagonist, often after a dose increase**
Relationship	Often clinically and biochemically indistinguishable; widely held to be the same syndrome, with NMS a drug-induced variant	
Decisive treatment	**Urgent ECT; do not delay**	Stop the antipsychotic, support, dantrolene/bromocriptine; ECT if refractory

Malignant catatonia and NMS overlap so completely that the same first moves apply; the discriminator is the drug history, not the presentation.

INDIA

ECT for catatonia is well established in Indian practice. AIIMS Clinical Methods in Psychiatry (2024) sets out that urgent modified ECT (mECT) is administered in malignant catatonia, so consent for mECT is taken as soon as possible; mECT may be given daily in severe cases and then reduced to alternate days or twice weekly as the catatonic syndrome declines, with maintenance mECT where needed. The lorazepam challenge (intravenous 1 to 2 mg over two minutes) is the standard first step, and the Bush-Francis Catatonia Rating Scale is named as the most used instrument to monitor catatonic signs. Overall prognosis is good, but delay in diagnosis and treatment raises morbidity, which is exactly why ECT is not delayed.

PEARL

ICD-11 places catatonia as a transdiagnostic grouping, not a subtype of schizophrenia: 6A40 catatonia associated with another mental disorder, 6A41 catatonia induced by substances or medications, and 6E69 secondary catatonia syndrome. This nosological move (catatonia can accompany mood disorders, psychoses or medical illness) is the high-yield point and reinforces the search for a treatable substrate before ECT.

HOLD THIS

ECT is the gold standard for catatonia (around 90% efficacy) and the definitive treatment for malignant or benzodiazepine-non-responsive catatonia; do not delay it, and track the response with the Bush-Francis scale.

GOOD TO REMEMBER

- **ECT in catatonia:** gold standard, efficacy around 90%; definitive for malignant and benzodiazepine-non-responsive catatonia; most improve within two to three treatments; maintenance ECT prevents relapse. Technique lives in the ECT and neurostimulation notes.
- **Lorazepam challenge:** initial 2 mg (IV 1 to 2 mg over two minutes in Indian practice), diagnostic and therapeutic; observe over 30 to 60 minutes; a positive response is the cue to arrange ECT.
- **Bush-Francis Catatonia Rating Scale (Bush 1996):** 23-item scale; items 1 to 14 = presence/absence screen; all 23 rated 0 to 3 for severity; used to identify catatonia and monitor response to the lorazepam challenge and ECT.
- **Malignant (lethal/pernicious) catatonia:** acute stupor or excitement with hyperthermia, autonomic instability, rigidity; often indistinguishable from NMS; urgent ECT can be lifesaving. Stauder eponym.
- **ICD-11 placement:** transdiagnostic grouping, 6A40 (with another mental disorder), 6A41 (substance/medication-induced), 6E69 (secondary catatonia syndrome).

Apply and consolidate

18 · Apply: four worked vignettes

Why this matters. Everything in these notes converges on a small number of bedside decisions, and the examiner tests them through short cases, not through recall of a criterion list. This closing topic runs four **worked vignettes**, each a brief scenario, the reasoning, then the resolution, that reassemble the moves already taught: the schizoaffective versus mood-with-psychosis gate, the delusional-disorder read, the catatonia lorazepam challenge, and the malignant-catatonia versus NMS emergency. Nothing new is introduced; the raw criteria live in the sibling topics and are cross-referenced, not re-derived.

Each vignette is deliberately compact and ends on the single discriminator that settles it, because that is how the case discussion is scored: not on how many features you can list, but on whether you name the one rule that decides the diagnosis. Treat every "Case:" below as a **worked example** to rehearse aloud, and hold the four clinical moves in the good-to-remember box at the close.

18.1 Vignette one: schizoaffective disorder versus mood with psychotic features

The commonest trap in the whole spectrum is to see psychosis and a mood episode together and reach for the schizoaffective label. The decision turns entirely on the two DSM-5-TR rules (Kaplan & Sadock 2024, DSM-5-TR 2022): Criterion B, a period of at least **two weeks** of delusions or hallucinations in the absence of a prominent mood episode; and Criterion C, mood-episode symptoms present for the majority of the total duration of the illness. The full mood-episode criteria are cross-referenced to the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes, and the disorder architecture to the Schizophrenia: aetiology, phenomenology, classification and course notes.

WORKED EXAMPLE

Case: A 34-year-old woman is admitted with a four-month history. For the first two months she had persecutory delusions and third-person auditory hallucinations with no disturbance of mood; over the following two months a full major depressive episode developed, and psychosis and depression have run together since.

Reasoning. Both phenomena are present, so the question is not "is there psychosis and mood" but "is the temporal architecture met". Criterion B asks for at least two weeks of psychosis without a prominent mood episode: here there were a full two months of pure psychosis before any mood change, so the gate is cleared. Criterion C asks that mood dominate the majority of the illness: depression has been present for two of the four months and continues, which is at least half. Both rules hold.

Resolution. Schizoaffective disorder, depressive type. Contrast the counter-case that resolves the other way: if psychosis had appeared only once the depressive episode began and had cleared when mood lifted, Criterion B would fail, there would be no two-week window of pure psychosis, and the diagnosis would be a major depressive episode with psychotic features, where psychosis is confined to the mood episode.

RULE **Two weeks of psychosis without a prominent mood episode is the gate.** Criterion B excludes mood-with-psychosis; Criterion C (mood for the majority of the illness) excludes schizophrenia; both must hold.

TRAP **Diagnosing schizoaffective from concurrent psychosis and mood alone.** Without the two-week pure-psychosis window, co-occurring psychosis and a mood episode are a mood disorder with psychotic features, not schizoaffective disorder.

18.2 Vignette two: delusional disorder versus paranoid schizophrenia

The delusional-disorder read is a discrimination against schizophrenia by what is *absent*. The positive requirement is a single-theme, characteristically non-bizarre delusional system present for at least one month in DSM-5-TR (three months in ICD-11 6A24), with functioning outside the delusion largely preserved and none of the other schizophrenia features (Kaplan & Sadock 2024, DSM-5-TR 2022, ICD-11 CDDR). The raw descriptive definition of a non-bizarre delusion is cross-referenced to the Psychometry, Assessment and Descriptive Psychopathology notes.

WORKED EXAMPLE

Case: A 42-year-old accountant is brought by his wife. For eight months he has been convinced that a colleague is quietly sabotaging his promotion, checking his emails and turning management against him. He is otherwise working, dressing and relating normally; there are no hallucinations, no thought disorder, no negative symptoms, and outside this one theme his conversation and affect are unremarkable.

Reasoning. The belief is plausible-in-kind, a non-bizarre persecutory theme, single and encapsulated, and it has run well beyond the one-month DSM-5-TR (and three-month ICD-11) threshold. The decisive point against paranoid schizophrenia is the preserved picture around the delusion: no prominent hallucinations, no formal thought disorder, no functional collapse. Schizophrenia would show a broader psychotic syndrome and deterioration; here there is a walled garden of one belief in an otherwise intact person.

Resolution. Delusional disorder, persecutory type. Had there been prominent ongoing auditory hallucinations, disorganisation or global functional decline, the diagnosis would shift to schizophrenia, whose criteria and course are owned by the Schizophrenia: aetiology, phenomenology, classification and course notes.

TRAP **Escalating an encapsulated non-bizarre delusion to schizophrenia.** A single-theme delusion with preserved function and no other psychotic features is delusional disorder; do not upgrade it on the strength of the delusion's conviction alone.

INDIA

Indian teaching leans on the ICD tradition, so the three-month non-bizarre-delusion template is the one most residents carry, and morbid jealousy and persecutory presentations are the delusional-disorder subtypes seen most often in clinic. The discrimination against schizophrenia is made the same way: preserved function outside the delusion and the absence of a wider psychotic syndrome.

18.3 Vignette three: catatonia and the lorazepam challenge

Catatonia is the syndrome the examiner most wants worked as a sequence: examine for the signs, exclude an organic cause, give the challenge, then treat with benzodiazepines. ICD-11 codes catatonia as a free-standing, transdiagnostic entity (6A40) requiring three or more signs from the decreased, increased and abnormal-activity clusters; DSM-5-TR cross-maps as three or more of twelve signs (ICD-11 CDDR, DSM-5-TR 2022). The individual signs, catalepsy, waxy flexibility (cerea flexibilitas), mutism, negativism, posturing, echophenomena, are set out with the Bush-Francis scale in the catatonia signs notes and not re-listed here.

WORKED EXAMPLE

Case: A 27-year-old man with known bipolar disorder is admitted mute and immobile. On examination he holds an arm where it is placed (catalepsy), resists passive movement, and shows waxy flexibility. Vitals are stable and he is afebrile.

Reasoning. Three or more signs are present, so the syndromic threshold is met. Before treating, exclude an organic or medical cause, the sign cluster is transdiagnostic and can be driven by encephalitis, metabolic derangement or medication, so a focused work-up (temperature, bloods including creatine kinase, and a screen for an organic driver) comes first. With no red flag for an organic emergency, proceed to the lorazepam challenge: 2 mg IV (1 to 2 mg in adults, lower in children and frail older adults) as a single diagnostic-and-therapeutic dose (Kaplan & Sadock 2024, Clinical Methods in Psychiatry 2024).

Resolution. A marked partial or full response, increased interaction and reduction of catatonic signs, typically within **30 minutes**, both confirms catatonia and opens treatment. Benzodiazepines are then first-line: scheduled lorazepam, titrated from the challenge dose. A positive response confirms the syndrome; sedation or no change does not rule it out. If catatonia is lorazepam-refractory or malignant, ECT is the definitive step, its technique cross-referenced to the ECT and neurostimulation notes.

2 mg IV	within 30 min	70 to 80%
STANDARD ADULT LORAZEPAM CHALLENGE DOSE	RESPONSE WINDOW THAT CONFIRMS CATATONIA	BENZODIAZEPINE EFFICACY FOR SYMPTOM REDUCTION

RULE **The lorazepam challenge is diagnosis and treatment in one.** A 2 mg IV dose that produces a marked response confirms catatonia and starts the benzodiazepine; response is judged by at least 50% improvement.

TRAP **Missing the organic cause.** Catatonia is transdiagnostic: exclude encephalitis, a metabolic cause and medication effects before assuming a primary psychiatric driver, and never reflexively reach for a high-potency antipsychotic.

18.4 Vignette four: malignant catatonia versus neuroleptic malignant syndrome

The emergency vignette is a febrile, rigid, dysautonomic patient, and the task is to reason to the discriminator and the first steps. Malignant catatonia is catatonic stupor with hyperthermia and autonomic instability, a potentially fatal state that at the bedside may be clinically indistinguishable from neuroleptic malignant syndrome, itself best regarded as a drug-induced variant of malignant catatonia (Maudsley Prescribing Guidelines 2021, DSM-5-TR 2022). NMS as an entity is owned by the Schizophrenia: management, antipsychotics and adverse effects notes and appears here only inside this differential.

WORKED EXAMPLE

Case: A 30-year-old man, three days into haloperidol for an acute psychosis, becomes febrile at 39.5 C with lead-pipe rigidity, fluctuating consciousness, labile blood pressure and a creatine kinase of several thousand units.

Reasoning. Fever, rigidity, autonomic instability and a raised CK are common to both malignant catatonia and NMS, so the syndromes overlap at the bedside. The discriminator that settles this presentation is the drug history: recent exposure to a dopamine-blocking antipsychotic points to NMS as the mechanism. Either way the immediate management is the same, because the two are on one continuum.

Resolution. Stop the antipsychotic first. Give a benzodiazepine (lorazepam) and start supportive care, IV fluids, cooling, monitoring, with ECT brought forward urgently if there is incomplete response or progression, since malignant catatonia can evolve fast. Where the underlying psychosis genuinely needs cover once the crisis settles, avoid a high-potency agent; the drug choice belongs to the management notes and the ECT technique to the ECT and neurostimulation notes.

RULE **The discriminator is the drug history; the first three moves are shared.** Recent antipsychotic exposure points to NMS, but for both: stop the antipsychotic, give a benzodiazepine, and move to urgent ECT if it does not settle.

TRAP **Treating malignant catatonia as if it were something other than NMS.** They sit on one continuum; do not withhold benzodiazepines or delay ECT while arguing the label, and never add a high-potency antipsychotic.

HOLD THIS

Four moves, four one-liners: schizoaffective needs at least two weeks of psychosis without a prominent mood episode plus mood for the majority; delusional disorder is a non-bizarre single-theme delusion with preserved function and nothing else; catatonia is three or more signs, exclude an organic cause, then a 2 mg IV lorazepam challenge; malignant catatonia and NMS are one continuum, so stop the antipsychotic, give a benzodiazepine and use urgent ECT.

GOOD TO REMEMBER

- **Schizoaffective versus mood-with-psychosis:** the move is the two-week gate. Diagnose schizoaffective only with at least **two weeks** of psychosis in the absence of a prominent mood episode (Criterion B) plus mood for the majority of the illness (Criterion C); otherwise it is a mood disorder with psychotic features.
- **Delusional disorder versus paranoid schizophrenia:** the move is to diagnose by what is absent. A non-bizarre single-theme delusion, at least one month (DSM-5-TR; three months in ICD-11), with preserved function and no other psychotic features; the number to hold is the one-month (ICD-11 three-month) threshold.
- **Catatonia and the lorazepam challenge:** the move is examine, exclude organic, challenge, treat. Three or more signs (ICD-11 6A40, transdiagnostic; DSM-5-TR three of twelve), then a **2 mg IV** lorazepam challenge with response in about **30 minutes**; benzodiazepines are first-line, symptom reduction **70 to 80%** (Kaplan & Sadock 2024).
- **Malignant catatonia versus NMS:** the move is treat the continuum, not the label. The discriminator is the antipsychotic drug history (NMS is the drug-induced variant); for both, stop the antipsychotic, give a benzodiazepine and use urgent ECT.

19 · Consolidate: mnemonic, retrieval and synthesis

Why this matters. A chapter this long is only as useful as the single thread the reader can pull at midnight before the case discussion. This closing topic does three things and nothing else: it hands over one **master mnemonic** that chains every entity in the block into an ordered walk, it sets a bank of answer-free recall prompts to force **active recall** rather than re-reading, and it names the whole-chapter **synthesis map** to be redrawn from memory. Nothing new is taught here. Every criterion, eponym and number below is owned and verified in the sibling topics and is compressed, not re-derived; the raw descriptive definitions of the delusions and misidentification phenomena stay cross-referenced to the Psychometry, Assessment and Descriptive Psychopathology notes, and the illness schizophrenia itself to the Schizophrenia: aetiology, phenomenology, classification and course notes.

Consolidation is a study step with an evidence base, not a decoration: chaining discrete facts onto one retrieval structure, then testing that structure against blank paper, is how a large block moves from recognition to recall. Treat the mnemonic as the spine, the retrieval prompts as the test, and the synthesis map as the object you must be able to draw with the book shut.

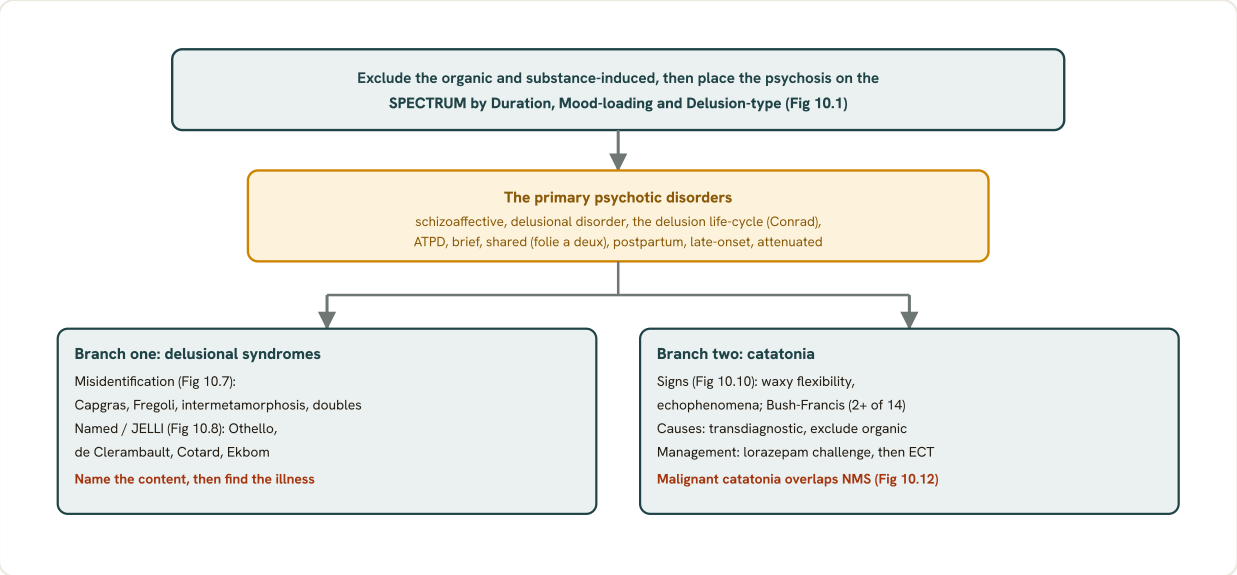


Fig 10.13 The whole-chapter synthesis map, to redraw from memory. The trunk is the spectrum decision tree and its primary psychotic disorders; branch one is the delusional syndromes (misidentification and the named monothematic set), held by content and direction; branch two is catatonia, run as a sequence from signs to causes to management to its malignant form. The gaps you cannot draw are the topics to revisit.

19.1 The master mnemonic: the whole chapter on one chain

The chain seeded at the orientation step now carries its full payload. The three-axis core (place the psychosis on the SPECTRUM by **D**uration, **M**ood-loading and **D**elusion-type) is the trunk; the named delusional syndromes and catatonia hang off it as the two branches the examiner tests by eponym and by sequence. Unpack every letter and the block is recoverable from a single string.

MNEMONIC

"SPECTRUM by D-M-D; then the DELUSIONAL syndromes; then CATATONIA MOVES."

SPECTRUM (the decision tree). First exclude the organic and substance-induced (the silent branch), then place the psychosis on the spectrum by the three axes. **D = Duration:** brief psychotic disorder under one month, schizophreniform one to six months (DSM-5-TR), schizophrenia six months or more (DSM-5-TR) or one month or more (ICD-11), with the acute and transient psychotic disorder (ATPD, ICD-11 6A23) off to the side, acute onset to the full picture within two weeks. **M = Mood-loading:** schizoaffective disorder needs a mood episode for the majority of the illness plus at least two weeks of psychosis without a prominent mood episode; psychosis only within mood episodes is a mood disorder with psychotic features. **D = Delusion-type:** a single non-bizarre delusion in an otherwise preserved person is delusional disorder.

The LIFE-CYCLE and the OTHER PRESENTATIONS. A primary delusion forms through Conrad's stages (Trema to Apophany to Apocalypse) and resolves by integration or sealing-over; and the block carries the compact presentations, the ACUTE and transient psychosis (bouffee delirante, cycloid psychosis), the BRIEF psychotic disorder, the SHARED delusion (folie a deux and its variants: imposee, communiquee, induite, simultanee), the PERINATAL (postpartum) psychosis, the LATE-onset and very-late-onset pictures (paraphrenia, partition delusions), and the ATTENUATED psychosis syndrome.

DELUSIONAL syndromes (branch two). The MISIDENTIFICATION set (Capgras, Fregoli, intermetamorphosis, subjective doubles, reduplicative paramnesia) and the named MONOTHEMATIC set (JELLI: Jealousy = Othello, Erotomania = de Clerambault, Loss-of-existence = Cotard, Little-organisms-Infest = Ekbom). Name the content, then find the illness.

CATATONIA MOVES (branch three). Read it as a sequence: the SIGNS (Kahlbaum's stupor, catalepsy, waxy flexibility, mutism, negativism, echophenomena; scored on the Bush-Francis Catatonia Rating Scale), the CAUSES (transdiagnostic, ICD-11 6A40/6A41/6E69, so exclude an organic driver), the MANAGEMENT (the lorazepam challenge, then benzodiazepines first-line, ECT if refractory), and the MALIGNANT form (Stauder's lethal catatonia, sitting on one continuum with NMS). "Moves" is the reminder that catatonia is the psychomotor syndrome that cuts across the whole grouping. D-M-D is the three-axis core the examiner rewards.

RULE **Walk the mnemonic in order, never by feature-count.** Exclude organic first, place on the spectrum by the three axes, then decide whether the picture is a named delusional content or catatonia; the order is the answer.

TRAP **Memorising the eponyms without the discriminators.** The chain is worthless if Capgras and Fregoli swap, or if Othello is called benign, or if a lorazepam-responsive catatonia is missed for want of the challenge; the letter must recall the rule, not just the name.

HOLD THIS

One string carries the block: place every psychosis on the SPECTRUM by Duration, Mood-loading and Delusion-type after excluding the organic; then work the named DELUSIONAL syndromes (misidentification and JELLI monothematic); then run CATATONIA as signs to causes to management to malignant form.

19.2 Retrieval practice: test the chain against blank paper

Reading the notes again feels like learning and mostly is not. The step that moves this block into recall is **retrieval practice**: shut the book, answer from memory, then check. The prompts below span the three bands (the spectrum and the primary psychotic disorders; the named delusional syndromes; catatonia). Work them as **active recall**, out loud or on paper, before you look anything up. The answers are deliberately absent; every prompt is answered somewhere in the sibling topics of this block.

RETRIEVAL PRACTICE, COVER THE ANSWERS

1. Name the three axes that separate every member of the schizophrenia spectrum, and state the silent branch you apply before you enter the tree.
2. Give the two DSM-5-TR criteria (B and C) that make a diagnosis schizoaffective disorder, and the one that separates it from a mood disorder with psychotic features.
3. State the duration thresholds that split brief psychotic disorder, schizophreniform disorder and schizophrenia in DSM-5-TR, and say where ICD-11 draws the schizophrenia line differently.
4. Define the acute and transient psychotic disorder (ICD-11 6A23) by its onset speed and course, and name its two classical antecedents in the European literature.
5. Give the positive criteria for delusional disorder and the single discriminator that separates it from paranoid schizophrenia.
6. Trace the life-cycle of a primary delusion through its named formation stages, and name the two ways it can resolve.
7. Name the shared-delusion syndrome and its four subtypes by the Latin terms, and state which member is the inducer versus the recipient.
8. State the incidence of postpartum psychosis per deliveries, the window in which most cases begin, and the single highest recurrence-risk factor.
9. Distinguish late-onset schizophrenia from very-late-onset schizophrenia-like psychosis, and name the delusion type classically tied to the older presentation.
10. Match each misidentification eponym (Capgras, Fregoli, intermetamorphosis, subjective doubles) to its core belief and its direction, and state the proportion of Capgras cases with an organic cause.
11. Unpack the JELLI monothematic set: give each eponym, its delusional content, and the one association or forensic risk to hold for each.
12. List the core catatonic signs and name the scale used to score them; then define waxy flexibility and negativism precisely.
13. Describe the lorazepam challenge: drug, dose, route, the response window that confirms catatonia, and the first-line treatment it opens.
14. State where catatonia lives in ICD-11 and why that placement is high-yield, and name the three organic categories you must exclude before calling it primary.
15. Give the one bedside discriminator between malignant catatonia and neuroleptic malignant syndrome, and the first three management moves the two share.

RULE **Answer before you check.** A prompt you can answer from memory is learned; a prompt you can only recognise once you read the answer is not, and re-reading will not fix it, only retrieval will.

19.3 The synthesis map: redraw the block from memory

The final consolidation object is a whole-chapter **synthesis map** to **redraw from memory**: a single figure with one trunk and three branches that you should be able to reproduce on blank paper without the notes open. The **trunk** is the spectrum decision tree, the primary psychotic disorders placed by the three axes (duration, mood-loading, delusion-type) after the organic and substance-induced are excluded, with schizoaffective, delusional disorder and the compact

presentations (acute and transient, brief, shared, perinatal, late-onset, attenuated) as its leaves. **Branch one** is the misidentification and named monothematic delusional syndromes, held by content and direction (Capgras versus Fregoli; the JELLI four). **Branch two** is catatonia as a sequence, signs to causes to management to the malignant form, drawn as the psychomotor syndrome that cuts transdiagnostically across the whole trunk. Redraw it, then check each branch against the good-to-remember boxes of the sibling topics; the gaps you find are the topics to revisit. This is the concept figure for the whole block (Fig 10.13), and drawing it from memory, not reading it, is the last consolidation step.

GOOD TO REMEMBER

- **The master mnemonic:** "SPECTRUM by D-M-D; then the DELUSIONAL syndromes; then CATATONIA MOVES." The whole-chapter chain: exclude organic, place on the spectrum by Duration, Mood-loading and Delusion-type, then the named delusional syndromes, then catatonia signs to causes to management to malignant form. The three-axis core (D-M-D) is the load-bearing part.
- **Retrieval practice:** the study move is to answer the 15 prompts from memory with the answers covered, out loud or on paper, then check; retrieval, not re-reading, is what fixes a large block. Every prompt is answered within the sibling topics of this block.
- **The synthesis map (Fig 10.13):** the object to redraw from memory is one trunk (the spectrum tree and primary disorders, by the three axes) and two branches (the misidentification and JELLI delusional syndromes; catatonia as signs to causes to management to malignant form). The gaps you cannot draw are the topics to revisit.
- **The high-yield anchors to carry:** schizoaffective needs at least **two weeks** of psychosis without prominent mood plus mood for the majority; delusional disorder is at least **one month** (ICD-11 **three months**) of a single non-bizarre delusion; up to **40%** of Capgras cases are organic; catatonia is the **2 mg IV** lorazepam challenge with response in about **30 minutes** and **70% to 80%** benzodiazepine efficacy; malignant catatonia and NMS are one continuum.

Previously asked

This territory is examined less as the long diagnose-and-manage essay of the schizophrenia papers and more as a steady stream of short notes and definitions: a named syndrome, a single disorder, or a discriminating feature. Catatonia is the most examinable single topic and has come as a full short note on its clinical features and, in the neuropsychiatry papers, as organic catatonia; postpartum psychosis and bouffee delirante have each been asked as named short notes. The delusional and misidentification syndromes recur as the definition-and-differentiate items the descriptive-psychopathology and clinical papers favour. The genuine questions on record are grouped by band below.

? HOW THIS TERRITORY IS ACTUALLY TESTED

Q **Other primary psychotic disorders.** These come as named short notes rather than long essays. "Postpartum psychosis" has been asked as a 10-mark note, and "bouffee delirante" as a 10-mark note that rewards knowing the acute-and-transient category it seeds. Schizoaffective disorder, delusional disorder and its subtypes, the acute and transient psychotic disorders, and the late-onset psychoses are the definition-and-criteria short notes this band yields; prepare each to be defined, placed on the spectrum by duration and mood-loading, and separated from schizophrenia. short note, recurring

Q **Delusional misidentification and named syndromes.** The eponymous syndromes are classic short-note and viva territory: define Capgras, Fregoli, De Clerambault (erotomania), Othello (delusional jealousy), Cotard and Ekbom, and name the core delusional content and the one association or risk. Othello syndrome carries a forensic angle worth stating. Prepare these as crisp keyed definitions, not essays. short note and viva, recurring

Q **Catatonia.** The most examinable single topic of the block. "Clinical features of catatonia" has been asked as a 10-mark note, and "organic catatonia" as a 10-mark note in the neuropsychiatry papers, rewarding the aetiological work-up and the exclusion of a medical or neurological cause. Build the signs, the lorazepam challenge, the transdiagnostic placement, and malignant catatonia and its differential from neuroleptic malignant syndrome to answer the note and the emergency question. short note, recurring

Prepare this material to be defined and discriminated, not just recited: the spectrum decision tree, the misidentification and named-syndrome grids, and the malignant-catatonia-versus-NMS differential in these notes are built to the way the topic is examined. The phenomenology, aetiology, criteria and course of schizophrenia itself are developed in the Schizophrenia: aetiology, phenomenology, classification and course notes; the antipsychotic drugs and neuroleptic malignant syndrome as an entity live in the Schizophrenia: management, antipsychotics and adverse effects notes; these notes own the other psychotic disorders, the delusional syndromes, and catatonia.

Quick review

The whole subject in one table	
THE SPECTRUM DECISION TREE	Exclude the organic and substance-induced first, then place the psychosis on three axes: duration, mood-loading and delusion-type. A prominent mood episode pulls out schizoaffective and mood-with-psychosis; a single non-bizarre delusion with preserved function is delusional disorder; the rest go on the duration ruler.
SCHIZOAFFECTIVE DISORDER	At least two weeks of psychosis in the absence of a prominent mood episode (DSM-5-TR Criterion B, excludes mood-with-psychosis) plus mood symptoms for the majority of the total illness (Criterion C, excludes schizophrenia). Bipolar type (F25.0) or depressive type (F25.1). A diagnosis of debated validity: at two years only about a third keep the label. Coined by Kasanin (1933).
DELUSIONAL DISORDER	One or more non-bizarre delusions for at least one month (DSM-5-TR; three months in ICD-11 6A24), function otherwise preserved, no other schizophrenia symptoms. Subtypes by theme: persecutory (commonest), grandiose, jealous (male-predominant, Othello), erotomanic (De Clerambault), somatic (Ekbom), mixed. Onset mid- to late-30s. Kendler's original five dimensions (conviction, extension, bizarreness, disorganisation, pressure) rate form, not content.
THE LIFE-CYCLE OF A DELUSION	Formation through Conrad's phases: trema (delusional mood, an uncanny atmosphere) precedes apophany (the crystallised delusional perception), then anastrophe and apocalypse. Jaspers' primary forms: delusional mood, delusional perception (Schneider's two-memberedness), the sudden autochthonous idea, delusional memory. Dissolution: Bleuler's double bookkeeping and double orientation, encapsulation, and the recovery styles sealing-over versus integration.
ACUTE AND TRANSIENT PSYCHOTIC DISORDER	ICD-11 6A23: abrupt onset to full psychosis within two weeks, no prodrome, a rapidly shifting polymorphic picture, no negative symptoms, duration not over three months, with a characteristically good outcome. The acute polymorphic form (with or without schizophrenia symptoms) is the prototype; bouffee delirante (the Magnan and Legrain tradition) is the French antecedent. Follow up: a minority become schizophrenia or a mood disorder.
BRIEF PSYCHOTIC AND SHARED DISORDERS	Brief psychotic disorder (DSM-5-TR): at least a day, under one month, full recovery, often post-stressor. Induced or shared delusional disorder (folie a deux): a delusion transferred from a dominant psychotic primary to a passive, isolated secondary; separation of the pair usually resolves the secondary's delusion.
PERINATAL AND LATE-ONSET PSYCHOSES	Postpartum psychosis: an acute, often bipolar-spectrum, fluctuating psychosis of the first two weeks, a psychiatric emergency for suicide and

The whole subject in one table	
	infanticide risk; admit, ideally with the baby. Late-onset schizophrenia-like psychosis (onset after 40) and very-late-onset (after 60, the old paraphrenia): commoner in women, with sensory impairment, isolation and partition delusions; exclude a neurodegenerative cause.
ATTENUATED PSYCHOSIS SYNDROME	A DSM-5-TR condition for further study (Section III), not a formal diagnosis: sub-threshold delusion-like ideas, unusual perceptions or disorganised speech with reality testing relatively intact. It names the at-risk mental state (detected by CAARMS or SIPS); only a minority transition (about 15% at one year, 20% at two years), so false-positive and stigma risks keep it out of the main manual.
THE SPECTRUM DIFFERENTIAL	Duration and mood-loading are the master discriminators: brief psychotic under one month, schizophreniform one to six months, schizophrenia six months or more (one month in ICD-11). Schizoaffective needs the two-week pure-psychosis window and mood for the majority; delusional disorder is a single non-bizarre delusion in an otherwise preserved person, against the broader decline of paranoid schizophrenia.
MISIDENTIFICATION SYNDROMES	Keyed on the core misidentification: Capgras (a familiar person seen as an identical impostor), Fregoli (one persecutor disguised inside strangers, the mirror image), intermetamorphosis (both appearance and identity swapped), subjective doubles (doubles of the self). A face-processing disconnection between recognition and the affective sense of familiarity, with a high rate of right-hemisphere or organic pathology (up to 40% of Capgras cases), so exclude an organic cause.
NAMED MONOTHEMATIC SYNDROMES	Content, not disorder (JELLI): De Clerambault (erotomania, another of higher status secretly in love), Othello (delusional jealousy, a real forensic risk of violence, commoner in men), Cotard (nihilistic, being dead or the organs lost, in severe psychotic depression), Ekbom (delusional infestation, the matchbox sign, presents to dermatology). Name the content, then find the illness.
CATATONIA: THE SIGNS	A transdiagnostic psychomotor syndrome, elicited not just observed. The classical Kahlbaum and modern signs across three clusters: decreased (stupor, mutism, negativism, posturing, catalepsy, waxy flexibility), increased or abnormal (stereotypies, mannerisms, echolalia, echopraxia, verbigeration), and the elicited opposites of will (automatic obedience, mitgehen, gegenhalten, ambitendency). Waxy flexibility is the classic sign. Bush-Francis scale: 23 items, first 14 the screen, two or more positive.
CATATONIA: AETIOLOGY	Psychiatric (mood disorders are commoner than schizophrenia), neurological (encephalitis, especially anti-NMDA-receptor encephalitis, seizures, stroke) and medical (metabolic, autoimmune, drug-related) causes; always exclude an organic cause. ICD-11 codes it transdiagnostically (6A40 with another

The whole subject in one table	
	disorder, 6A41 substance-induced, 6E69 secondary), not as a subtype of schizophrenia, which is the shift from ICD-10.
CATATONIA: MANAGEMENT	The lorazepam challenge (1 to 2 mg IV, response usually within 10 minutes) is diagnostic and therapeutic; benzodiazepines are first-line (70 to 80% efficacy), with supportive care and treatment of the cause. Antipsychotics can worsen catatonia and precipitate the malignant form, so they are used with caution. ECT for lorazepam-refractory or malignant catatonia (about 90% efficacy).
MALIGNANT CATATONIA AND NMS	Malignant (lethal) catatonia is catatonic stupor plus fever and autonomic instability, a fatal emergency described by Stauder (1934). It overlaps so completely with neuroleptic malignant syndrome that many treat them as one entity (NMS a drug-induced malignant catatonia). The drug history only leans the label: catatonic signs first, no antipsychotic needed, lean to malignant catatonia; a recent antipsychotic with lead-pipe rigidity leans to NMS. For both: stop the antipsychotic, benzodiazepines, ECT early.
ECT AND THE RATING SCALE	ECT is the treatment for malignant and benzodiazepine-non-responsive catatonia and should not be delayed; the technique is developed in the ECT and neurostimulation notes. The Bush-Francis Catatonia Rating Scale (a 14-item screen and a fuller severity scale) identifies catatonia and monitors the response to the lorazepam challenge and to ECT.
APPLY AND CONSOLIDATE	Four worked cases: schizoaffective versus mood-with-psychosis by the two-week gate, a delusional-disorder read against paranoid schizophrenia, a catatonia worked through the lorazepam challenge, and a malignant-catatonia versus NMS emergency. Then the master mnemonic (place on the spectrum by duration, mood-loading and delusion-type, then the delusional syndromes, then catatonia), answer-free retrieval prompts, and the three-branch synthesis map to redraw from memory.

References

The content is grounded in the standard clinical and descriptive-psychopathology texts (the source hierarchy below), which anchor the settled facts on the criteria, the delusional syndromes and catatonia; the nosology follows ICD-11 (CDDR) primary with DSM-5-TR cross-mapped. Every diagnostic criterion, duration threshold, eponym attribution and named figure has been checked against these sources. Each journal PMID here was verified against PubMed this build, matched on title, first author and year; any identifier that did not resolve to the cited paper was corrected or dropped rather than guessed. The classic historical papers that seed the syndromes (Kasanin, Langfeldt, Conrad, Kahlbaum, Capgras and Reboul-Lachaux, Courbon and Fail, Stauder, Schneider) have no stable PubMed record and are cited by author, title and year.

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PART IV

IV

Mood Disorders: Classification, Depressive and Bipolar Syndromes, Neurobiology

Mood disorder defined and divided: the depressive and bipolar syndromes, their course, and the biology beneath them.

01 Mood disorders: classification and nosology

02 Depressive disorders: clinical syndromes

03 Bipolar and related disorders

04 Mood disorders: neurobiology and aetiology

05 Discriminate, apply and consolidate

PAPER II

Mood disorders: classification, depressive and bipolar syndromes, neurobiology

Five sections · one complete notes document

This material opens the mood block, gathering into one document how the mood disorders are classified, the full set of depressive and bipolar clinical syndromes, the guideline-anchored management of each, and the neurobiology that underlies them. The first band is **classification and nosology**: the ICD-11 episode-based architecture and how it cross-maps to ICD-10 and DSM-5-TR, the unipolar-versus-bipolar distinction and the detailed Akiskal bipolar spectrum, the historical Kraepelinian dichotomy, and the epidemiology. The second band is **depressive disorders**: major depressive disorder and its criteria and specifiers, persistent depressive disorder, the melancholic, atypical, psychotic and catatonic subtypes, seasonal affective disorder, peripartum depression and premenstrual dysphoric disorder, and the guideline-anchored management of depression. The third band is **bipolar and related disorders**: bipolar I and the manic episode, bipolar II and hypomania, cyclothymia, mixed features and rapid cycling, course and prognosis and the special populations, the management of bipolar disorder across acute mania, bipolar depression and maintenance, and the interleaved differential that separates the mood syndromes. The fourth band is **neurobiology and aetiology**: the monoamine, HPA-axis, neurotrophic, glutamatergic, inflammatory and genetic hypotheses, each taught with its evidence and its limitation, the neuroimaging and limbic-cortical circuit model, and the psychological theories. The examinable skill is discrimination and reasoning: to place a mood presentation by episode type and polarity, to tell the syndromes and subtypes apart, to reach for the right guideline-recommended treatment, and to explain the mechanisms without overclaiming them.

HOW TO USE THESE NOTES

Read the five bands as one continuous account of mood disorder from its classification through the syndromes and their management to the underlying neurobiology. The **classification** band gives the episode-based map and the detailed Akiskal spectrum that orients everything after it. The **depressive** and **bipolar** bands teach each syndrome against its mimics, and every named syndrome and subtype ends with a **Good to remember** box giving what it is, the core criteria or the one discriminating feature, and the one number or eponym to hold; each of those two bands closes with a guideline-anchored **management** topic led by the CANMAT guidelines and stating the Indian Psychiatric Society and NICE positions, on the where-to-treat, target-by-phase, modes-of-treatment spine. The **neurobiology** band teaches each hypothesis with both its supporting evidence and its limitation, so no mechanism is overclaimed. Figures declare one axis and code it in colour: **petrol** marks structure and the neutral case, **coral** marks the trap or the danger, and **marigold** highlights the number or eponym to hold. Several boundaries are worth stating up front: the individual drug pharmacology, the treatment-resistant algorithms and the pharmacotherapy detail are taught in the Mood disorders: pharmacotherapy notes and are cross-referenced here rather than repeated; the HPA-axis mechanics, the monoamine pathway anatomy and the neuroimaging principles live in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes, applied here to mood; the mood-with-psychotic-features boundary against schizoaffective disorder and the catatonia entity live in the Other psychotic disorders, delusional syndromes and catatonia notes, which cross-refers back to the mood-episode criteria owned here; the technique of electroconvulsive therapy lives in the ECT and neurostimulation notes; clinical suicide risk assessment lives in the Somatic-symptom, sexual, impulse-control disorders and suicide notes; and the raw descriptive definitions of the mood symptoms live in the Psychometry, Assessment and Descriptive Psychopathology notes. This is doctor-facing revision, so the full technical vocabulary is used, and every criterion, threshold, dose-free guideline recommendation, and number is verified against a source.

Mood disorders: classification and nosology

1 · Orientation: classifying the mood disorders

Why this matters. The mood disorders are the largest single block in the affective syllabus, and they are also the block most vulnerable to a snapshot error: a clinician who diagnoses from how the patient looks today, without the longitudinal history, will call a bipolar depression "major depression" and start the wrong drug. The whole modern nosology is built to stop exactly that. It is **episode-based**: you name the mood **episode** first, then let the lifetime pattern of episodes name the disorder. This orienting topic builds the **classification of mood** disorders as one map, seeds the master mnemonic that chains the entire chapter, and hands the reader the two master axes, polarity and episode type, against which everything downstream is placed.

The governing idea, which the examiner rewards over and over: everything in this family is a disturbance of mood that persists over time, so you never separate the disorders by "is the mood low or high" at a single visit but by which episodes have occurred across the person's life and in what pattern. Nosology here is given ICD-11 primary (the current CDDR grouping "mood

disorders"), with the DSM-5 (the DSM-5-TR) labels cross-mapped, because the two systems split the family into different chapters and the difference is itself examinable; ICD-10 is flagged where the exams still lean on it. The raw descriptive definitions of the individual mood symptoms, and the rating scales, are owned by the Psychometry, Assessment and Descriptive Psychopathology notes and are cross-referenced here, not re-derived; this chapter is the canonical home of the depressive-episode and manic-episode diagnostic criteria themselves.

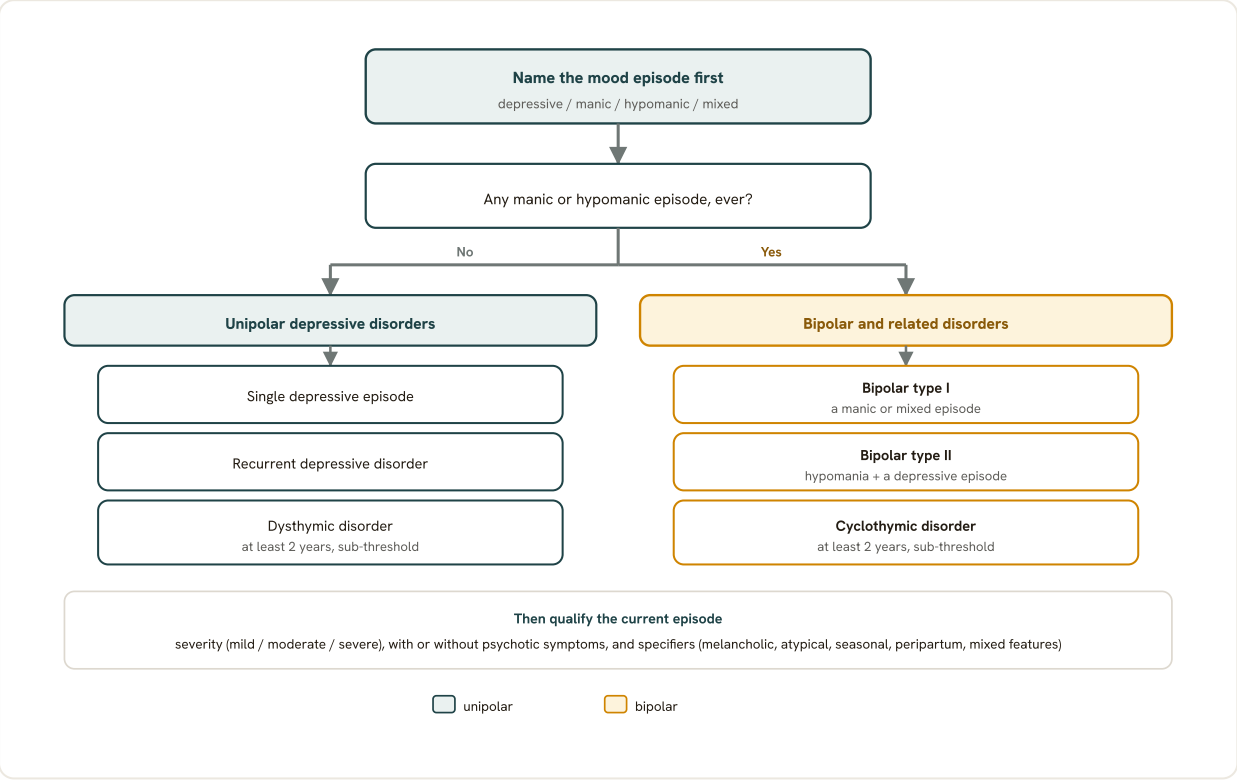


Fig 11.1 The ICD-11 episode-based mood-classification map. Name the current mood episode first, then split on polarity: any lifetime manic or hypomanic episode moves the patient into the bipolar column permanently, otherwise the illness is unipolar. The lifetime pattern of episodes then names the disorder, and a severity, psychotic-symptom and specifier layer is added to the current episode.

1.1 The episode is the atom: mood disorders are built on episodes

The single most important structural fact is that in ICD-11 the **mood episode** is the building block of the diagnosis, not a diagnosis in its own right. The ICD-11 CDDR states it plainly: "mood episodes are not independently diagnosable entities, and therefore do not have their own diagnostic codes"; rather, they are the components out of which the bipolar and depressive disorders are assembled (ICD-11 CDDR). There are four episode types the reader must hold: the depressive episode, the manic episode, the hypomanic episode and the mixed episode. A disorder is then defined by which of these episodes have occurred and how they pattern over time (ICD-11 CDDR; Kaplan & Sadock 2024). This is why the correct diagnostic move is always two-step: identify the episode in front of you, then interrogate the lifetime history for the episodes that reclassify it.

RULE **Name the episode first, then let the pattern of episodes name the disorder.** Depressive, manic, hypomanic or mixed is the atom; the lifetime pattern is the molecule.

TRAP **Do not diagnose a "disorder" from a cross-sectional snapshot.** A depressed patient today is a depressive episode; whether the disorder is unipolar or bipolar is decided only by the past history of a hypomanic or manic episode.

1.2 The four mood episodes and their duration thresholds

Before the disorders come the episodes, and the examiner tests the duration threshold of each as a reflex fact. A **depressive episode** requires the core mood or anhedonia change plus associated symptoms persisting for a period of **at least two weeks** (ICD-11 CDDR; DSM-5-TR major depressive episode). A **manic episode** is an extreme elevated, expansive or irritable mood with increased activity or energy lasting **at least one week** (or any duration if hospitalisation is needed), and by its severity it causes marked impairment, needs intensive treatment, or carries psychotic features (ICD-11 CDDR; DSM-5-TR). A **hypomanic episode** is the same symptom picture at lesser severity, without marked impairment, hospitalisation or psychosis; ICD-11 requires it "for at least several days", while DSM-5-TR sets a firm floor of **at least four consecutive days** (ICD-11 CDDR; DSM-5-TR). A **mixed episode** is prominent manic and depressive symptoms occurring simultaneously or alternating rapidly within the same episode (ICD-11 CDDR). The full criterion lists for the depressive and manic episodes are laid out in their own topics that follow; the point here is that the episode, with its threshold, is the unit of classification.

at least 2 wk	at least 1 wk	at least 4 days	several days
DEPRESSIVE EPISODE	MANIC EPISODE	HYPOMANIC (DSM-5-TR)	HYPOMANIC (ICD-11)

GOOD TO REMEMBER

- **Depressive episode:** low mood or anhedonia plus associated symptoms for **at least two weeks**; the depressive atom; criteria taught in full in this chapter.
- **Manic episode:** elevated, expansive or irritable mood with raised activity for **at least one week** (any duration if hospitalised), with marked impairment, need for intensive treatment, or psychosis; the defining episode of bipolar type I.
- **Hypomanic episode:** the manic symptom picture below the impairment or psychosis threshold; ICD-11 "several days", DSM-5-TR **at least four days**; the defining episode of bipolar type II.
- **Mixed episode:** prominent manic and depressive symptoms simultaneously or rapidly alternating within one episode; places the patient in bipolar type I.

1.3 Master axis one, polarity: the unipolar versus bipolar split

The first and most consequential axis is **polarity**: has the person ever crossed into the manic or hypomanic pole. On one side sit the unipolar depressive disorders, where the lifetime course contains depressive episodes only. On the other sit the **bipolar spectrum** disorders, where at least one manic or hypomanic episode has occurred (Kaplan & Sadock 2024). This single question splits the entire block, because it decides the treatment logic: an antidepressant is a reasonable first move in unipolar depression but is the classic error in a bipolar depression, where it risks a switch and is not the anchor of care. ICD-11 encodes the split at the top level of its grouping, dividing "mood disorders" into **bipolar and related disorders** and **depressive disorders** (ICD-11 CDDR). The detailed soft-bipolar gradation between the two poles, the Akiskal spectrum, is

developed in the unipolar-versus-bipolar-spectrum topic that follows; here it is enough to hold that polarity is the master cut.

TRAP **Never close a depression assessment without screening for a past hypomanic or manic episode.** An unscreened past hypomania is what silently reclassifies a "unipolar" depression as bipolar type II.

1.4 Master axis two, episode type and pattern: how the pattern names the disorder

Given polarity, the second axis reads the **episode type and its pattern over time**, and this is what actually assigns the diagnostic label. Within the unipolar depressive disorders, a first and only depressive episode is single episode depressive disorder, whereas a history of at least two depressive episodes separated by several months of relative euthymia is recurrent depressive disorder (ICD-11 CDDR). Within the bipolar disorders, one lifetime manic or mixed episode is sufficient for bipolar type I disorder (a depressive episode is not required), while bipolar type II disorder requires at least one hypomanic and at least one depressive episode with no history of a manic or mixed episode (ICD-11 CDDR; DSM-5-TR). Two chronic, sub-threshold patterns close the family: cyclothymic disorder, a persistent instability of hypomanic and depressive periods over **two years or more** that never meets full episode criteria and never includes a manic or mixed episode, and dysthymic disorder (persistent depressive disorder), a persistent depressed mood lasting **two years or more** that stays below the full depressive-episode threshold for most of that time (ICD-11 CDDR).

RULE **One manic or mixed episode is bipolar type I, full stop.** Bipolar type II needs a hypomania plus a depression and no manic or mixed episode ever; a manic episode anywhere in the history overrides the type II label.

GOOD TO REMEMBER

- **Single episode depressive disorder (6A70):** one lifetime depressive episode, no manic or hypomanic history; becomes recurrent on the second episode.
- **Recurrent depressive disorder (6A71):** **at least two** depressive episodes separated by several months of relative euthymia; the unipolar recurrent form (DSM-5-TR: major depressive disorder, recurrent).
- **Bipolar type I disorder (6A60):** at least one lifetime **manic or mixed** episode; a depressive episode is not required for the diagnosis; the discriminator is the full manic episode.
- **Bipolar type II disorder (6A61):** at least one **hypomanic** and at least one **depressive** episode, with **no** manic or mixed episode ever; the discriminator is a hypomania in a patient who has never been fully manic.
- **Cyclothymic disorder (6A62):** mood instability of hypomanic and depressive periods over **two years or more**, never meeting full episode criteria, no manic or mixed episode; the sub-threshold bipolar pattern.
- **Dysthymic disorder (6A72):** persistent depressed mood for **two years or more** below the full depressive-episode threshold; the sub-threshold unipolar pattern (DSM-5-TR: persistent depressive disorder).

1.5 Master axis three and four, severity and the psychotic and other specifiers

Once polarity and episode pattern have named the disorder, two further axes describe the current episode. **Severity** grades the current depressive episode as mild, moderate or severe on the number and intensity of symptoms and the impact on functioning, with the rule that a mild depressive episode by definition carries no psychotic symptoms (ICD-11 CDDR). The **psychotic specifier** then marks a moderate or severe episode as "with" or "without psychotic symptoms" (delusions or hallucinations), the mood-congruent guilt, poverty, nihilistic and persecutory delusions of depression being the classic examples (ICD-11 CDDR). Other examinable specifiers layered on top include the melancholic, atypical, seasonal, peripartum, mixed-features and rapid-cycling patterns, each of which steers prognosis and treatment. The full handling of mood with psychotic features, and the boundary with schizoaffective disorder, is cross-referenced to the Other psychotic disorders, delusional syndromes and catatonia notes.

PEARL

ICD-11 and DSM-5-TR both let an antidepressant-emergent (or ECT-, light- or rTMS-emergent) manic or hypomanic syndrome that **persists beyond the physiological effect of the treatment** count as a true manic or hypomanic episode, and therefore reclassify the patient as bipolar. A switch that resolves the moment the drug is stopped does not (ICD-11 CDDR; DSM-5-TR).

1.6 The three frameworks cross-mapped: ICD-11, DSM-5-TR and ICD-10

The reader needs to hold all three systems (the icd-11, the dsm-5 and the icd-10) because Indian examinations still cite ICD-10 alongside the newer manuals. ICD-11 gathers everything under a single superordinate "mood disorders" grouping split into bipolar-and-related and depressive disorders. DSM-5-TR, by contrast, breaks the same content into **two separate chapters**, "Bipolar and Related Disorders" and "Depressive Disorders", and deliberately places the bipolar chapter as a bridge between schizophrenia and depression (Kaplan & Sadock 2024; DSM-5-TR). ICD-10 used the older label "mood [affective] disorders" (F30 to F39) with "bipolar affective disorder" as a single unified category and no separate bipolar type II code, and it grouped the recurrent depressive and persistent (dysthymia, cyclothymia) forms alongside. The map below is the object to memorise: read each row across the three columns and note where the systems diverge.

ENTITY (CONCEPT)	ICD-11	DSM-5-TR	ICD-10 (STILL EXAMINED)
Superordinate grouping	**Mood disorders (one grouping, two sub-blocks)**	Two chapters: Bipolar and Related; Depressive	Mood [affective] disorders (F30 to F39)
Single depressive episode	Single episode depressive disorder (6A70)	Major depressive disorder, single episode	**Depressive episode (F32)**
Recurrent unipolar depression	Recurrent depressive disorder (6A71)	Major depressive disorder, recurrent	Recurrent depressive disorder (F33)
Chronic low-grade depression	Dysthymic disorder (6A72)	**Persistent depressive disorder (dysthymia)**	Dysthymia (F34.1)

ENTITY (CONCEPT)	ICD-11	DSM-5-TR	ICD-10 (STILL EXAMINED)
Manic-pole disorder, full mania	Bipolar type I disorder (6A60)	Bipolar I disorder	**Bipolar affective disorder (F31); no separate type**
Hypomania plus depression	Bipolar type II disorder (6A61)	Bipolar II disorder	**No distinct code (subsumed under F31)**
Chronic mood instability	Cyclothymic disorder (6A62)	Cyclothymic disorder	Cyclothymia (F34.0)

The mood-classification cross-map: the same clinical entities as they are coded across the three frameworks; the highlighted cell flags where a system diverges most from the others.

1.7 Two entities the DSM parks with depression: DMDD and PMDD

Two categories sit in the DSM-5-TR Depressive Disorders chapter that the reader should place now and expand later. Disruptive mood dysregulation disorder is a childhood-onset presentation of chronic, severe persistent irritability with frequent temper outbursts, placed among the depressive disorders to capture children who would otherwise be over-diagnosed as bipolar; it is a differential guard rather than a bipolar entity (DSM-5-TR). Premenstrual dysphoric disorder is a luteal-phase mood disturbance recurring across most menstrual cycles and remitting after menses; DSM-5-TR lists it as a depressive disorder, while ICD-11 codes it in the genitourinary chapter and cross-lists it under mood disorders for reference (ICD-11 CDDR; DSM-5-TR). Both are named here only to fix their place on the map; their criteria are developed in their own topics.

1.8 The classification map assembled: reading a stem in order

The axes chain into an ordered walk, and reading them in this order is the fastest route through any placement stem. First, characterise the current **episode** and confirm it meets threshold (depressive at two weeks, manic at one week, hypomanic at four days or several days, or mixed). Second, ask the **polarity** question: has there ever been a manic or hypomanic episode, which pulls the patient off the unipolar track and onto the bipolar spectrum. Third, read the **pattern**: one versus recurrent for the depressive disorders; manic-or-mixed (type I) versus hypomanic-plus-depressive (type II) for the bipolar disorders; and the two-year sub-threshold patterns (cyclothymia, dysthymia) for the chronic low-grade presentations. Fourth, layer the **severity and specifiers** (psychotic, melancholic, atypical, seasonal, peripartum, mixed-features, rapid-cycling) onto the named disorder. This ordered map is the concept figure for the whole chapter, Fig 11.1, the ICD-11 episode-based mood-classification tree.

WORKED EXAMPLE

A 26-year-old woman presents with a three-week depressive episode: low mood, anhedonia, poor sleep, hopelessness. Walk the map. The episode meets threshold (over two weeks). Now the polarity question: on careful history she describes a five-day period last year of reduced need for sleep, overactivity, rapid speech and uncharacteristic confidence that friends noticed but that caused no hospitalisation, no psychosis and no marked impairment, a hypomanic episode. She has therefore had a hypomanic plus a depressive episode and no manic or mixed episode: the diagnosis is bipolar type II disorder, currently in a depressive episode, not major depressive disorder. Miss the hypomania on the snapshot and you would start an antidepressant alone, the classic bipolar-depression error.

MNEMONIC

"EPISODE first, then POLARITY; CLASSIFY, DEPRESS, then BIPOLAR; MANAGE by phase; MECHANISM with its limit."

The master chain for the whole chapter. Start from the mood EPISODE and its threshold, then split on POLARITY (unipolar versus bipolar spectrum). Then work the chapter in order: CLASSIFY the family on this map, then the DEPRESSive syndromes (single, recurrent, dysthymia, the specifiers), then the BIPOLAR syndromes (type I, type II, cyclothymia and the Akiskal spectrum). Then MANAGE by phase, guideline-anchored (acute, continuation, maintenance for depression; acute mania, bipolar depression, maintenance for bipolar). Finish on the neurobiology, where every MECHANISM is held together with its LIMITation (monoamine, HPA, neurotrophic, gene-environment). Episode, then polarity, is the two-beat core the examiner rewards.

1.9 Management and neurobiology: where they live in the chapter

Management in this chapter is taught guideline-first, led by the CANMAT recommendations with the Indian Psychiatric Society (the IPS guidelines) and NICE positions stated alongside, and organised on a LOCUS (where to treat), FOCUS (the phase target) and MODUS (the modes of treatment) spine (CANMAT 2016; CANMAT 2018). Those recommendations are developed in the two management topics; the guideline-level headline to carry from the outset is that unipolar depression is treated by phase (acute, continuation, maintenance) with a second-generation antidepressant plus evidence-based psychotherapy first-line, while bipolar disorder is treated by presentation (acute mania, bipolar depression, maintenance) around lithium and the atypical antipsychotics and anticonvulsant mood stabilisers, with antidepressant monotherapy avoided (CANMAT 2016; CANMAT 2018). The deep drug pharmacology, the full dosing, the adverse-effect profiles and the treatment-resistant algorithms are owned by the Mood disorders: pharmacotherapy notes and are cross-referenced, not duplicated here. The neurobiology band teaches each hypothesis with its supporting evidence and its limitation; the HPA-axis mechanics, the monoamine pathway anatomy and the neuroimaging principles are grounded in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes, with the mood application taught here.

INDIA

Mood disorders are among the commonest presentations in Indian outpatient psychiatry, and the National Mental Health Survey of India 2015 to 2016 (Gururaj et al. 2016) remains the anchor epidemiological source cited in the exams; depressive disorders were among the most prevalent categories it identified. For severe, psychotic or treatment-resistant depression and for acute mania, ECT is widely available and heavily used across Indian teaching hospitals, a point returned to in the management and the ECT and neurostimulation notes. This chapter is largely generic; where any brand is named it leads with the Indian brand, but drug branding belongs to the Mood disorders: pharmacotherapy notes.

GOOD TO REMEMBER

- **Classification of mood disorders:** ICD-11 superordinate "mood disorders" split into bipolar-and-related and depressive disorders; DSM-5-TR splits the same content into two separate chapters; ICD-10 uses F30 to F39.
- **Episode-based architecture:** the mood episode (depressive, manic, hypomanic, mixed) is the atom; it has no code of its own; the lifetime pattern of episodes names the disorder.
- **Polarity:** the master split; depressive episodes only is unipolar, any manic or hypomanic episode places the patient on the bipolar spectrum.
- **Diagnostic order:** episode and threshold, then polarity, then pattern, then severity and specifiers; the map is Fig 11.1.

HOLD THIS

Name the mood episode first (depressive, manic, hypomanic or mixed), split on polarity (unipolar versus bipolar spectrum), and only then let the lifetime pattern of episodes name the disorder: the modern nosology is episode-based, never a snapshot.

2 · ICD-11 changes in mood disorders

Nosology is examined every sitting, and the mood chapter is where the classifications diverge most usefully. The **icd-11 changes** in mood disorders are not cosmetic: they reorganise the whole block around the mood episode as the unit of definition, they re-tool how a mixed presentation is coded, and they tighten the severity and psychotic-symptom qualifiers. This topic teaches what actually moved from ICD-10 to ICD-11, cross-maps to DSM-5-TR, and flags where Indian exams and clinics still sit on the older categorical structure.

One warning up front. A common revision error is to import the DSM change into ICD-11. DSM-5 deleted its old mixed episode and turned mixed states into a specifier; ICD-11 did something different. Read the two systems as distinct so you do not answer an ICD-11 stem with a DSM-5 fact. The raw descriptive definitions of the individual mood symptoms and the rating scales are carried in the Psychometry, Assessment and Descriptive Psychopathology notes; here we teach the classification and the discrimination.

2.1 The episode-based architecture: the mood episode as the building block

The core move. ICD-11 defines the mood disorders from a small set of **mood episode** descriptions and then builds the disorders on top of them, an **episode-based architecture** (ICD-

11 CDDR 2024). There are four episode types: the depressive episode, the manic episode, the mixed episode and the hypomanic episode. A disorder is then a pattern of these episodes over time: a single depressive episode, recurrent depressive disorder, bipolar type I (defined by at least one manic or mixed episode) or bipolar type II (a hypomanic episode plus a depressive episode). DSM-5-TR made the same architectural shift, folding the episode definitions into the disorder criteria to streamline bedside use (DSM-5-TR 2022).

RULE **Episode first, disorder second.** In ICD-11 you diagnose the current mood episode, then name the disorder from the lifetime episode pattern.

2.2 The mixed presentation: ICD-11 keeps a mixed episode, DSM-5 does not

The pivot fact. ICD-11 retains a standalone mixed episode as one of its four episode types (ICD-11 CDDR 2024). A mixed episode is diagnosed when several prominent manic and several prominent depressive symptoms occur simultaneously, or alternate rapidly, for most of the day nearly every day for at least about two weeks; it qualifies bipolar type I disorder (code 6A60 current episode mixed) and cross-walks to ICD-10 F31.6, bipolar affective disorder current episode mixed. DSM-5-TR, by contrast, deleted the old DSM-IV mixed episode and replaced it with a **mixed features** specifier that is applied to a depressive, manic or hypomanic episode when at least three symptoms of the opposite pole are present through most of the episode (DSM-5-TR 2022). So the two systems reach a similar clinical idea by opposite routes: ICD-11 by a dedicated episode, DSM-5 by a specifier.

COMMON TRAP

Do not say ICD-11 abolished the mixed episode. That is the DSM-5 change. ICD-11 kept a mixed episode; what disappears is the ICD-10 idea of a separate residual mixed affective category divorced from the bipolar course.

2.3 Mixed features as a qualifier, not a separate category

How to hold both systems. The exam-safe formulation is that a **mixed features** presentation is a qualifier on an episode, not a free-standing mixed disorder. In DSM-5-TR it is literally the "with mixed features" specifier on a manic, hypomanic or major depressive episode. In ICD-11 the same clinical reality is captured either as a mixed episode within a bipolar disorder or, for subthreshold contrapolar symptoms, through the symptomatic specifiers attached to the current episode. Either way the mixed state is coded onto the episode, never as an orphan diagnosis floating outside the mood-episode framework.

RULE **Mixed = a qualifier on an episode.** In ICD-11 a mixed presentation attaches to the episode within a bipolar disorder; it is not a separate "mixed disorder".

TRAP **ICD-10 logic under ICD-11.** Applying the old ICD-10 mixed-episode reasoning as if it were an independent category, rather than treating the mixed state as an episode-level qualifier, is the classic error.

2.4 The depressive episode: prominence and persistence

The threshold. An ICD-11 depressive episode requires a cluster of characteristic symptoms present nearly every day for **at least two weeks**, drawn from an affective cluster (depressed mood, or markedly reduced interest or pleasure), a cognitive-behavioural cluster (reduced concentration, worthlessness or guilt, hopelessness, recurrent thoughts of death or suicidality) and a neurovegetative cluster (disrupted sleep, appetite or weight change, psychomotor change, reduced energy) (ICD-11 CDDR 2024). The chronic depressive forms are coded separately: ICD-11 dysthymic disorder is a sub-threshold condition (persistent depressed mood for at least two years with additional, usually milder, symptoms and no full depressive episode during the first two years), whereas a full-threshold depressive episode that itself persists for two years or more is flagged by the "with persistent depressive episode" specifier; the two are opposites, and dysthymia is developed in the persistent depressive disorder topic. The prominence-and-persistence framing, symptoms both prominent enough and present nearly every day across the two-week window, is what distinguishes an episode from a normal reaction to adversity.

at least two weeks	at least 1 week	at least several days
DEPRESSIVE EPISODE DURATION	MANIC EPISODE DURATION	HYPOMANIC EPISODE DURATION

2.5 Severity grading and the psychotic-symptoms qualifier

The two axes. ICD-11 grades the current depressive episode as mild, moderate or severe on the number and severity of symptoms and the functional impact. Superimposed on that, moderate and severe episodes are further qualified as **without psychotic symptoms** or with psychotic symptoms, meaning the presence or absence of delusions or hallucinations (ICD-11 CDDR 2024). By definition a mild depressive episode carries no psychotic symptoms. This decouples severity from psychosis and is a genuine change from ICD-10, where the presence of psychotic symptoms in a depressive episode automatically forced the episode to be rated as severe. The mood-congruent versus mood-incongruent quality of those psychotic symptoms, and the schizoaffective boundary, belong to the Other psychotic disorders, delusional syndromes and catatonia notes.

> **PEARL**
> In ICD-11 you can have a moderate depressive episode with psychotic symptoms; in ICD-10 that combination did not exist, because psychosis pushed the episode straight to severe. This is a favourite single-best-answer discriminator.

2.6 The manic and hypomanic episodes, and the bipolar backbone

The bipolar definers. The manic episode requires euphoric, irritable or expansive mood with increased activity or energy, most of the day nearly every day, for **at least 1 week** (or any duration if hospitalisation is needed, or shortened by effective treatment), plus several additional symptoms; one manic or mixed episode is sufficient to define bipolar type I disorder. The hypomanic episode is the milder, non-impairing, non-psychotic form lasting **at least several days**, and a hypomanic episode with a depressive episode defines bipolar type II disorder (ICD-11 CDDR 2024). A useful ICD-11 detail: if a patient has had past manic or mixed episodes, the

one-week duration is not required to call a current manic episode. The detailed Akiskal soft-bipolar spectrum that sits behind these categories is developed in the unipolar-versus-bipolar-spectrum topic.

TRAP **Calling a hypomania a mania.** Impairment, psychosis or a need for hospitalisation moves the episode out of hypomania; without them, a several-day elevation is hypomanic, and the disorder is bipolar II, not bipolar I.

2.7 Cross-map to DSM-5-TR and the ICD-10 flag

Three-system literacy. DSM-5-TR keeps mixed features as a specifier (at least three opposite-pole symptoms on a manic, hypomanic or major depressive episode) and adds its own changes: the bereavement exclusion was removed from major depressive disorder, and premenstrual dysphoric disorder and disruptive mood dysregulation disorder sit within the depressive disorders (DSM-5-TR 2022). ICD-10, still the working system in many Indian settings and in a good share of exam material, retains the older categorical structure, with the mixed affective state coded F31.6 within bipolar affective disorder and psychosis forcing a severe rating. Knowing which system a stem is written in is half the answer.

FEATURE	ICD-10	ICD-11	DSM-5-TR
Organising unit	Episode plus disorder, loosely linked	**Mood episode as the building block, episode-based architecture**	Episode definitions folded into disorder criteria
Mixed presentation	F31.6 mixed affective episode within bipolar	**Retains a standalone mixed episode (qualifies bipolar I)**	**Mixed episode deleted; "with mixed features" specifier**
Depressive episode duration	At least two weeks	At least two weeks, nearly every day	At least two weeks (major depressive episode)
Severity and psychosis	**Psychosis forces a severe rating**	**Severity and the without psychotic symptoms / with psychotic symptoms qualifier are separate**	Severity and psychotic-features specifier separate
Bipolar II as a named type	Not a distinct category	Bipolar type II disorder present	Bipolar II disorder present
Exam relevance in India	**Still widely used clinically and in question banks**	Increasingly examined; the current WHO system	Cross-mapped; common in MCQ discriminators

The three-system grid: the hit cells are the discriminators most likely to be tested.

INDIA

Many Indian training programmes, case records and question banks still run on ICD-10, so a candidate must hold both the ICD-10 categorical structure and the ICD-11 episode-based architecture in parallel. When a stem quotes an F-code (for example F31.6 or F32), it is an ICD-10 item; when it talks about a mixed episode qualifying bipolar type I or a "moderate depressive episode with psychotic symptoms", it is ICD-11.

MNEMONIC

D-M-M-H

The four ICD-11 mood episodes, in the CDDR order: Depressive, Manic, Mixed, Hypomanic. Hold that the Mixed one survives in ICD-11 but not in DSM-5, and you will not swap the two systems.

GOOD TO REMEMBER

- **Episode-based architecture:** ICD-11 builds mood disorders from four mood episodes (depressive, manic, mixed, hypomanic); diagnose the episode, then the disorder from the lifetime pattern.
- **ICD-11 mixed episode:** retained as a distinct episode type; prominent manic and depressive symptoms together or rapidly alternating; qualifies bipolar type I (6A60 current episode mixed, cross-walks to ICD-10 F31.6).
- **DSM-5-TR mixed features:** the DSM-IV mixed episode was deleted; a "with mixed features" specifier now attaches to a manic, hypomanic or major depressive episode when at least three opposite-pole symptoms are present.
- **ICD-11 depressive episode:** characteristic symptoms nearly every day for at least two weeks across affective, cognitive-behavioural and neurovegetative clusters.
- **Severity and psychosis:** ICD-11 grades mild / moderate / severe and separately flags without psychotic symptoms or with psychotic symptoms; mild has no psychosis; unlike ICD-10, psychosis no longer forces a severe rating.
- **ICD-10 flag:** retains the older categorical structure (F31.6 mixed, psychosis forcing severe), still the working system in many Indian settings.

HOLD THIS

ICD-11 keeps a mixed episode and codes any mixed presentation as a qualifier on an episode within a bipolar disorder; DSM-5 deleted the mixed episode and made mixed features a specifier, so never answer an ICD-11 stem with the DSM-5 abolition.

3 · Unipolar versus bipolar and the Akiskal spectrum

The single most consequential act in assessing any depressed patient is deciding which of two illnesses you are looking at. **Unipolar** disorder has depressive episodes only; **bipolar** disorder has, somewhere in the history, a manic or hypomanic episode. That one fact reorganises the whole clinical picture, the family history, the expected course and, above all, the treatment, because the wrong answer means an antidepressant given alone to a patient who needed a mood stabiliser (Kaplan & Sadock 2024). The exam rewards the resident who can recite the point-by-point contrast and who reflexively screens every depression for a past hypomanic episode.

Beyond the clean unipolar/bipolar dichotomy lies a graded territory. Hagop Akiskal argued that bipolarity is not an on/off category but a continuum, the **bipolar spectrum**, whose milder end (the **soft bipolar** spectrum) shades imperceptibly into what looks like ordinary unipolar depression (Akiskal 2007). This topic lays that whole numbered spectrum out *before* you enter bipolar I proper, so you can see the terrain the diagnosis sits in. The raw descriptive definitions of the mood symptoms and the rating scales referenced here sit in the Psychometry, Assessment and Descriptive Psychopathology notes; the full manic and depressive episode criteria are taught in this chapter's own manic-episode and depressive-episode topics.

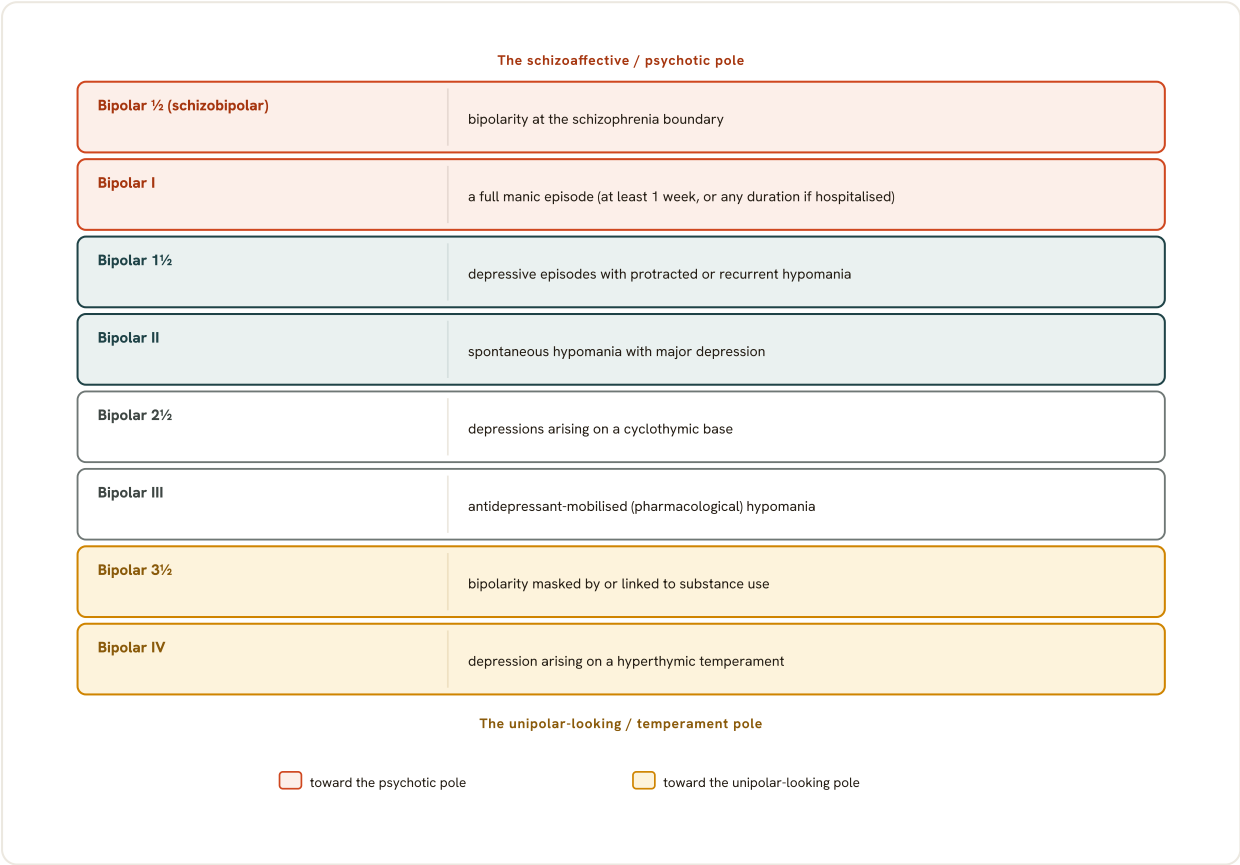


Fig 11.2 Akiskal's soft-bipolar spectrum, laid out before bipolar I proper. Read the fractions as rungs from the schizoaffective and psychotic pole at the top (bipolar one-half, then classic bipolar I) down through the temperament- and trigger-defined softer forms (protracted hypomania, spontaneous hypomania, cyclothymic depressions, antidepressant-mobilised and substance-linked bipolarity) to depression on a hyperthymic temperament, which looks unipolar on the surface. Only bipolar I, bipolar II and cyclothymia are formal ICD-11 categories; the numbered types are a lens for vigilance.

3.1 The definitional dividing line

One question decides it. The boundary is categorical and historical: has the patient *ever* had a manic or hypomanic episode? If yes, the disorder is bipolar and remains bipolar for life, even during a depressive presentation; if no, and only depressive episodes have ever occurred, it is unipolar (major depressive) disorder (Kaplan & Sadock 2024). A manic episode in ICD-11 lasts at least **1 week** (or any duration if hospitalisation is required) and defines bipolar type I disorder; a hypomanic episode is milder, without marked impairment or psychosis, and defines bipolar type II disorder when it occurs with major depression. ICD-11 requires a hypomanic episode to last **at least several days** and does not fix a day-count; DSM-5-TR requires **at least 4 consecutive**

days. The full criteria for both episodes are taught in this chapter's manic-episode and depressive-episode topics.

RULE **Ever high, then bipolar.** A single lifetime manic or hypomanic episode moves the patient into the bipolar column permanently, however depressed they look today.

3.2 Why the distinction is clinical, not academic

Bipolar and unipolar depressions differ across the board. They separate on temperament, sex ratio, age of onset, episode shape and drug response, and Kaplan & Sadock's Table 13.3-8 crystallises the contrast (Kaplan & Sadock 2024). Bipolar depression tends to be earlier in onset, more recurrent with shorter episodes, more often retarded and hypersomnic, and it carries the risk that an antidepressant will flip the mood; unipolar depression tends to be later, less recurrent with longer episodes, more often agitated and insomnic. Hold the discriminators below.

AXIS	BIPOLAR DEPRESSION	UNIPOLAR DEPRESSION
History of mania/hypomania (definitional)	**Yes**	**No**
Temperament and personality	Cyclothymic and extroverted	Dysthymic and introverted
Sex ratio	**Roughly equal**	**More women than men**
Age of onset	Teens, 20s and 30s	30s, 40s and 50s
Postpartum episodes	More common	Less common
Onset of episode	Often abrupt	More insidious
Number of episodes	**Numerous**	**Fewer**
Duration of episode	3 to 6 months	3 to 12 months
Psychomotor activity	**Retardation over agitation**	**Agitation over retardation**
Sleep	Hypersomnia over insomnia	Insomnia over hypersomnia
Response to most antidepressants	**Can induce hypomania or mania**	**Antidepressant effect, low switch risk**
Lithium carbonate	Prophylactic	Adjunctive at best

Kaplan & Sadock Table 13.3-8, differentiating bipolar from unipolar depressions. The italicised discriminators are the ones examiners test; the switch risk in the last two rows is why the unipolar/bipolar call changes management.

TRAP **Never diagnose bipolar II without a hypomanic episode.** Recurrent, early, retarded, hypersomnic depression *suggests* bipolarity, but the diagnosis needs a documented hypomanic episode, not a temperament or a hunch.

3.3 Every depression must be screened for past hypomania

Hypomania hides. Patients rarely volunteer hypomania. It is ego-syntonic, experienced as a welcome rebound from depression or as a pleasant, short-lived good spell, and many bipolar patients recoil from the word ("I am not a manic-depressive") (Kaplan & Sadock 2024). Benazzi and Akiskal advised asking first about *behavioural activation*: distinct sustained periods of

unusual energy, reduced sleep need, racing vivid thinking, over-talkativeness or disinhibition that others noticed, and only then anchoring the mood change to those periods. Collateral history from family is often decisive. Because hypomania is missed, apparent unipolar depression is frequently misclassified bipolar depression, and the screen is the safeguard.

WORKED EXAMPLE

A 26-year-old woman presents with her third episode of low mood since age 19: each time she sleeps 11 hours, feels leaden and slowed, and craves carbohydrate. She denies ever being "manic". On careful screening for behavioural activation she recalls two week-long spells of needing only 4 hours of sleep, redecorating the flat overnight and talking so fast that friends teased her, with no impairment. That is a hypomanic episode. The diagnosis is bipolar type II disorder, and an antidepressant alone would have been the wrong first move.

3.4 The bipolar spectrum and Akiskal's soft bipolar concept

A continuum, not a switch. From 1987, Akiskal propagated the idea of a soft bipolar spectrum, heavily dependent on temperament and managed with mood stabilisers rather than conventional antidepressants (Kaplan & Sadock 2024). The core intuition is that hypomania comes in three empirically recognised patterns, each defining a place on the spectrum: hypomania that *heralds the termination* of a retarded depression (bipolar II), hypomania that *alternates with mini-depressions* (cyclothymic disorder), and hypomania as an *elevated habitual baseline* (hyperthymic temperament) (Kaplan & Sadock 2024). Around these, Akiskal arranged a numbered spectrum of intermediate forms that bridge from schizoaffective territory at one pole to depression on a sunny temperament at the other. Lay the whole thing out before bipolar I so the softer forms are visible as variants, not exceptions.

SPECTRUM TYPE	DEFINING FEATURE	TEMPERAMENT OR TRIGGER
Bipolar one-half (schizobipolar)	**Bipolarity at the schizophrenia boundary; the schizobipolar pole of the affective-to-psychotic continuum**	Overlap with schizoaffective territory (Companion to Psychiatric Studies)
Bipolar I	**Full manic episode (at least 1 week, or any duration if hospitalised)**	Manic diathesis; classic manic-depressive illness
Bipolar one-and-a-half	**Depressive episodes with protracted or recurrent hypomania**	Prolonged hypomanic states
Bipolar II	**Spontaneous hypomania with major depression**	Hypomania heralding the end of a retarded depression
Bipolar two-and-a-half	**Depressions arising on a cyclothymic base (cyclothymic depressions)**	Cyclothymic temperament

SPECTRUM TYPE	DEFINING FEATURE	TEMPERAMENT OR TRIGGER
Bipolar III	**Antidepressant-associated or pharmacological hypomania (hypomania only ever mobilised by treatment)**	Antidepressant, or other somatic antidepressant treatment, as trigger
Bipolar three-and-a-half	**Bipolarity masked by, or associated with, substance use**	Stimulants, alcohol or other substances
Bipolar IV	**Depression arising on a hyperthymic temperament**	Hyperthymic (habitually cheerful, energetic) temperament

Akiskal's numbered soft bipolar spectrum, ordered before bipolar I proper. Read top to bottom as a slide from the schizophrenia boundary, through the classic manic pole, into progressively softer temperament- and trigger-defined forms that look unipolar on the surface (Akiskal 2007; Kaplan & Sadock 2024).

RULE **The spectrum is a screening mandate.** Because bipolarity shades continuously into apparent unipolar depression, every depression is screened for past hypomania, for a bipolar family history and for a hyperthymic or cyclothymic temperament.

3.5 Bipolar III and the temperaments that underwrite the soft forms

Trigger and temperament, not just episodes. Two Akiskal types are pure "reveal" phenomena: bipolar III is bipolarity that surfaces only as hypomania mobilised by an antidepressant (or other antidepressant treatment), and bipolar three-and-a-half is bipolarity tangled with substance use, where stimulants or alcohol both mask and mimic the mood swing (Kaplan & Sadock 2024). The softest end rests on affective temperaments. The cyclothymic temperament swings between cheerful and sad moods and occurs in roughly **4% to 6%** of young adults; the hyperthymic temperament, in which the person is habitually cheerful, energetic and confident, occurs in perhaps **2% to 5%** of young adults and is the base on which bipolar IV depressions arise (Kaplan & Sadock 2024). A depressed patient on a lifelong sunny, driven baseline is bipolar IV, not simply unipolar.

at least several days ICD-11 HYPOMANIC EPISODE	**at least 4 days** DSM-5-TR HYPOMANIC EPISODE	**4% to 6%** CYCLOTHYMIC TEMPERAMENT (YOUNG ADULTS)	**2% to 5%** HYPERTHYMIC TEMPERAMENT (YOUNG ADULTS)

3.6 Clinical use and the controversy of over-inclusiveness

Powerful lens, blunt instrument. The spectrum's clinical value is precisely that it teaches you to look for softer bipolarity behind an apparent unipolar depression: the recurrent early-onset retarded depression with a cyclothymic temperament, a bipolar family history, atypical (hypersomnic, hyperphagic, leaden) features, and antidepressant-mobilised highs are all soft-bipolar signals (Kaplan & Sadock 2024). Atypical features are so common in bipolar, especially bipolar II, that some treat them as markers of soft bipolar disorder, and it is clinically wise to exclude bipolar II before settling on major depressive disorder where hostile-labile features predominate (Kaplan & Sadock 2024). The controversy is over-inclusiveness: a spectrum with fuzzy edges risks re-labelling ordinary unipolar depression, temperament or personality variation as bipolarity, over-diagnosing the condition and exposing patients to mood stabilisers they may

not need. Neither DSM-5-TR nor ICD-11 adopts Akiskal's numbered types as formal categories; the operational nosology recognises only bipolar I, bipolar II and cyclothymic disorder, with the rest captured under "other specified" bipolar and related disorder. The spectrum is a heuristic for vigilance, not a licence to diagnose bipolarity from temperament alone.

COMMON TRAP

Treating an apparent unipolar depression that is really soft bipolar with an antidepressant alone. In bipolar depression, an antidepressant can induce hypomania, mania, mixed states or increased cycling; the deep pharmacology and the bipolar-depression treatment sit in the Mood disorders: pharmacotherapy notes, but the screening reflex belongs here.

PEARL

Hypomania "tends to recur (happiness does not)." A recurrent, distinct, ego-syntonic high, especially one that ends a retarded depression or is mobilised by an antidepressant, is the soft-bipolar signal that reclassifies the depression (Kaplan & Sadock 2024).

MNEMONIC

HALF-STEPS UP THE SPECTRUM

Read the fractions as rungs: bipolar one-half (schizobipolar) sits below bipolar I (mania); one-and-a-half is protracted hypomania; II is spontaneous hypomania with depression; two-and-a-half is cyclothymic depressions; III is antidepressant-mobilised hypomania; three-and-a-half is substance-linked bipolarity; IV is depression on a hyperthymic temperament.

INDIA

In Indian practice the soft-bipolar signal that changes management most often is the missed antidepressant-mobilised hypomania (Akiskal's bipolar III): a "treatment-resistant" or repeatedly relapsing depression that briefly brightened, over-brightened, on each antidepressant trial. Careful behavioural-activation questioning and family collateral, rather than a new drug, is what reclassifies it. The formal categories used are the ICD-11 ones (bipolar type I, bipolar type II, cyclothymic disorder); the numbered Akiskal types are taught as a lens, not coded as diagnoses.

GOOD TO REMEMBER

- **Unipolar disorder:** depressive episodes only, no lifetime mania or hypomania; discriminator is the negative hypomania screen; hold "depression only."
- **Bipolar disorder:** at least one lifetime manic (bipolar I) or hypomanic (bipolar II) episode; discriminator is the ever-high history; hold that one manic/hypomanic episode fixes the diagnosis for life.
- **Bipolar type I:** full manic episode; discriminator is mania lasting at least 1 week (or any duration if hospitalised); hold the 1-week manic threshold.
- **Bipolar type II:** spontaneous hypomania plus major depression; discriminator is a documented hypomanic episode without a full manic episode; hold "hypomania at least 4 days (DSM-5-TR), at least several days (ICD-11)."
- **Bipolar spectrum:** the continuum from strict unipolar to bipolar I; discriminator is graded rather than categorical bipolarity; hold Akiskal as the eponym.
- **Soft bipolar spectrum (Akiskal):** the milder end, temperament-driven, mood-stabiliser-managed; discriminator is bipolarity behind apparent unipolar depression; hold the numbered types one-half through IV.
- **Bipolar III:** antidepressant-associated (pharmacological) hypomania; discriminator is hypomania only ever mobilised by treatment; hold "antidepressant as trigger."
- **Bipolar IV:** depression on a hyperthymic temperament; discriminator is a lifelong cheerful, energetic baseline; hold the hyperthymic-temperament prevalence 2% to 5% of young adults.

HOLD THIS

Unipolar means depressive episodes only; a single lifetime manic or hypomanic episode makes it bipolar for life, so screen every depression for past hypomania, a bipolar family history and a hyperthymic or cyclothymic temperament before you commit to a unipolar diagnosis or an antidepressant.

4 · The Kraepelinian dichotomy and historical concepts

Why this matters. The whole modern nosology of the functional psychoses rests on one nineteenth-century decision: that **manic-depressive insanity** and dementia praecox are two separate diseases. That decision, the **kraepelinian** dichotomy, is the founding **historical concept** of the field, and the examiner rewards two things about it: that it was drawn on **course and outcome**, not on the cross-sectional symptom picture, and that a century of genetics and phenomenology has since blurred the line it drew. Getting both halves right, the origin and the erosion, is the whole of this topic.

This is a history-and-concepts topic, so it is taught around the people and the ideas, but with the exam-relevant discriminator kept sharp throughout: what each contributor actually claimed, and the one fact to hold about each. It is placed as the opener of the mood block because it explains why the block is organised by longitudinal pattern at all. The raw descriptive definitions of the mood symptoms and the rating scales are owned by the Psychometry, Assessment and Descriptive Psychopathology notes; the mood-with-psychotic-features presentations and the schizoaffective boundary are developed in the Other psychotic disorders, delusional syndromes and catatonia notes and are only sketched here as the place where the dichotomy breaks down.

4.1 Kraepelin's move: dividing the functional psychoses by course, not cross-section

The central figure in the history of psychiatric nosology is Emil Kraepelin, professor of psychiatry in Heidelberg from 1891 and in Munich from 1903 (Kaplan & Sadock 2024). Kraepelin had little use for theory or morbid anatomy and placed the diagnostic interest of psychiatry at the bedside, above all on the **course and outcome** of the illness (Kaplan & Sadock 2024). On that basis he stated, in the sixth edition of his textbook in 1899, that the two great endogenous diseases were manic-depressive insanity, a mood disorder that ran an episodic course with recovery between episodes, and dementia praecox, a progressive deteriorating illness of young onset later renamed schizophrenia by Bleuler (Kaplan & Sadock 2024; Companion 2010). The decisive point, and the one the examiner tests, is that he separated them not by how they looked on any one day, since both could show psychosis, but by their **longitudinal trajectory**: episodic with inter-episode recovery on the one side, progressive downhill deterioration on the other (Tasman 2015).

RULE **Kraepelin divided the functional psychoses by course, not by cross-section.** Episodic illness with recovery between episodes became manic-depressive insanity; progressive deterioration became dementia praecox.

MNEMONIC

"COURSE, not the CROSS-SECTION."

Kraepelin's whole innovation in one line. Two patients can look identical on the day you meet them, both psychotic, both agitated; what tells the diseases apart is the shape of the illness over years. Recover and relapse means manic-depressive insanity; grind steadily downhill means dementia praecox. When a stem asks what Kraepelin used to draw the dichotomy, the answer is course and outcome.

4.2 Manic-depressive insanity: what Kraepelin actually meant by it

A common trap is to read Kraepelin's manic-depressive insanity as the modern "bipolar disorder". It is not. Kraepelin's concept was deliberately broad: it took in the whole domain of periodic and circular insanity, simple mania, hypomania and the greater part of what was then called melancholia, and crucially it grouped together all severe recurrent mood illness **regardless of polarity**, so that a person with recurrent severe depression and no mania at all still fell inside manic-depressive insanity (Kaplan & Sadock 2024). In other words, Kraepelin lumped what modern systems split into unipolar and bipolar into a single unified disease, unified by its episodic, recovering course. Holding this is what lets the reader see why the later unipolar-bipolar split (4.4) was a genuine division of Kraepelin's category, not a footnote to it.

TRAP **Kraepelin's manic-depressive insanity is not DSM "bipolar disorder".** His category included recurrent unipolar depression too; it was polarity-blind and unified all episodic mood illness under one course-based label.

GOOD TO REMEMBER

- **Emil Kraepelin (1856 to 1926):** the father of descriptive psychiatric nosology; the discriminating feature is that he classified by **course and outcome**; the one date to hold is **1899**, the edition in which he stated the dichotomy.
- **Manic-depressive insanity:** Kraepelin's episodic, recovering endogenous mood disease; the discriminating feature is an episodic course with inter-episode recovery; the trap is that it was **polarity-blind** and included recurrent unipolar depression, not only bipolar illness.
- **Dementia praecox:** the progressive, deteriorating psychosis of young onset; the discriminating feature is a downhill course to defect; renamed **schizophrenia** by Bleuler in 1908.

4.3 The earlier French contributors: Falret and Baillarger

Kraepelin synthesised, he did not invent from nothing, and the examiner likes the two French alienists whose descriptions of the alternating illness preceded him by decades. In 1854 Jean-Pierre Falret described folie circulaire, "circular insanity", the recurring cycle of mania and depression with lucid intervals between (Companion 2010). In the same year, and famously presented only about two weeks before Falret's account, Jules Baillarger described folie a double forme, "insanity in two forms", the occurrence of mania and depression as two faces of a single illness (Companion 2010). It is from these two descriptions that the contemporary concept of recurrent oscillation between mania and depression emerged, later given its more explicit and unifying definition by Kraepelin as manic-depressive psychosis (Companion 2010). For the exam, hold the pairing: Falret with folie circulaire, Baillarger with folie a double forme, both 1854, both French, both antecedents of the Kraepelinian synthesis.

GOOD TO REMEMBER

- **Jean-Pierre Falret, folie circulaire (1854):** "circular insanity", the cyclical recurrence of mania and depression with lucid intervals; the eponym to hold is **folie circulaire**.
- **Jules Baillarger, folie a double forme (1854):** "insanity in two forms", mania and depression as two forms of one illness, described about two weeks before Falret; the eponym to hold is **folie a double forme**.

4.4 Leonhard's unipolar-bipolar split: the seed of the modern distinction

The modern division of Kraepelin's unified category into two diseases came from Karl Leonhard, a pupil of Karl Kleist (Kaplan & Sadock 2024). In his 1948 textbook Leonhard proposed the term **bipolar** for illness that alternates between depression and mania, setting it apart from a **unipolar** depression that shows only the depressive pole; he developed the split in his 1957 book, The Classification of the Endogenous Psychoses, arguing that unipolar depression had a different psychopathology from the bipolar variety (Kaplan & Sadock 2024). Leonhard grounded the distinction phenomenologically and then corroborated it with family data: mania occurred more often in the relatives of manic-depressive (bipolar) patients than in the relatives of unipolar patients, an early example of validating a purely descriptive split with an external correlate (Tasman 2015). This unipolar-bipolar distinction, carried into the literature by investigators such as Angst, Perris, Winokur and others, is what DSM-III inherited in 1980 when it anchored "bipolar disorder" as a disease separate from "major depression" (Kaplan & Sadock 2024).

Leonhard is therefore the bridge from the single Kraepelinian category to the two-axis modern classification.

RULE **Kraepelin lumped, Leonhard split.** Leonhard (1948) added the unipolar-versus-bipolar axis inside Kraepelin's manic-depressive category, and that split, not the dichotomy itself, is what the modern bipolar-versus-unipolar distinction descends from.

GOOD TO REMEMBER

- **Karl Leonhard:** introduced the **unipolar versus bipolar** split of the mood disorders; the discriminating claim is that bipolar (alternating) illness is a different disease from unipolar (depression-only) illness; the date to hold is **1948** for the term "bipolar", with the fuller account in his 1957 Classification of the Endogenous Psychoses.

4.5 The erosion of the strict dichotomy: shared genetics and overlapping neurobiology

The examiner's second demand is that the dichotomy is no longer treated as absolute. The **kraepelinian dichotomy** holds well for classic cases but breaks down at the boundaries, and modern psychiatric genetics is the main reason (Tasman 2015). Family, twin and molecular studies show that schizophrenia and bipolar disorder **share a substantial portion of their genetic liability**, with overlapping susceptibility loci rather than two cleanly separate genetic architectures, so the two poles do not breed true as fully distinct diseases (Craddock & Owen 2005). The neurobiology tells the same story: overlapping findings across the two conditions rather than a clean biological border. This body of evidence is what led Craddock and Owen to their landmark paper title, "The beginning of the end for the Kraepelinian dichotomy" (Craddock & Owen 2005), the reference to cite in any answer on this theme. The practical reading is that the dichotomy is best held as a useful clinical approximation, valid at the extremes, rather than a statement of two biologically watertight categories.

PEARL

The single reference to name when a stem asks about the erosion of the dichotomy is Craddock and Owen's 2005 editorial in the British Journal of Psychiatry, "The beginning of the end for the Kraepelinian dichotomy" (Craddock & Owen 2005). It marshalled the shared-genetics evidence into the argument that the two Kraepelinian diseases are not genetically separate.

4.6 The intermediate presentations: schizoaffective and psychotic mood on a continuum

The clinical face of the erosion is the population of **boundary cases** that will not sort cleanly into either Kraepelinian box. Kraepelin himself acknowledged that some patients showed features of both, and Bleuler proposed that manic-depressive illness and schizophrenia lie on a **continuum with no sharp border**, with patients often exhibiting characteristics of both and running a course midway between (Tasman 2015). The category that formalises this middle ground is schizoaffective disorder, the recognised diagnostic home for presentations that carry both prominent mood and prominent schizophrenia-type psychotic features (Tasman 2015). Alongside it sit the mood episodes **with psychotic features**, where a severe depressive or manic episode carries delusions or hallucinations and so blurs the phenomenological line between a

mood disorder and a psychotic one. Together, the shared genetics, the overlapping neurobiology and these intermediate schizoaffective and psychotic-mood presentations place the two Kraepelinian poles on a continuum rather than in separate boxes. The detailed criteria and the schizoaffective boundary itself are developed in the Other psychotic disorders, delusional syndromes and catatonia notes.

TRAP **Do not treat the dichotomy as absolute.** Shared genetic liability, overlapping neurobiology and the intermediate schizoaffective and psychotic-mood presentations blur the line; the boundary cases are the rule, not an exception, and the dichotomy is now read as a continuum.

GOOD TO REMEMBER

- **Bleuler continuum:** the proposal that manic-depressive illness and schizophrenia lie on a single continuum with no sharp border; the discriminating idea is boundary cases running a course midway between the two.
- **Schizoaffective disorder:** the recognised diagnostic home for mixed mood-and-psychosis presentations; the discriminating feature is prominent mood and prominent schizophrenia-type psychotic features together; criteria owned by the Other psychotic disorders, delusional syndromes and catatonia notes.

HOLD THIS

Kraepelin (1899) split the functional psychoses by **course and outcome**, episodic manic-depressive insanity versus progressive dementia praecox; Leonhard (1948) then split that mood category into **unipolar and bipolar**; and shared genetics with the intermediate schizoaffective and psychotic-mood cases has since turned the strict dichotomy into a **continuum**.

INDIA

The Kraepelinian course-based logic is the backbone of the ICD system used across Indian teaching hospitals, and the emphasis on longitudinal course over the cross-sectional picture is exactly why a careful lifetime history, not a single mental-state snapshot, is the taught standard for separating a recurrent mood disorder from schizophrenia in Indian practice.

5 · Epidemiology of mood disorders

Why this matters. The **epidemiology of mood** disorders is high-yield precisely because the numbers separate the two illnesses. Major depressive disorder is common, skews female roughly two to one, and tends to begin in adult life; bipolar disorder is a good deal rarer, has a roughly equal sex ratio, and starts earlier. An examiner tests whether you can quote the right figure for the right disorder, and whether you resist the classic error of transplanting a Western prevalence onto an Indian population. This topic teaches the population picture: prevalence, the **sex ratio**, the **age of onset**, the burden, the comorbidity and mortality, and the Indian data from the National Mental Health Survey.

The raw descriptive definitions of the mood symptoms and the rating scales that generate these prevalence estimates sit in the Psychometry, Assessment and Descriptive Psychopathology notes; here the concern is the population-level distribution. Clinical suicide risk assessment and safety

planning are developed in the Somatic-symptom, sexual, impulse-control disorders and suicide notes; the mortality figures below are the epidemiological headline only.

5.1 Major depressive disorder: how common

Common, and commoner in women. Major depressive disorder is among the most prevalent psychiatric disorders. Kaplan & Sadock give a **lifetime prevalence** in the region of **5% to 17%** across community surveys, with a widely quoted point (current) prevalence of roughly **2% to 3%** in men and **5% to 9%** in women (Kaplan & Sadock 2024). The single most robust epidemiological fact is the sex difference: depression is about **twice** as common in women as in men, the classic 2:1 female-to-male ratio, a finding that holds across most countries and cultures and is thought to reflect a mix of hormonal, psychosocial and help-seeking factors (Kaplan & Sadock 2024). Hold the prevalence as a range rather than a single figure, because surveys differ by method and case definition.

RULE **Depression is commoner in women, about two to one.** The 2:1 female preponderance in major depressive disorder is the most reproducible single fact in mood epidemiology.

5.2 Major depressive disorder: when it starts

Adult onset, spread wide. The **age of onset** of major depressive disorder spans the whole adult lifespan, but the bulk of first episodes cluster in the twenties to thirties, and community data show first onset can occur from adolescence into later life (Kaplan & Sadock 2024). Older texts quote a mean age of onset around 40, but a large share of patients now present with a first episode in the twenties and thirties, and depression rising in younger cohorts is a recognised secular trend. The clinical point for the exam is that depression is not confined to any single decade: an adolescent first episode and a late-life first episode are both fully compatible with the diagnosis, and the peak of new onsets sits in early to middle adult life.

GOOD TO REMEMBER

- **Major depressive disorder:** the commonest mood disorder; the discriminating epidemiological feature is the 2:1 female preponderance; hold lifetime prevalence roughly 5% to 17% and onset clustering in the twenties to thirties.
- **Sex ratio in depression:** women to men about 2:1; the discriminator from bipolar is that bipolar is roughly equal; hold "twice as common in women."
- **Age of onset in depression:** spread across adult life, peak in the twenties to thirties; the discriminator from bipolar is that depression starts later on average; hold "adult onset, wide range."

5.3 Bipolar disorder: rarer, equal by sex, earlier

Less common, and different in shape. Bipolar disorder is substantially less prevalent than unipolar depression. Bipolar type I disorder has a lifetime prevalence of around **1%** in community surveys, and the figure rises when the wider **bipolar spectrum** (bipolar II and subthreshold forms) is counted, with combined spectrum estimates commonly cited in the region of a few percent (Kaplan & Sadock 2024). Two population features distinguish bipolar from unipolar disorder and are examined directly: the sex ratio in bipolar I is roughly **equal** between men and women, unlike the female excess of depression, and the age of onset is earlier, typically

in the **late teens to twenties**, with a frequently quoted mean around the early twenties (Kaplan & Sadock 2024). A first manic episode presenting for the first time in later life should prompt a search for a secondary (organic or substance-related) cause.

TRAP **Do not quote a Western prevalence as an Indian one.** The community surveys behind the 5% to 17% depression figure and the 1% bipolar I figure are largely Western; for India, cite the National Mental Health Survey, not a US or European number.

2:1	5% to 17%	about 1%	roughly equal
FEMALE-TO-MALE RATIO, DEPRESSION	LIFETIME PREVALENCE, MAJOR DEPRESSION	LIFETIME PREVALENCE, BIPOLAR I	SEX RATIO, BIPOLAR DISORDER

5.4 The unipolar versus bipolar epidemiological contrast

Three axes separate them. The population profiles of the two disorders diverge on prevalence, sex ratio and age of onset, and this triad is the crux of the topic (Kaplan & Sadock 2024). The clean contrast is worth holding as a grid, because a single swapped cell (calling the bipolar sex ratio female-predominant, or making depression the earlier-onset illness) is exactly the kind of error the exam punishes. The full clinical differentiation of bipolar from unipolar depression, temperament, episode shape and drug response, is taught in this chapter's unipolar-versus-bipolar-spectrum topic; here the axes are purely epidemiological.

AXIS	MAJOR DEPRESSIVE DISORDER (UNIPOLAR)	BIPOLAR DISORDER
Lifetime prevalence	**Higher, roughly 5% to 17%**	**Lower, about 1% for bipolar I; more for the spectrum**
Sex ratio	**Women to men about 2:1**	**Roughly equal**
Age of onset	Twenties to thirties, wide adult range	**Earlier: late teens to twenties**
Family history	Positive, but weaker loading than bipolar	Strong bipolar loading, highly heritable

The three epidemiological discriminators between unipolar and bipolar disorder. Read across the italicised cells: depression is commoner and female-skewed with later onset; bipolar is rarer, sex-equal and earlier (Kaplan & Sadock 2024).

5.5 Burden, comorbidity and mortality

A leading cause of disability, and a lethal illness. Mood disorders carry a burden out of proportion to their visibility. Depression is consistently ranked a **leading cause of years lived with disability** worldwide in the Global Burden of Disease analyses, and both depressive and bipolar disorders sit high on the disability tables because they are prevalent, recurrent and disabling during episodes (Kaplan & Sadock 2024). Comorbidity is the rule, not the exception: anxiety disorders and substance use disorders co-occur heavily with both depression and bipolar disorder, worsening course and outcome. Mortality has two strands the exam expects. The first is suicide: mood disorders, especially with mixed features or comorbid substance use, carry a markedly raised suicide risk, and a substantial share of completed suicides occur in people with a mood disorder. The second is cardiovascular and other physical mortality, so that people with

severe mood disorders, and bipolar disorder in particular, have a shortened life expectancy driven partly by cardiovascular and metabolic disease. The clinical assessment of suicide risk itself is developed in the Somatic-symptom, sexual, impulse-control disorders and suicide notes.

PEARL

The mortality of a mood disorder is not only from suicide. The excess deaths in bipolar disorder are driven substantially by cardiovascular and metabolic disease, which is why physical-health monitoring is part of long-term care, not an afterthought (Kaplan & Sadock 2024).

5.6 The Indian picture and the treatment gap

Cite the National Mental Health Survey, and flag the gap. For Indian data the anchor source is the National Mental Health Survey of India 2015 to 2016 (Gururaj et al. 2016), conducted across twelve states by NIMHANS. It reported an overall **lifetime prevalence** of mental disorders of **13.7%** and a current (point) prevalence of **10.6%** (Kaplan & Sadock 2024). Depressive disorders were among the most prevalent categories identified, and bipolar disorder was found at a lower prevalence, consistent with the global unipolar-over-bipolar pattern. The survey's headline public-health finding is the enormous **treatment gap**: for mental disorders overall the gap runs in the region of **70% to 92%**, meaning the great majority of people with a diagnosable disorder receive no treatment (Kaplan & Sadock 2024). India also has fewer than the desirable number of psychiatrists, well short of the target of three per 100,000 population, which frames the service context in which mood disorders go untreated.

INDIA

Quote the National Mental Health Survey 2015 to 2016 (Gururaj et al. 2016) as the Indian anchor: overall lifetime prevalence of mental disorders 13.7%, current prevalence 10.6%, and a treatment gap of roughly 70% to 92% for mental disorders overall. Depressive disorders were among the most prevalent categories, and bipolar disorder was less prevalent, mirroring the global picture. The exact NMHS point estimates specific to depressive disorders and to bipolar affective disorder (the disorder-specific prevalence percentages, rather than the all-disorder totals) could not be verified from the parsed sources and are flagged under gaps; describe them as "depression among the commonest, bipolar less common" rather than quoting an unverified percentage. For severe, psychotic or treatment-resistant depression and for acute mania, electroconvulsive therapy is widely available and heavily used across Indian teaching hospitals, a point returned to in the management topics and the ECT and neurostimulation notes.

TRAP **Never present a US or European mood-disorder prevalence as the Indian figure.** For India the number to give is the National Mental Health Survey estimate and its treatment gap, not the Western 5% to 17% or 1% quoted for depression and bipolar I.

MNEMONIC

DEPRESSION IS FEMALE AND LATER, BIPOLAR IS EQUAL AND EARLIER

Depression: commoner (5% to 17%), Female-skewed (2:1), Later onset (twenties to thirties). Bipolar: rarer (about 1% for bipolar I), Equal sex ratio, Earlier onset (late teens to twenties). Two illnesses, opposite on sex and onset.

HOLD THIS

Major depression is common (lifetime roughly 5% to 17%), twice as common in women, and starts in the twenties to thirties; bipolar disorder is rarer (about 1% for bipolar I), has a roughly equal sex ratio, and starts earlier in the late teens to twenties, and for India you quote the National Mental Health Survey with its 70% to 92% treatment gap, never a Western number.

Depressive disorders: clinical syndromes

6 · Major depressive disorder

Why this matters. **Major depressive disorder** is the commonest severe mood diagnosis in the syllabus and the canonical home of the depressive-episode criteria: the psychotic-disorders notes cross-refer here for the depressive pole of schizoaffective disorder, so the criteria are taught here in full. The examiner tests three reflexes on **mdd**: the exact criterion set for a **depressive episode**, the specifier that reshapes prognosis and treatment, and the single move that keeps the diagnosis honest, screening every depression for a past hypomanic episode before the label is applied. Miss that screen and a bipolar depression is mislabelled unipolar and mistreated from the outset.

The structure to hold is a nesting: the **depressive episode** is the atom of criteria; **major depressive disorder** (ICD-11: single episode depressive disorder or recurrent depressive disorder) is the disorder built from one or more such episodes with no lifetime manic or hypomanic episode. Nosology is given ICD-11 primary with the DSM-5 (the DSM-5-TR) criteria cross-mapped, because the two manuals word the same episode slightly differently and that difference is itself examinable. The raw descriptive definitions of the individual mood symptoms and the rating scales are owned by the Psychometry, Assessment and Descriptive Psychopathology notes and cross-referenced here, not re-derived.

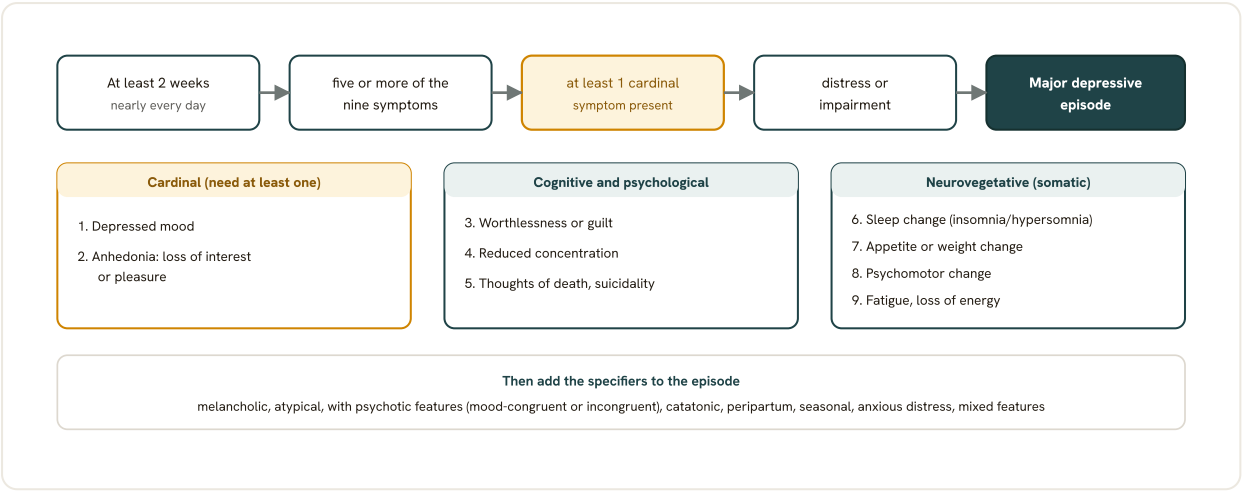


Fig 11.3 Major depressive disorder: the criteria gate and the specifier set. The episode needs at least two weeks, five or more of the nine symptoms including at least one cardinal symptom (depressed mood or anhedonia), and distress or impairment. The nine symptoms fall into a cardinal, a cognitive and psychological, and a neurovegetative cluster, and the diagnosed episode is then qualified with the specifiers.

6.1 The depressive episode: the two-week floor and the two cardinal symptoms

Every diagnosis in this family begins with a depressive episode, and the episode has a fixed duration floor. Both manuals require the symptom cluster to persist over the same period of **at least two weeks**, most of the day and nearly every day, representing a change from previous functioning (DSM-5-TR; ICD-11 CDDR). Within that window the episode is anchored on two **cardinal symptoms**: **depressed mood** (subjective sadness, emptiness or hopelessness, or observed tearfulness; in children and adolescents this may be irritability) and anhedonia, a markedly diminished interest or pleasure in all or almost all activities. DSM-5-TR requires that at least one of the five counted symptoms be one of these two cardinals; ICD-11 requires at least one symptom from its affective cluster, which carries the same two cardinals (DSM-5-TR; ICD-11 CDDR). This is the non-negotiable spine: two weeks, and at least one cardinal symptom present.

RULE **A major depressive episode needs at least two weeks and five of nine symptoms including one cardinal symptom.** No cardinal (depressed mood or anhedonia), no episode, however many other symptoms are counted.

6.2 The five of nine rule: the DSM-5-TR nine-symptom set

DSM-5-TR builds the episode from a count: the **five of nine** rule. Five or more of the following nine symptoms must have been present during the same two-week period, at least one being depressed mood or anhedonia (DSM-5-TR major depressive episode). The nine, verbatim in substance, are: (1) depressed mood; (2) markedly diminished interest or pleasure (anhedonia); (3) significant weight or appetite change (a change of more than **5% of body weight** in a month, or decreased or increased appetite); (4) insomnia or hypersomnia; (5) psychomotor agitation or retardation, observable by others; (6) fatigue or loss of energy; (7) feelings of worthlessness or excessive or inappropriate guilt, which may be delusional; (8) diminished ability to think, concentrate or decide; and (9) recurrent thoughts of death, recurrent suicidal ideation, or a suicide attempt or specific plan. The episode also requires clinically significant distress or impairment (criterion B) and is not attributable to a substance or another medical condition

(criterion C). The classic grouping the examiner rewards: two cardinal (mood, anhedonia), four neurovegetative (sleep, appetite or weight, energy, psychomotor), and three cognitive (worthlessness or guilt, concentration or indecision, and thoughts of death or suicidality).

at least 2 wk	5 of 9	1 cardinal	2:1
DEPRESSIVE EPISODE	DSM-5-TR SYMPTOM COUNT	MOOD OR ANHEDONIA REQUIRED	FEMALE-TO-MALE RATIO

WORKED EXAMPLE

A 34-year-old man reports three weeks of low mood and loss of interest in everything he used to enjoy, with early-morning waking, a 4 kg weight loss, fatigue, poor concentration and recurrent thoughts that his family would be better off without him. Count it: depressed mood and anhedonia (both cardinals), plus insomnia, weight loss, fatigue, concentration loss and death thoughts, which is seven of nine over more than two weeks, with impairment and no medical cause. This meets a major depressive episode. Now the mandatory next step, before the label major depressive disorder is written: screen the lifetime history for any past hypomanic or manic episode.

6.2b The ICD-11 wording and its small differences from DSM-5-TR

ICD-11 describes the same episode through **three symptom clusters** rather than a flat list of nine, and the reader should be able to name them (ICD-11 CDDR). The **affective cluster** carries depressed mood and anhedonia (the two cardinals) and, additionally, hopelessness about the future. The **cognitive-behavioural cluster** carries reduced concentration and indecisiveness, beliefs of low self-worth or excessive guilt (which may be delusional), and recurrent thoughts of death or suicidal ideation. The **neurovegetative cluster** carries disrupted or excessive sleep, appetite or weight change, psychomotor agitation or retardation, and reduced energy or fatigue. ICD-11 requires several symptoms present most of the day, nearly every day, for at least two weeks, with at least one from the affective cluster. The small differences that get examined: DSM-5-TR fixes a hard count of five of nine, whereas ICD-11 speaks of "several" symptoms across the clusters rather than a rigid arithmetic threshold; ICD-11 adds hopelessness as an explicit affective item; and both share the same two-week floor and the same cardinal anchoring. ICD-10 (F32, still cited in Indian exams) used a slightly different structure of core plus additional symptoms with a somatic syndrome specifier, and is flagged here.

TRAP **Do not diagnose major depressive disorder without excluding a past hypomanic episode.** A single unscreened hypomania in the history reclassifies the patient as bipolar type II, and the missed bipolarity changes first-line treatment entirely.

6.3 Severity grading and the with-psychotic-features distinction

Once an episode is confirmed, severity is graded as **mild, moderate or severe** on the number and intensity of symptoms and the impact on functioning (ICD-11 CDDR; DSM-5-TR). ICD-11 fixes a clean rule the examiner likes: a mild depressive episode by definition carries **no** psychotic symptoms, so psychosis can occur only in a moderate or severe episode (ICD-11 CDDR). The **with-psychotic-features** distinction then marks a moderate or severe episode as "with" or "without psychotic symptoms" (delusions or hallucinations). The classic depressive delusions are

mood-congruent and self-referential: guilt (falsely blaming oneself for wrongdoing), poverty or ruin, nihilistic delusions (Cotard-type beliefs that body organs or the self do not exist), and delusions of deserved punishment or impending disaster (ICD-11 CDDR; Kaplan & Sadock 2024). Perhaps 10% to 20% of depressed adults have psychotic symptoms, and psychotic depression carries a differential treatment response and a higher risk of progression to bipolar illness (Kaplan & Sadock 2024). The full handling of mood with psychotic features and the boundary with schizoaffective disorder is cross-referenced to the Other psychotic disorders, delusional syndromes and catatonia notes.

GOOD TO REMEMBER

- **Depressive episode:** low mood or anhedonia plus associated symptoms, most of the day nearly every day, for **at least two weeks**; DSM-5-TR requires **five of nine** including one cardinal.
- **Mild severity:** few symptoms above threshold, limited functional impact; by definition **no psychotic symptoms** (ICD-11).
- **Moderate severity:** intermediate symptom count and impairment; may be with or without psychotic symptoms.
- **Severe severity:** most symptoms present with marked impairment; may carry psychotic features; the number to hold is the psychotic-depression prevalence of roughly **10% to 20%** of depressed adults.

6.4 The specifiers: melancholic, atypical and mixed features

The specifiers refine a confirmed episode and steer prognosis and treatment; each is defined briefly here, with the fuller subtype detail owned by the next topic. Melancholic features require loss of pleasure or loss of reactivity to pleasurable stimuli, plus at least three of: depressed mood with a distinct quality of despair, mood worse in the morning, early-morning awakening, marked psychomotor change, significant anorexia or weight loss, and excessive guilt (DSM-5-TR; Kaplan & Sadock 2024). Atypical features are the mirror image, defined by **mood reactivity** plus at least two of: increased appetite or weight gain, hypersomnia, leaden paralysis, and a long-standing pattern of interpersonal rejection sensitivity; these reverse-vegetative signs carry an affinity with bipolar II, so atypicality should prompt a careful bipolar screen (DSM-5-TR; Akiskal 2007). Mixed features mark a depressive episode carrying at least three concurrent manic or hypomanic symptoms that do not themselves meet an episode threshold; it blurs the unipolar-bipolar boundary and flags heightened bipolar risk (DSM-5-TR; Kaplan & Sadock 2024).

6.5 The specifiers continued: psychotic, catatonic, peripartum, seasonal and anxious distress

The remaining specifiers complete the set. The **psychotic** specifier is split into **mood-congruent** psychotic features (delusions or hallucinations whose content fits the depressed mood, the guilt, poverty and nihilistic themes) and **mood-incongruent** features (content not consonant with depression, e.g. persecutory or thought-insertion themes), the incongruent pattern carrying a worse prognosis (DSM-5-TR; Kaplan & Sadock 2024). Catatonic features mark an episode dominated by the catatonic syndrome (stupor, mutism, negativism, posturing, waxy flexibility), with the catatonia entity itself owned by the Other psychotic disorders, delusional syndromes and catatonia notes. Peripartum onset applies when the episode begins during pregnancy or within four weeks of delivery in DSM-5-TR, with the wider perinatal frame cross-referenced to

the Perinatal/women's mental health and emergency psychiatry notes. Seasonal pattern marks a regular temporal relationship of episodes to a time of year (classically autumn-winter onset with spring remission). Anxious distress requires at least two of tension, restlessness, difficulty concentrating from worry, fear that something awful may happen, and fear of loss of control, and it predicts a worse course and higher suicide risk (DSM-5-TR).

SPECIFIER	DEFINING FEATURE	THE ONE DISCRIMINATOR TO HOLD
Melancholic	Loss of pleasure or reactivity plus 3 or more of despair, AM-worse mood, early waking, psychomotor change, anorexia or weight loss, guilt	**Non-reactive mood plus early-morning awakening and diurnal (AM-worse) variation**
Atypical	Mood reactivity plus 2 or more of hyperphagia or weight gain, hypersomnia, leaden paralysis, rejection sensitivity	**Reactive mood and reverse-vegetative signs; a bipolar-II red flag**
Mixed features	Depressive episode with 3 or more concurrent subthreshold manic or hypomanic symptoms	**Manic symptoms inside the depression; blurs into the bipolar spectrum**
Psychotic, mood-congruent	Delusions or hallucinations consonant with depression (guilt, poverty, nihilism)	Content fits the depressed mood
Psychotic, mood-incongruent	Delusions or hallucinations not consonant with depression (e.g. persecution, passivity)	**Incongruent content; worse prognosis**
Catatonic	Episode dominated by the catatonic syndrome (stupor, mutism, negativism, posturing)	Catatonia overlaid on the mood episode
Peripartum onset	Onset in pregnancy or within 4 weeks of delivery (DSM-5-TR)	**The four-week postpartum window (DSM-5-TR)**
Seasonal pattern	Regular seasonal timing of episodes (classically autumn-winter)	Temporal, not symptomatic, definition
Anxious distress	2 or more of tension, restlessness, worry-driven poor concentration, fear of something awful, fear of loss of control	**Predicts worse course and higher suicide risk**

The MDD specifier map: each specifier with its defining feature and the single discriminator to hold; the highlighted cell is the fact the examiner tests.

GOOD TO REMEMBER

- **Melancholic:** loss of pleasure or reactivity plus 3 or more classic features; the eponymic marker is non-reactive mood with early-morning awakening and AM-worse diurnal variation.
- **Atypical:** mood reactivity plus 2 or more reverse-vegetative signs (hyperphagia, hypersomnia, leaden paralysis, rejection sensitivity); the number to hold is 2 features, and it is a bipolar-II red flag.
- **Mixed features:** depressive episode with 3 or more concurrent subthreshold manic or hypomanic symptoms; flags bipolar risk.
- **Psychotic (mood-congruent vs incongruent):** congruent content fits the mood (guilt, poverty, nihilism); incongruent content carries a worse prognosis.
- **Catatonic:** episode dominated by the catatonic syndrome; the entity is owned by the psychotic-disorders and catatonia notes.
- **Peripartum:** onset in pregnancy or within **4 weeks** of delivery (DSM-5-TR).
- **Seasonal:** regular seasonal timing of episodes, classically autumn-winter onset with spring remission.
- **Anxious distress:** 2 or more anxiety items; predicts worse course and higher suicide risk.

6.6 Course concepts: single versus recurrent, relapse versus recurrence

Major depressive disorder is defined longitudinally as well as cross-sectionally. A first and only lifetime episode is single episode depressive disorder (DSM-5-TR: major depressive disorder, single episode); a history of at least two depressive episodes separated by several months of relative euthymia is recurrent depressive disorder (DSM-5-TR: recurrent). Two course words are examined and are not interchangeable: **relapse** is the return of symptoms of the same, still-active episode during the continuation window before full recovery, whereas **recurrence** is a genuinely new episode arising after a period of full recovery (Kaplan & Sadock 2024). This distinction drives the management phases: continuation treatment targets relapse of the index episode, while maintenance treatment targets recurrence of a new one. Recurrence is common: the majority of patients with a first major depressive episode will experience further episodes over a lifetime, and each additional episode raises the risk of the next.

6.7 Treatment-resistant depression as a course concept

Treatment-resistant depression is best held at this stage as a course concept, not a management algorithm. The working definition the examiner expects is failure to achieve adequate response after at least two antidepressant trials of adequate dose and duration within the current episode (Kaplan & Sadock 2024). It matters here because it reshapes prognosis and prompts a re-examination of the diagnosis itself (missed bipolarity, an unaddressed psychotic feature, a comorbidity, or non-adherence are the commonest reasons a depression appears resistant). The staged pharmacological approach to treatment-resistant depression, the augmentation and switching strategies, and the deep drug detail are owned by, and cross-referenced to, the Mood disorders: pharmacotherapy notes and are not duplicated here.

COMMON TRAP

Before labelling a depression "treatment-resistant", re-screen for a past hypomanic episode and for undetected psychotic features. A bipolar depression treated with antidepressant monotherapy, or a psychotic depression treated without an antipsychotic or ECT, will look resistant when the real error is a missed specifier or missed polarity, not true pharmacological resistance.

6.8 Suicide: the key risk, and the neuroendocrine correlate

Suicide is the dominant risk of major depressive disorder and the reason severity, psychotic features and anxious distress all matter clinically; recurrent thoughts of death and suicidality are one of the nine episode symptoms, and active suicidal ideation is common in a depressive episode where it is rare in normal grief (Kaplan & Sadock 2024). The structured clinical assessment of suicide risk and safety planning is owned by the Somatic-symptom, sexual, impulse-control disorders and suicide notes and cross-referenced here. One laboratory correlate is examined as a biological marker of the depressive state: the dexamethasone suppression test (DST). One milligram of dexamethasone is given orally at 11 PM and plasma cortisol measured the next day; a plasma cortisol above **5 micrograms per decilitre** (nonsuppression) is the abnormal, positive result, reflecting HPA-axis overactivity (Kaplan & Sadock 2024). Its limitation, and the reason it is not a diagnostic test, is its poor specificity: nonsuppression occurs in many other conditions, so a positive DST supports but never confirms a depressive diagnosis. The HPA-axis mechanics behind the test are owned by the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the mood application is held here.

INDIA

Depressive disorders are among the commonest presentations in Indian outpatient psychiatry, and the National Mental Health Survey of India 2015 to 2016 (Gururaj et al. 2016) remains the anchor epidemiological source cited in the exams, with depressive disorders among the most prevalent categories it identified. For severe, psychotic or treatment-resistant depression, ECT is widely available and heavily used across Indian teaching hospitals; the ECT technique is owned by the ECT and neurostimulation notes. This chapter is largely generic and names no brand for major depressive disorder itself; drug branding, Indian brand first, belongs to the Mood disorders: pharmacotherapy notes.

6.9 Management pointer and the criteria-and-specifiers map

Management of major depressive disorder is taught guideline-first, led by the CANMAT recommendations with the Indian Psychiatric Society (the IPS guidelines) and NICE positions stated alongside, and organised by phase (acute, continuation, maintenance); the guideline-level headline to carry from the outset is a second-generation antidepressant plus an evidence-based psychotherapy first-line, with the full detail developed in the depression-management topic and cross-referenced there (CANMAT 2016). The whole diagnostic object of this topic assembles into a single map: the two-week floor and the two cardinal symptoms at the centre, the five of nine count around them, the three symptom groups (cognitive, neurovegetative and the worthlessness-guilt and suicidality items), the severity grading with the psychotic split, and the

ring of specifiers. That map is the concept figure for this topic, Fig 11.3, the MDD criteria and specifiers map.

MNEMONIC

SIG E CAPS (plus the two cardinals)

The eight neurovegetative and cognitive counters that sit around the two cardinal symptoms (depressed mood, anhedonia): **S**leep change, loss of **I**nterest (anhedonia, a cardinal), **G**uilt or worthlessness, **E**nergy loss or fatigue, **C**oncentration loss, **A**ppetite or weight change, **P**sychomotor change, and **S**uicidality. Count five or more over two weeks, with at least one cardinal, and the depressive episode is met.

HOLD THIS

A depressive episode is at least two weeks, five of nine symptoms, and at least one cardinal symptom (depressed mood or anhedonia); and no major depressive disorder is diagnosed until a past hypomanic or manic episode has been excluded.

7 · Persistent depressive disorder and double depression

Why this matters. **Persistent depressive disorder** is the low-intensity, high-chronicity end of the depressive spectrum, and the examiner tests it precisely because it is so easy to under-read. Where major depressive disorder is a break from the premorbid self that the patient can date to a month or a season, **dysthymia** is a chronically low mood that has become the background weather of the person's life, present most of the time for years and often mistaken for temperament rather than illness (Kaplan & Sadock 2024). The single reflex to build here is that the diagnostic principle is **chronicity, not severity**: a milder syndrome that is defined by its duration, carried by a fixed two-year floor.

Two named entities live in this topic and each ends with a good-to-remember line: **persistent depressive disorder** (the DSM-5 merger of chronic major depression and dysthymia, ICD-11 dysthymic disorder) and **double depression**, a major depressive episode breaking out on top of underlying dysthymia. Nosology is given ICD-11 primary with the DSM-5 (the DSM-5-TR) cross-mapped and ICD-10 flagged where Indian exams still use it. The raw descriptive definitions of the individual mood symptoms are owned by the Psychometry, Assessment and Descriptive Psychopathology notes and cross-referenced here, not re-derived; the deep pharmacology and treatment-resistance algorithms belong to the Mood disorders: pharmacotherapy notes.

7.1 The core criterion: chronic low mood for two years

The defining criterion of persistent depressive disorder is a chronic, low-grade depressed mood, present for most of the day, on more days than not, for a period of at least **two years** (in children and adolescents the mood may be irritable and the duration threshold falls to at least **one year**) (DSM-5-TR; ICD-11 CDDR). During that depressed period the patient must carry **two or more** associated depressive symptoms from a short list, and, crucially, must never have been symptom-free for more than **two months** at a time across the whole two-year span (DSM-5-TR). It is this "never free for more than two months" clause that makes the disorder persistent rather than

recurrent: the low mood is a near-continuous state, not a series of discrete episodes with clean euthymia between them.

RULE **Persistent depressive disorder is chronicity at lower intensity.** The diagnostic hallmark is duration, low mood for at least two years, never symptom-free for more than two months, not the depth of any one day.

7.2 The two-or-more symptoms and the associated features

Once the chronic low mood over two years is established, the diagnosis needs **two or more** of the associated symptoms present during the depressed period (DSM-5-TR; ICD-11 CDDR). The list is a compact, mostly neurovegetative and cognitive set: poor appetite or overeating, insomnia or hypersomnia, low energy or fatigue, low self-esteem, poor concentration or difficulty making decisions, and feelings of hopelessness. The syndrome must cause clinically significant distress or functional impairment, and the usual exclusions apply: it cannot be diagnosed if there has ever been a manic, hypomanic or mixed episode (which would move the patient to the bipolar side), and it is not better explained by a psychotic disorder, a substance, or another medical condition (DSM-5-TR; Kaplan & Sadock 2024).

Depressed mood

Low mood most of the day, more days than not, for at least two years; the anchoring criterion.

Two or more associated symptoms

Appetite change, sleep change, low energy, low self-esteem, poor concentration or indecision, hopelessness.

The two-month rule

Never symptom-free for longer than two months across the two-year span; this is what makes it persistent.

7.3 The DSM-5 merger and the ICD-11 dysthymic disorder

The nosological headline the examiner rewards is the **DSM-5 merger**: DSM-IV kept chronic major depressive disorder and dysthymic disorder as separate categories, and DSM-5 collapsed both into a single umbrella, persistent depressive disorder, on the reasoning that the two could not be reliably distinguished and predicted the same chronic course (DSM-5-TR; Kaplan & Sadock 2024). DSM-5-TR then re-captures the old distinctions through course specifiers, most importantly "with pure dysthymic syndrome" (full major-depressive criteria not met in the last two years) versus "with persistent major depressive episode" (full criteria met throughout the whole two-year period) and the two "intermittent major depressive episode" variants. ICD-11 does **not** merge: it keeps a discrete dysthymic disorder, defined as a persistent depressed mood lasting at least two years with additional depressive symptoms that do not meet the threshold for a depressive episode, and it stipulates that a depressive episode must not have been present during the first two years of the disturbance (ICD-11 CDDR). ICD-10 used the label dysthymia (F34.1) in the same spirit, and is flagged here because Indian exams still cite it.

SYSTEM	LABEL	STRUCTURAL STANCE
DSM-5-TR	Persistent depressive disorder	**Merges chronic MDD and dysthymia into one umbrella; old distinctions live on as course specifiers**
ICD-11	Dysthymic disorder	**Keeps it discrete; no depressive episode in the first two years**
ICD-10	Dysthymia (F34.1)	Persistent mild depression below episode threshold; still cited in Indian exams

The nosology map for persistent depressive disorder: DSM-5 merges, ICD-11 keeps dysthymic disorder discrete, and the highlighted cells are the discriminators the examiner tests.

at least 2 years	2 or more	at most 2 months
CHRONIC LOW MOOD FLOOR	ASSOCIATED SYMPTOMS	LONGEST SYMPTOM-FREE GAP

GOOD TO REMEMBER

- **Persistent depressive disorder:** chronic low-grade depressed mood for at least **two years** (one year in children and adolescents) with **two or more** depressive symptoms, never symptom-free for more than **two months**; the DSM-5 merger of chronic MDD and dysthymia, ICD-11 dysthymic disorder.
- **Dysthymia:** the older name for the same chronic sub-threshold depression; the one number to hold is the two-year floor, and ICD-11 requires no depressive episode in the first two years.

7.4 Double depression: a major depressive episode on underlying dysthymia

Double depression is the term for a **major depressive episode superimposed on underlying dysthymia** (or persistent depressive disorder), so that an acute episode erupts on a chronically depressed baseline and, on remitting, the patient returns not to euthymia but to the antecedent dysthymic floor (Kaplan & Sadock 2024). Kaplan & Sadock illustrate exactly this as one of the graphic courses of depression: recurrent major depression overlapping an underlying dysthymic disorder, with a return to that dysthymia between episodes. The clinical importance is the **incomplete inter-episode recovery**: because baseline is never normal mood, "recovery" from the acute episode still leaves residual depressive symptoms, and this is the mechanism behind its poorer prognosis. In the Collaborative Depression Study follow-up, patients with double depression had depressive symptoms roughly **three-quarters** of the time over follow-up (Judd et al. 1998, cited in Tasman), and double depression is listed as a marker of treatment resistance and of recurrence or relapse (Kaplan & Sadock 2024).

WORKED EXAMPLE

A 41-year-old woman describes feeling flat, tired and hopeless "for as long as I can remember, at least the last four years", never really well but coping. Over the past six weeks she has slid further: pervasive anhedonia, early-morning waking, a 5 kg weight loss, poor concentration and passive death wishes, now meeting full major-depressive-episode criteria. This is double depression: a major depressive episode on top of established dysthymia. The trap is to treat only the acute episode and, when the florid symptoms lift, to call her recovered, when in fact she has merely returned to her dysthymic baseline and remains at high risk of the next episode.

TRAP **Do not dismiss persistent depressive disorder as "just personality" and under-treat it.** The chronic low mood is a treatable illness, not a fixed trait; missing it, or stopping at partial recovery in double depression, leaves the patient chronically symptomatic and at high relapse risk.

GOOD TO REMEMBER

- **Double depression:** a major depressive episode superimposed on underlying dysthymia; the discriminating feature is incomplete inter-episode recovery (return to the dysthymic floor, not to euthymia), and the number to hold is symptoms roughly **three-quarters** of follow-up time, marking a poorer prognosis (Judd et al. 1998).

7.5 Clinical significance: high burden despite lower severity, and the management pointer

The paradox of persistent depressive disorder is a **high cumulative burden despite lower per-day severity**. Because the illness is chronic, its total load of impairment, its comorbidity (with anxiety disorders, substance use, and personality pathology) and its association with disability accrue over years even though no one day looks dramatic (Kaplan & Sadock 2024). Chronicity, not intensity, is the burden. On management, the one-line pointer is that persistent depressive disorder is treated with the same broad tools as major depression, combining pharmacotherapy with structured psychotherapy, with specifically chronic-depression-oriented psychotherapy (of the CBASP type) and antidepressants both used, and combined treatment often outperforming either alone; the detailed drug selection, dosing and treatment-resistance algorithms are owned by the Mood disorders: pharmacotherapy notes and are cross-referenced, not duplicated here (Kaplan & Sadock 2024).

PEARL

The single most useful discriminator at the bedside is the course shape: major depression is an *episode* the patient can date to a month or a season and from which they return to their usual self; dysthymia is a *trait-like* chronic low mood that has become their normal, and double depression is the episode breaking out on that chronic floor and sinking back into it.

HOLD THIS

Persistent depressive disorder is depression defined by duration, not depth: low mood for at least two years, never symptom-free for more than two months; a major depressive episode on that dysthymic baseline is double depression, and its chronicity, incomplete recovery and comorbidity are the burden.

8 · The depressive subtypes

Why this matters. Once a **depressive episode** is confirmed, the examiner tests whether the reader can read its **clinical shape**: the same five-of-nine episode splits into recognisable subtypes that carry different biology, different prognosis and, downstream, different treatment. This topic is the keyed grid of those subtypes. Four earn their own line and their own keyword: **melancholic** depression, **atypical depression**, **psychotic depression** and **catatonic depression**. Each is a DSM-5-TR specifier applied to an episode whose core criteria are owned by the major depressive disorder topic and cross-referenced here, not re-derived; the raw descriptive definitions of the individual mood symptoms are owned by the Psychometry, Assessment and Descriptive Psychopathology notes.

The single organising axis to carry through the whole grid is **mood reactivity**. Melancholic depression loses it; atypical depression keeps it. That one contrast, non-reactive versus reactive mood, is the pivot the examiner returns to, and it maps onto the older endogenous-versus-neurotic split and onto the more biological versus more bipolar-spectrum poles of the depressive syndrome (Kaplan & Sadock 2024; Akiskal 2007). Psychotic and catatonic depression then layer a second dimension on top, the presence of psychosis or of the catatonic syndrome, marking the most severe end of the range.

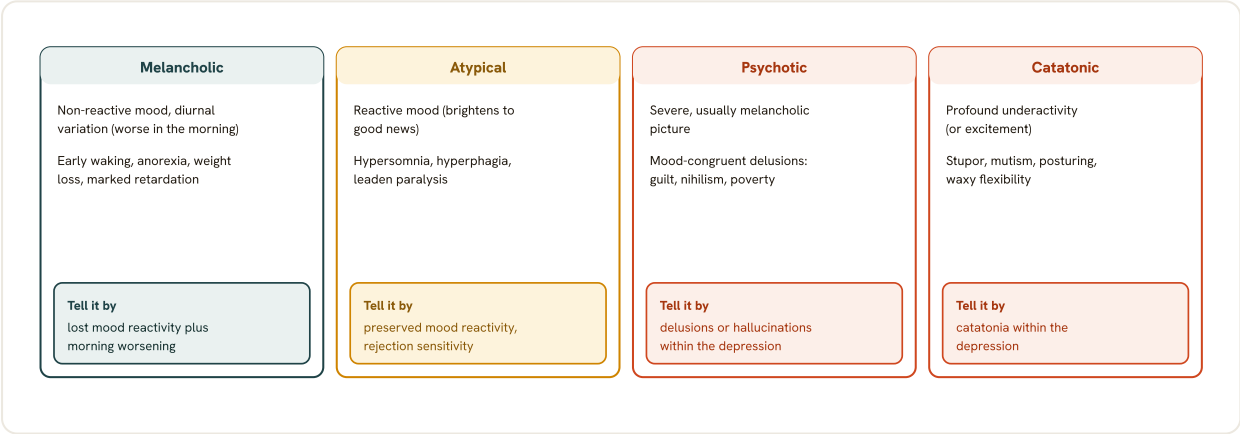


Fig 11.4 The depressive subtypes, keyed on the one feature that tells each apart. The pivotal contrast is mood reactivity: melancholic depression loses it (with morning worsening and early waking), atypical depression keeps it (with reversed vegetative signs and rejection sensitivity). Psychotic depression adds mood-congruent delusions, and catatonic depression adds catatonic signs within the episode. The catatonia entity itself is developed in the Other psychotic disorders, delusional syndromes and catatonia notes.

8.1 Melancholic depression: the non-reactive, more biological picture

Melancholic depression (DSM-5-TR: **with melancholic features**; the older term is endogenous depression) is the classic severe, biological presentation. The DSM-5-TR specifier has a two-part structure the reader should be able to reproduce (DSM-5-TR; Kaplan & Sadock 2024). Criterion A requires **one** of: loss of pleasure in all or almost all activities, or a lack of reactivity to usually pleasurable stimuli (mood does not brighten even temporarily when something good happens). Criterion B then requires **three or more** of six features: a distinct quality of depressed mood (profound despondency, despair, moroseness, or an empty mood, experienced as qualitatively different from ordinary sadness); depression regularly worse in the morning, the diurnal variation; early-morning awakening at least **2 hours** before the usual time; marked psychomotor

agitation or retardation observable by others; significant anorexia or weight loss; and excessive or inappropriate guilt. The signature to hold is the cluster: non-reactive mood plus a distinct quality of mood, plus the AM-worse diurnal variation and early-morning waking, plus marked psychomotor change, anorexia and weight loss and excessive guilt. Melancholia is more frequent in inpatients than outpatients, in more severe rather than milder episodes, and in episodes carrying psychotic features (DSM-5-TR).

RULE **Melancholic loses mood reactivity; atypical keeps it. Reactivity is the pivot.** A non-reactive mood with a distinct quality, morning worsening and early waking points melancholic; a mood that still brightens to good events points away from it.

GOOD TO REMEMBER

- **Melancholic depression:** the non-reactive, more biological depression; DSM-5-TR needs loss of pleasure or loss of reactivity plus **3 or more** of distinct-quality mood, AM-worse diurnal variation, early-morning awakening, marked psychomotor change, anorexia or weight loss, and excessive guilt; the one discriminating feature to hold is **non-reactive mood** with early-morning awakening.

8.2 Atypical depression: reactive mood and the reverse-vegetative signs

Atypical depression (DSM-5-TR: **with atypical features**) is the mirror image, and its name is historical rather than a claim of rarity: it is atypical only in contrast to the classical agitated, endogenous presentations that were the norm when depression was rarely diagnosed in outpatients (DSM-5-TR). Criterion A is the defining feature, **mood reactivity**, the capacity for mood to brighten in response to actual or potential positive events, sometimes to euthymia for extended periods if circumstances stay favourable. Criterion B then requires **two or more** of four features: significant weight gain or increased appetite (hyperphagia); hypersomnia (an extended night sleep or daytime napping totalling at least 10 hours a day, or at least 2 hours more than when well); leaden paralysis, a heavy, leaden or weighted-down feeling usually in the arms or legs; and a long-standing pattern of interpersonal rejection sensitivity that is present whether or not the person is depressed and causes real social or occupational impairment (DSM-5-TR). This last feature is a trait with early onset that persists through adult life, which is why it is long-standing rather than episode-bound. Criterion C requires that the episode not meet criteria for melancholic features or catatonia in the same episode: the two are defined as mutually exclusive.

Two downstream facts are examinable. First, atypical features carry an affinity with the **bipolar spectrum**: the reverse-vegetative signs of hypersomnia and hyperphagia are overrepresented in bipolar II depression, so an atypical picture should prompt a careful screen for a past hypomanic episode (DSM-5-TR bipolar II text; Akiskal 2007). Second, the historical anchor: atypical depression was defined by the Columbia group precisely because these patients responded to MAOIs where they responded poorly to tricyclics, phenelzine outperforming imipramine and placebo in their trials (Kaplan & Sadock 2024). The drug detail is cross-referred forward to the Mood disorders: pharmacotherapy notes; here only the responsiveness pattern is held.

TRAP **Do not dismiss reversed vegetative signs as "not real depression".** Hypersomnia and hyperphagia are the core of a defined subtype (atypical depression), not evidence against a mood disorder; reading them as trivial misses a bipolar-spectrum red flag.

GOOD TO REMEMBER

- **Atypical depression:** depression with **preserved mood reactivity** plus **2 or more** of hyperphagia or weight gain, hypersomnia, leaden paralysis, and long-standing rejection sensitivity; associated with the bipolar spectrum; the eponymic anchor to hold is the historical **MAOI** responsiveness (Columbia group).

8.3 Psychotic depression: a depressive episode with delusions or hallucinations

Psychotic depression (DSM-5-TR: **with psychotic features**) is a major depressive episode in which delusions or hallucinations are present at any time during the episode. It is a marker of severity, not a separate disorder, and it can occur in the context of both unipolar and bipolar depression (Maudsley 2021). The psychotic content is usually **mood-congruent**: the delusions and hallucinations track typical depressive themes of personal inadequacy, guilt, disease, death, nihilism (the Cotard-type belief that organs or the self do not exist, or that one is dead), poverty or ruin, and deserved punishment or impending disaster (DSM-5-TR; Kaplan & Sadock 2024). Sometimes the content is **mood-incongruent**, not consonant with depression (for example persecutory or passivity themes, or a mixture); the incongruent pattern carries a worse prognosis. Psychotic depression has a lifetime prevalence of roughly **1%**, is frequently under-diagnosed, and carries greater illness severity, longer episodes, poorer long-term outcome and a substantially higher suicide risk than non-psychotic depression (Maudsley 2021).

The boundary that must be drawn cleanly is against schizoaffective disorder and the wider mood-with-psychosis territory: when psychotic and mood symptoms are present the rule is whether the psychosis is confined to the mood episode (mood disorder with psychotic features) or extends beyond it. That whole mood-with-psychotic-features boundary and the schizoaffective decision are owned by the Other psychotic disorders, delusional syndromes and catatonia notes and cross-referred there. The management, which differs from non-psychotic depression, is an antidepressant plus an antipsychotic, or electroconvulsive therapy; the guideline-level detail is a pointer to the Mood disorders: pharmacotherapy notes and the ECT technique to the ECT and neurostimulation notes.

PEARL

Psychotic depression needs a different treatment from non-psychotic depression and is commonly missed because clinicians do not ask about mood-congruent delusions of guilt, poverty or nihilism. An antidepressant alone under-treats it; the evidence-based options are an antidepressant plus an antipsychotic, or ECT, developed in the Mood disorders: pharmacotherapy notes.

GOOD TO REMEMBER

- **Psychotic depression:** a major depressive episode **with delusions or hallucinations**, usually mood-congruent (guilt, nihilism, poverty, deserved punishment), sometimes incongruent (worse prognosis); the number to hold is a lifetime prevalence near **1%**, and it is treated with an antidepressant plus an antipsychotic or with ECT.

8.4 Catatonic depression: a depressive episode with catatonia

Catatonic depression (DSM-5-TR: **with catatonia**) is a depressive episode dominated by the catatonic syndrome, coded in DSM-5-TR with an additional catatonia code. Clinically it presents with the catatonic signs overlaid on the mood episode: stupor, mutism, negativism, posturing, waxy flexibility, and in the extreme a depressive stupor. It sits at the severe, biological end of the depressive range alongside melancholia and psychosis. The catatonia entity itself, its full sign list, its differential across mood, psychotic and organic causes, and its management (the benzodiazepine challenge and ECT), is owned by the Other psychotic disorders, delusional syndromes and catatonia notes and is cross-referred there; the catatonic-depression subtype, catatonia arising specifically within a depressive episode, is owned here.

GOOD TO REMEMBER

- **Catatonic depression:** a depressive episode **with catatonia** (stupor, mutism, negativism, posturing, waxy flexibility), the most severe motor pole of depression; the catatonia entity is cross-referred to the psychotic-disorders and catatonia notes, the subtype is owned here.

8.5 The keyed subtypes grid

The four named subtypes assemble into a single keyed grid, each row carrying its defining feature and the one discriminator the examiner tests. Read down the reactivity axis first (melancholic non-reactive, atypical reactive), then the psychosis and catatonia layer on top.

SUBTYPE	DEFINING FEATURE	THE ONE DISCRIMINATOR TO HOLD
Melancholic depression	Loss of pleasure or loss of reactivity, plus 3 or more of distinct-quality mood, AM-worse variation, early-morning awakening, marked psychomotor change, anorexia or weight loss, excessive guilt	**Non-reactive mood with early-morning awakening and AM-worse diurnal variation; the more biological picture**
Atypical depression	Mood reactivity preserved, plus 2 or more of hyperphagia or weight gain, hypersomnia, leaden paralysis, long-standing rejection sensitivity	**Reactive mood plus reverse-vegetative signs; bipolar-spectrum affinity; historical MAOI responsiveness**
Psychotic depression	Major depressive episode with delusions or hallucinations, usually mood-congruent (guilt, poverty, nihilism, deserved punishment)	**Presence of psychosis; needs antidepressant plus antipsychotic, or ECT; lifetime prevalence near 1%**

SUBTYPE	DEFINING FEATURE	THE ONE DISCRIMINATOR TO HOLD
Catatonic depression	Depressive episode dominated by the catatonic syndrome (stupor, mutism, negativism, posturing, waxy flexibility)	**Catatonia overlaid on the mood episode; entity cross-referred, subtype owned here**

The depressive-subtypes grid: each named subtype with its defining feature and the single discriminator to hold; the highlighted cell is the fact the examiner tests. This is the concept figure for this topic, Fig 11.4.

3 of 6 MELANCHOLIC B-FEATURES	**2 of 4** ATYPICAL B-FEATURES	**about 1%** PSYCHOTIC DEPRESSION LIFETIME	**2 hours** EARLY-MORNING AWAKENING

WORKED EXAMPLE

A 52-year-old woman has three weeks of severe low mood that does not lift even when her grandchildren visit, wakes at 4 AM (about 2 hours early), feels worst in the mornings, is visibly slowed, has lost 5 kg and voices intense guilt about being a burden. The non-reactive mood, early-morning awakening, AM-worse diurnal variation, psychomotor retardation, weight loss and guilt read as melancholic depression. Contrast a 28-year-old man whose mood still brightens when friends call, who sleeps 11 hours, eats more than usual, describes his legs as leaden, and has a lifelong hypersensitivity to rejection: preserved reactivity plus two reverse-vegetative features read as atypical depression, and prompt a screen for a past hypomanic episode.

MNEMONIC

Melancholic goes DOWN, Atypical goes UP

Melancholic runs the vegetative signs **down**: appetite and weight down (anorexia), sleep down (early-morning awakening), mood down and non-reactive. Atypical runs them **up**: appetite up (hyperphagia), sleep up (hypersomnia), and mood still able to lift (reactive). The reverse-vegetative direction, plus preserved reactivity, is the whole of the atypical picture.

HOLD THIS

Melancholic depression loses mood reactivity (with a distinct-quality mood, AM-worse variation, early-morning awakening at least 2 hours early); atypical depression keeps mood reactivity (with hyperphagia, hypersomnia, leaden paralysis, rejection sensitivity); psychotic depression adds mood-congruent delusions and catatonic depression adds the catatonic syndrome.

9 · Seasonal affective disorder and chronobiology

Why this matters. **Seasonal affective disorder** is a small-print but reliably examined corner of the mood block, and it is examined for a precise reason: it is not a separate disorder but a course specifier, and the discriminator is temporal, not symptomatic. The reflex the examiner rewards is that a **seasonal pattern** requires a regular relationship between mood episodes and a time of year across several years, not a single bad winter. Around it sits the **chronobiology** of mood, the clearest worked example in psychiatry of a circadian mechanism translated into a diagnosis and a physical treatment.

The mechanics of the master clock, the suprachiasmatic nucleus and the molecular clock genes are owned by the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the raw descriptive definitions of the mood symptoms are owned by the Psychometry, Assessment and Descriptive Psychopathology notes. Held here is the mood application: how disrupted **circadian** and sleep-wake rhythms feed seasonal and non-seasonal relapse, and how **light therapy** exploits that biology. The deep drug detail and chronotherapy pharmacology are cross-referred to the Mood disorders: pharmacotherapy notes.

9.1 Seasonal affective disorder and the seasonal pattern specifier

Seasonal affective disorder (SAD), the term introduced by Rosenthal and colleagues, describes recurrent depressive episodes with a regular seasonal onset and remission, classically an autumn-winter onset with spring-summer recovery (Kaplan & Sadock 2024; Companion 2010). Both manuals code it not as a distinct entity but as a course specifier on a recurrent mood disorder: DSM-5-TR calls it **with seasonal pattern**, ICD-11 codes it as with seasonal pattern of mood episode onset (6A80.4), and each can attach to recurrent depressive disorder or to bipolar disorder (DSM-5-TR; ICD-11 CDDR). The DSM-5-TR requirement is the crux and is worth holding precisely: a regular temporal relationship between the onset of episodes and a particular time of year, full remission (or a switch to the opposite pole) also at a characteristic time of year, this pattern present for at least the last **two years** with no non-seasonal episodes in that period, and seasonal episodes substantially outnumbering any non-seasonal episodes over the lifetime (DSM-5-TR). The winter episodes carry a characteristic symptom skew toward **atypical features**: hypersomnia, hyperphagia with carbohydrate craving, weight gain, leaden fatigue and low mood, rather than the insomnia and anorexia of melancholia (Kaplan & Sadock 2024; Companion 2010). Prevalence rises with latitude, a correlation used as circumstantial evidence for a light-dependent mechanism (New Oxford 2020).

RULE **A seasonal pattern is defined by a regular temporal relationship across years, not by symptoms in one winter.** DSM-5-TR needs the pattern over at least the last two years with no intervening non-seasonal episodes, and seasonal episodes outnumbering non-seasonal ones lifetime.

TRAP **Do not label any winter low mood as SAD.** A single dark-month dip, or a depression that merely happens to fall in winter once, is not a seasonal pattern; the specifier is refused unless the temporal regularity is documented across years and non-seasonal episodes are effectively absent.

9.2 The summer pattern and the differential

The autumn-winter form dominates, but a less common **summer pattern** exists, with episodes beginning in spring or summer and remitting in autumn or winter; it tends to carry the reverse profile of insomnia, reduced appetite, weight loss and agitation rather than the atypical reverse-vegetative signs of winter SAD (DSM-5-TR; Kaplan & Sadock 2024). Two differentials keep the diagnosis honest. First, a mood disturbance that recurs each year because of a recurring psychosocial stressor tied to a season, for example a predictable seasonal workload or an anniversary reaction, is explicitly excluded: the specifier does not apply where the seasonality

reflects a season-linked stressor rather than an endogenous pattern (DSM-5-TR; Shorter Oxford 2018). Second, the very status of SAD as a discrete syndrome has been questioned, since some community studies fail to confirm a specific winter-depression syndrome and instead find a milder general seasonality of mood in the population; the specifier remains, but the reader should know the construct is not uncontested (Companion 2010).

9.3 Chronobiology and the circadian theories of mood

Chronobiology is the study of biological rhythms, and circadian rhythms, with a period of about a day, are entrained to the light-dark cycle by the suprachiasmatic nucleus acting on time cues (zeitgebers), the most powerful of which is light (Kaplan & Sadock 2024). Two overlapping hypotheses connect this to seasonal depression. The **reduced-light hypothesis** holds that the shorter photoperiod of winter, less light reaching the retina and the suprachiasmatic nucleus, drives the winter episode, which fits the latitude gradient and the response to added bright light (New Oxford 2020; Kaplan & Sadock 2024). The **phase-shift hypothesis** (Lewy and colleagues) is more specific: it proposes that in winter SAD the internal circadian clock, and in particular the timing of nocturnal melatonin secretion, drifts into a phase delay relative to the sleep-wake cycle, and that correctly timed morning bright light works by **phase-advancing** the clock back into alignment (Kaplan & Sadock 2024). Melatonin, synthesised from serotonin and secreted at night by the pineal under suprachiasmatic control, is the central rhythm signal, and its mistimed secretion is the mechanistic hinge of the phase-shift account (New Oxford 2020).

PEARL

The phase-shift hypothesis predicts the clinical instruction. If winter SAD is a phase-delayed clock, then light must be given in the **morning** to phase-advance it; morning bright light is more effective than evening light in most trials, and this timing logic, not the raw brightness alone, is the examinable point (Kaplan & Sadock 2024).

9.4 Social rhythm disruption and circadian relapse in both poles

Beyond the seasonal case, disrupted rhythms feed relapse across the mood disorders, and the framework the examiner names is the social rhythm disruption model of Ehlers, Frank and colleagues. The claim is that regular daily **social zeitgebers**, consistent bedtimes, mealtimes and first daily social contact, stabilise the underlying circadian and sleep-wake rhythm, and that a life event which disrupts these social rhythms (bereavement, shift work, a transmeridian flight, a new infant) destabilises the biological rhythm and can precipitate a mood episode (Kaplan & Sadock 2024). In bipolar disorder the link is sharpest at the manic pole: sleep loss and circadian disruption can trigger the rapid onset of mania, which is why protecting sleep and regularising routine is central to relapse prevention (New Oxford 2020). This is the rationale for interpersonal and social rhythm therapy (IPSRT), which combines interpersonal psychotherapy with behavioural stabilisation of the daily schedule to smooth social rhythms and lengthen time to relapse; the psychotherapy detail itself sits with management, but the mechanism belongs here (Frank et al.; Kaplan & Sadock 2024).

HOLD THIS

Seasonal affective disorder is a course specifier, not a separate disorder: a regular seasonal onset and remission across at least two years, a winter form skewed to atypical features, explained by a phase-delayed circadian clock, and treated first-line with morning bright light.

9.5 Light therapy: the first-line pointer for seasonal depression

Light therapy (phototherapy) is the established first-line treatment for winter seasonal depression: daily exposure to **bright light, typically in the morning**, using a light box delivering of the order of **10,000 lux** for about 30 minutes, or lower intensities such as 5,000 lux for longer, timed to phase-advance the delayed clock (Kaplan & Sadock 2024; Shorter Oxford 2018). It is best evidenced in SAD with atypical winter features and has also shown benefit in non-seasonal depression (Tasman 2015). It is generally well tolerated; the main cautions are theoretical switch risk in bipolar patients and eye considerations, and its overall specificity over dim-light control has at times been hard to disentangle from placebo, so the reader should present it as first-line but not miraculous (Companion 2010; New Oxford 2020). The comparative drug choice for seasonal depression, notably the SSRI and agomelatine options and the use of chronotherapeutic techniques such as sleep-phase advance and adjunctive melatonin, is cross-referred to the Mood disorders: pharmacotherapy notes and given at guideline level only there.

at least 2 yr	10,000 lux	morning
DSM-5-TR SEASONAL PATTERN	STANDARD LIGHT-BOX DOSE	TIMING TO PHASE-ADVANCE

INDIA

Classic winter seasonal affective disorder is far less prominent in Indian practice than in high-latitude countries, consistent with the latitude gradient: most of India lies in low latitudes with a small seasonal photoperiod swing, so the syndrome is uncommon and light therapy is a niche rather than a routine tool in Indian psychiatry. This chapter names no brand for it; drug branding, Indian brand first, belongs to the Mood disorders: pharmacotherapy notes.

GOOD TO REMEMBER

- **Seasonal affective disorder:** recurrent depression with regular seasonal onset and remission; it is a **course specifier** (DSM-5-TR: with seasonal pattern; ICD-11 6A80.4), not a separate disorder; the number to hold is the DSM-5-TR requirement of the pattern over at least the last **two years** with no non-seasonal episodes.
- **Winter (autumn-winter) pattern:** the common form; the discriminating feature is **atypical** symptoms, hypersomnia, hyperphagia and carbohydrate craving; the eponym to hold is Rosenthal.
- **Summer pattern:** the uncommon form; spring or summer onset with the reverse profile of insomnia, poor appetite, weight loss and agitation.
- **Phase-shift hypothesis:** winter SAD as a phase-**delayed** circadian clock with mistimed melatonin; the eponym is Lewy, and it predicts that **morning** light corrects it.
- **Social rhythm disruption model:** loss of regular social zeitgebers destabilises the circadian rhythm and precipitates episodes; the names are Ehlers and Frank, and the therapy is IPSRT.
- **Light therapy:** first-line for winter SAD; bright light, morning, of the order of **10,000 lux**; well tolerated but of debated specificity over dim-light control.

10 · Peripartum and postpartum depression

Why this matters. A depressive episode arising around childbirth is one of the highest-yield mood-syndrome vignettes in the exam, because it packages three separable things the examiner wants you to keep apart: a genuine mood disorder carrying a course specifier, a benign self-limited adjustment (the blues), and a psychiatric emergency (postpartum psychosis). The single reflex being tested is that **peripartum** is a *specifier on a mood episode*, not a free-standing diagnosis, and that behind the soft label "postnatal depression" may hide a bipolar depression or an evolving psychosis that changes management completely.

Hold the terminology first. **Peripartum** (use "peripartum") is the DSM-5-TR onset window; **postpartum depression** (use "postpartum depression"), also called **postnatal depression** (use "postnatal depression"), is the clinical entity of a depressive episode after delivery. This topic owns the perinatal *mood* syndrome and its screening and management pointer; the wider perinatal frame (perimenopause, perinatal anxiety, the obstetric liaison picture) is cross-referenced to the Perinatal/women's mental health and emergency psychiatry notes, and postpartum psychosis proper is owned by the Other psychotic disorders, delusional syndromes and catatonia notes. The raw descriptive definitions of the depressive symptoms and the rating scales are owned by the Psychometry, Assessment and Descriptive Psychopathology notes.

10.1 The entity: a depressive episode with a peripartum-onset specifier

There is no separate criterion set for "postpartum depression": the depressive episode is diagnosed by the standard criteria (taught in full in the major depressive disorder topic), and childbirth is captured by a peripartum-onset specifier. In DSM-5-TR the specifier "with peripartum onset" applies when the onset of mood symptoms occurs during pregnancy or in the **4 weeks** following delivery (DSM-5-TR). The manual deliberately uses "peripartum" rather than "postpartum" because about **50%** of postpartum major depressive episodes actually begin before delivery, so pregnancy-onset and delivery-onset episodes are grouped together (DSM-5-TR). Clinically the episode often declares itself within the first months rather than the first four weeks, which is why the strict specifier window and the looser clinical reality are both examinable.

RULE **Peripartum is a specifier, not a diagnosis.** Diagnose the depressive episode on standard criteria, then add "with peripartum onset" if it began in pregnancy or within four weeks of delivery (DSM-5-TR).

10.2 ICD-11 nosology and the ICD-10 flag

ICD-11 handles the perinatal picture differently: it does not use an onset specifier but provides a grouping, **6E20** mental and behavioural disorders associated with pregnancy, childbirth or the puerperium **without psychotic symptoms**, and **6E21** the same **with psychotic symptoms**, applied when a mood (or other mental) syndrome arises during pregnancy or within about **6 weeks** after delivery and cannot be better classified elsewhere (ICD-11 CDDR). Note the small discriminator the examiner likes: the DSM-5-TR window is **4 weeks** postpartum, whereas the ICD-11 puerperal window is roughly **6 weeks**. ICD-10 (F53, mental and behavioural disorders

associated with the puerperium not elsewhere classified, still cited in Indian exams) is flagged here. Nosology is given ICD-11 primary with DSM-5-TR cross-mapped.

SYSTEM	HOW CHILDBIRTH IS CODED	THE ONSET WINDOW TO HOLD
DSM-5-TR	Course specifier "with peripartum onset" on the mood episode	**Pregnancy or within 4 weeks of delivery**
ICD-11	6E20 (without psychotic symptoms) / 6E21 (with psychotic symptoms)	**Pregnancy or about 6 weeks after delivery (puerperium)**
ICD-10	F53 puerperal mental disorders not elsewhere classified (exam legacy)	Puerperium (flagged for older exams)

How each system codes a peripartum mood episode; the highlighted cells are the two onset windows the examiner contrasts.

10.3 The three-way distinction: blues versus depression versus psychosis

The core discrimination of this topic is a three-way one, and getting it right is the whole exam point. The postpartum blues (maternity blues, "baby blues") is **not a mental disorder**: sudden mood changes, tearfulness in the absence of true depression, mild sleep disturbance and even transient confusion, with **no functional impairment**, appearing in the first days after delivery and self-limiting, typically improving within a week without treatment (DSM-5-TR). It is common, affecting a large proportion of new mothers. **Postpartum depression** is a full depressive episode with the standard duration and symptom threshold, causing impairment and needing treatment. Postpartum psychosis is a separate psychiatric emergency, typically resembling a manic or mixed episode with psychotic features, strongly associated with bipolar I disorder, of sudden onset in the first days to weeks, carrying a rare but real risk of infanticide when driven by command hallucinations to harm the infant or delusions that the infant is possessed (DSM-5-TR). The entity itself is owned by the Other psychotic disorders, delusional syndromes and catatonia notes; it is contrasted here because the whole safety of the topic turns on not mistaking one for another.

FEATURE	POSTPARTUM BLUES	POSTPARTUM DEPRESSION	POSTPARTUM PSYCHOSIS
Status	Not a disorder; physiological	Mood disorder (depressive episode)	**Psychiatric emergency**
Typical onset	First few days postpartum	Within weeks to first months (peripartum window)	**First few days to 2 weeks, abrupt**
Duration	Self-limited, resolves within a week	Persistent, meets episode threshold	Rapidly progressive without treatment
Impairment	None	Present	Severe
Psychosis	Absent	Absent (unless severe with psychotic features)	**Defining; command hallucinations, delusions about the infant**

FEATURE	POSTPARTUM BLUES	POSTPARTUM DEPRESSION	POSTPARTUM PSYCHOSIS
Core association	Physiological postpartum change	Past depression, poor support	**Bipolar I disorder**
Action	Reassurance, watchful waiting	Screen, treat, safeguard	Urgent admission, treat as emergency

The three-way peripartum differential; the highlighted cells carry the discriminators that separate an emergency from an illness from a normal adjustment.

TRAP **Do not let "postnatal depression" hide a bipolar depression or an evolving postpartum psychosis.** An abrupt, fluctuating, psychotic or manic-tinged postpartum presentation is an emergency, not a low mood; always ask about past hypomania before you reach for an antidepressant.

10.4 Epidemiology and the prevalence numbers to hold

Perinatal depression is common, not rare. Postpartum depression occurs in approximately **15%** of women (Tasman 2015). DSM-5-TR frames the risk temporally: about **9%** of women will experience a major depressive episode between conception and birth, and the best estimate for a major depressive episode between birth and 12 months postpartum is just below **7%** (DSM-5-TR). Postpartum psychosis is far rarer, occurring in roughly **1 in 500 to 1 in 1,000** deliveries and more common in primiparous women (DSM-5-TR).

~15%	4 weeks	~50%	1 in 500 to 1,000
POSTPARTUM DEPRESSION PREVALENCE	DSM-5-TR PERIPARTUM WINDOW	OF POSTPARTUM MDES BEGIN BEFORE DELIVERY	POSTPARTUM PSYCHOSIS (DELIVERIES)

10.5 Risk factors and the recurrence figures

The risk factors cluster into psychiatric history, social support and obstetric or psychosocial stress. The strongest is a **past depressive or bipolar illness**: women with a history of major depression carry a **10% to 25%** risk of an episode of postpartum depression (Tasman 2015). A prior postpartum depression is the single most predictive marker, carrying about a **50%** risk of another episode with subsequent births, which makes eliciting that history essential (Tasman 2015). The other established risks are **poor social support** (an unsupportive partner, isolation), and **obstetric and psychosocial stressors** (a difficult delivery, an unwell or unwanted infant, poverty, marital conflict, and life events around the birth). For postpartum psychosis specifically, once a woman has had a psychotic postpartum episode the recurrence risk with each subsequent delivery is between **30% and 50%**, and a personal or family history of bipolar I disorder markedly raises the risk (DSM-5-TR).

RULE **Ask about the last delivery.** A prior postpartum depression carries roughly a 50% recurrence risk with the next birth, and a prior postpartum psychosis carries a 30% to 50% recurrence risk; the obstetric psychiatric history is the highest-yield question you can ask.

10.6 Impact on mother-infant bonding and child development

The reason perinatal depression is prioritised in public health is that it does not affect the mother alone. Untreated maternal depression impairs **mother-infant bonding** and the quality of early interaction, and is associated with poorer **child developmental outcomes**, including effects on the infant's emotional, cognitive and behavioural development, mediated through reduced responsive caregiving and disturbed early attachment (Tasman 2015; New Oxford Textbook 2020). This dyadic impact is the argument for universal screening and for treating the mother as the route to protecting the child, and it is why the topic is examined as a maternal-and-infant problem rather than a maternal one.

10.7 Screening: the Edinburgh Postnatal Depression Scale

Because a new mother is sleep-deprived and preoccupied, and may not distinguish a drift from the blues into a mood disorder, active **screening** (use "screening") is standard rather than waiting for spontaneous complaint. The instrument to name is the Edinburgh Postnatal Depression Scale (EPDS), a 10-item self-report questionnaire developed for detecting postnatal depression (Cox et al. 1987), deliberately weighted away from the somatic symptoms (sleep, appetite, fatigue) that are confounded by normal new motherhood and towards the mood and cognitive items (New Oxford Textbook 2020; Companion to Psychiatric Studies 2010). It is a screen, not a diagnostic test: a positive EPDS flags a woman for a full clinical assessment, and any endorsement of the self-harm item is acted on directly. The structured suicide risk assessment and safety planning are owned by the Somatic-symptom, sexual, impulse-control disorders and suicide notes; the descriptive detail of the scales is owned by the Psychometry, Assessment and Descriptive Psychopathology notes.

RULE **Screen every perinatal woman, and always ask about past hypomania before an antidepressant.** Use the EPDS to screen; a prior hypomanic episode reclassifies the depression as bipolar and changes first-line treatment.

10.8 Management principles as a guideline pointer

Management is given here at guideline level only; the drug detail (mechanisms, dosing, adverse effects, interactions and treatment-resistant algorithms) is owned by the Mood disorders: pharmacotherapy notes, and the ECT technique by the ECT and neurostimulation notes. Three principles carry the exam answer. First, for **mild to moderate** postpartum depression, a **psychological therapy is first-line**: CANMAT recommends offering CBT or interpersonal therapy, individual or group, as first-line treatment for mild to moderate postpartum depression in breastfeeding women (CANMAT 2016). Second, when an antidepressant is needed in a **breastfeeding** woman, sertraline is the preferred agent: CANMAT lists citalopram, escitalopram or sertraline as the preferred antidepressants for postpartum depression in breastfeeding women, and the British Association for Psychopharmacology similarly prefers sertraline because of its low transfer into breast milk and low rate of reported adverse effects (CANMAT 2016; BAP 2015). Third, for **severe, psychotic or treatment-resistant** perinatal depression, ECT is considered, and breastfeeding can continue during ECT (CANMAT 2016). NICE similarly places psychological interventions first for mild to moderate perinatal depression and reserves

antidepressants and ECT for more severe or refractory illness, weighing risks and benefits with the woman. The Indian Psychiatric Society (use "Indian Psychiatric Society") clinical practice guidelines for depression (Gautam et al. 2017, the IPS guidelines) endorse the same phase-based, therapy-first-for-milder-illness framework; the specific perinatal breastfeeding-antidepressant recommendation could not be separately confirmed in the IPS text available here and is therefore named without a specific IPS agent claim rather than invented. The wider perinatal management frame is cross-referenced to the Perinatal/women's mental health and emergency psychiatry notes.

SITUATION	GUIDELINE RECOMMENDATION (FIRST-LINE)	SOURCE
Mild to moderate postpartum depression	**CBT or interpersonal therapy (individual or group), first-line**	CANMAT 2016; NICE
Antidepressant needed, breastfeeding	**Sertraline preferred (also citalopram, escitalopram); low breast-milk transfer**	CANMAT 2016; BAP 2015
Severe, psychotic or treatment-resistant	**Consider ECT; breastfeeding may continue during ECT**	CANMAT 2016
Any perinatal depression, before starting a drug	Screen for past hypomania; safeguard mother and infant	General principle

The guideline-anchored management pointer for peripartum depression; the highlighted cells are the three first-line moves the examiner rewards.

INDIA

Perinatal depression is a substantial and under-recognised problem in Indian settings, where the disorder is often expressed somatically and detected late, and where limited social support and obstetric or psychosocial stress are common; community screening with the Edinburgh Postnatal Depression Scale is used in Indian research and district mental health work, and comparative data have historically suggested perinatal mood disturbance is at least as common in lower-resource settings as in higher-resource ones (Shorter Oxford Textbook 2018). For severe, psychotic or treatment-resistant perinatal depression, ECT is widely available across Indian teaching hospitals and is a practical option, with breastfeeding continued. This chapter is generic and names no brand; drug branding, Indian brand first, belongs to the Mood disorders: pharmacotherapy notes. A verified India-specific perinatal prevalence figure from the National Mental Health Survey could not be confirmed in the sources available here and is not asserted.

WORKED EXAMPLE

A 27-year-old woman is brought at three weeks postpartum with two weeks of low mood, anhedonia, guilt about being a "bad mother", poor sleep beyond the infant's demands, and thoughts that the baby would be better off without her. She is fully oriented with no fluctuation of awareness and no delusions or hallucinations. Count the episode: this meets a depressive episode, and because onset is within four weeks of delivery it is major depressive disorder, with peripartum onset (DSM-5-TR). Now the two mandatory moves before treatment: screen the lifetime history for any past hypomanic episode (to catch a bipolar depression), and act on the passive death wish with a formal risk assessment. Because she is breastfeeding and this is moderate, offer a psychological therapy first-line, and if an antidepressant is needed prefer sertraline (CANMAT 2016). Had she instead been abruptly perplexed, elated at times, and convinced the infant was possessed, the answer would pivot to a suspected postpartum psychosis and urgent admission.

GOOD TO REMEMBER

- **Peripartum-onset specifier (DSM-5-TR):** a depressive episode with onset in pregnancy or within **4 weeks** of delivery; a specifier, not a separate diagnosis; about **50%** of postpartum episodes begin before delivery.
- **Postpartum (postnatal) depression:** a full depressive episode after childbirth, prevalence approximately **15%**; needs treatment; the number to hold is the roughly **50%** recurrence with the next birth.
- **Postpartum blues:** not a disorder; tearful mood swings in the first days, self-limiting within a week, no impairment, no treatment.
- **Postpartum psychosis:** a psychiatric emergency, abrupt, manic or mixed with psychotic features, strongly tied to bipolar I, **1 in 500 to 1,000** deliveries; owned by the psychotic-disorders notes.
- **ICD-11:** 6E20 (without psychotic symptoms) / 6E21 (with psychotic symptoms), puerperal window about **6 weeks**.
- **Screening scale:** the Edinburgh Postnatal Depression Scale (EPDS), a 10-item self-report screen (Cox et al. 1987).
- **Management (guideline):** psychological therapy first-line for mild to moderate; sertraline the preferred antidepressant in breastfeeding; ECT for severe or psychotic cases (CANMAT 2016).

MNEMONIC

BLUES vs BLUE MOOD vs BREAK

Three B's for the three-way split: **BLUES** is benign and brief (self-limits within a week, no impairment); **BLUE MOOD** is the depression proper (a true episode, screen and treat); **BREAK** is the psychotic break (postpartum psychosis, an emergency, bipolar-linked). If the mother is breaking with reality, it is the third B and it is urgent.

PEARL

The word "peripartum" is itself the teaching point: DSM-5-TR chose it over "postpartum" precisely because half of these episodes start in pregnancy. If the vignette gives you low mood that began in the third trimester and worsened after delivery, that is still "with peripartum onset", not a new postnatal illness.

HOLD THIS

Peripartum is a specifier on a depressive episode (pregnancy or within 4 weeks of delivery, DSM-5-TR): screen every perinatal woman with the EPDS, ask about past hypomania before any antidepressant, prefer sertraline in breastfeeding, and never let "postnatal depression" mask a bipolar depression or an evolving postpartum psychosis.

11 · Premenstrual dysphoric disorder

Why this matters. **Premenstrual dysphoric disorder** is the affective disorder the examiner tests to see whether the candidate understands that the diagnosis is made by **prospective timing**, not by a plausible history. It is a cluster of marked affective and physical symptoms, irritability, mood lability, depressed mood and anxiety alongside physical symptoms, that is confined to the **luteal phase** of the menstrual cycle and remits shortly after the onset of menses, returning the woman to a symptom-free follicular baseline (DSM-5-TR; Kaplan & Sadock 2024). The whole clinical identity of the entity rests on that cyclical on-off pattern locked to the cycle.

The board-relevant points are three: the luteal-phase confinement with post-menstrual remission, the requirement that the diagnosis be **confirmed by prospective daily rating** over at least two cycles rather than accepted from a single retrospective account, and the split nosological placement, DSM-5 filing it among the depressive disorders while ICD-11 places it in the gynaecological chapter with a cross-listing back into the mood grouping. The raw descriptive definitions of the individual mood symptoms and the rating scales are owned by the Psychometry, Assessment and Descriptive Psychopathology notes; the wider frame of women's reproductive-cycle mood disturbance sits with the Perinatal/women's mental health and emergency psychiatry notes; the detailed pharmacology of the SSRIs belongs to the Mood disorders: pharmacotherapy notes.

11.1 The entity: luteal-phase symptoms that remit after menses

Premenstrual dysphoric disorder (PMDD, abbreviated pmdd) is defined by a symptomatic cluster that appears in the final premenstrual (luteal) week for **most menstrual cycles of the preceding year**, begins to improve within a few days of the onset of menses, and becomes minimal or absent in the post-menstrual (follicular) week (DSM-5-TR; Kaplan & Sadock 2024). DSM-5-TR (Criterion A) requires at least **5 of 11** symptoms in that premenstrual week; Criterion B requires that at least **one** of them be from the affective core, marked affective lability, marked irritability or anger, marked depressed mood or hopelessness, or marked anxiety or tension; Criterion C supplies the remaining symptoms, decreased interest, poor concentration, lethargy, appetite change or food cravings, hypersomnia or insomnia, a sense of being overwhelmed, and physical symptoms such as breast tenderness or swelling, joint or muscle pain, bloating or weight gain (DSM-5-TR). Criterion D requires significant distress or functional interference, and Criterion E requires that the symptoms not be merely a premenstrual exacerbation of another disorder, though PMDD may co-occur with one.

RULE **PMDD is confirmed by prospective luteal-phase rating, not recall.** The symptoms must be timed to the luteal phase and shown, by daily charting across at least two cycles, to remit after menses; the pattern, not the symptom list, is the diagnosis.

11.2 Prospective daily rating over at least two cycles confirms it

The criterion that separates a rigorous diagnosis from a guess is DSM-5-TR Criterion F: the timing described in Criterion A must be **confirmed by prospective daily ratings** during at least two symptomatic cycles, because a provisional diagnosis made from history alone is unreliable and frequently overturned once the woman actually charts her symptoms against her cycle (DSM-5-TR; Kaplan & Sadock 2024). Retrospective report over-attributes ordinary premenstrual complaints to the luteal phase and cannot demonstrate the post-menstrual remission that defines the disorder; only prospective daily rating over at least two cycles establishes the luteal-phase confinement and the return to a symptom-free follicular baseline. This is why the prospective chart, not the presenting story, is the operative test.

TRAP **Diagnosing PMDD from a single retrospective history.** A convincing account of premenstrual irritability is not the diagnosis; without at least two cycles of prospective daily rating the timing is unconfirmed and the label is premature.

11.3 Placement (DSM-5 depressive, ICD-11 gynaecological with a cross-listing) and management pointer

The nosology is the classic split the examiner probes. DSM-5 (and DSM-5-TR) places premenstrual dysphoric disorder as a full diagnosis **within the depressive disorders** chapter, treating it as a mood disorder proper (DSM-5-TR; Shorter Oxford Textbook of Psychiatry). ICD-11 (GA34.41) does the opposite: it classifies PMDD primarily in the grouping of premenstrual disturbances in Chapter 16 on diseases of the genitourinary system, but **cross-lists** it (secondary-parents it) into the depressive disorders grouping so that clinicians reading the mood section still find it (ICD-11 CDDR). ICD-10 carried the older, looser "premenstrual tension syndrome" and did not require prospective confirmation, and is flagged because Indian exams still cite it. On management, the one-line pointer is that SSRIs are first-line, given either continuously or restricted to luteal-phase dosing, with roughly two-thirds of women responding; the detailed drug pharmacology, dosing and next-line options (including the GnRH agonists reserved for SSRI non-responders) are owned by, and cross-referenced to, the Mood disorders: pharmacotherapy notes (Kaplan & Sadock 2024).

SYSTEM	PLACEMENT	CONFIRMATION STANCE
DSM-5-TR	**Depressive disorders chapter (a mood disorder proper)**	Criterion F: prospective daily ratings over at least two cycles
ICD-11 (GA34.41)	**Chapter 16 genitourinary (premenstrual disturbances), cross-listed into depressive disorders**	Luteal-phase symptoms confirmed against the cycle
ICD-10	Premenstrual tension syndrome (gynaecological)	No prospective-charting requirement; still cited in Indian exams

Placement map for PMDD: DSM-5 files it among the depressive disorders, ICD-11 in the gynaecological chapter with a cross-listing back to mood, and only the modern systems demand prospective confirmation.

5 of 11	at least 2 cycles	about 5%
SYMPTOMS, LUTEAL WEEK	PROSPECTIVE DAILY RATING	SEVERE PREMENSTRUAL SYMPTOMS

GOOD TO REMEMBER

- **Premenstrual dysphoric disorder (PMDD):** a luteal-phase cluster of marked affective (irritability, mood lability, depressed mood, anxiety) and physical symptoms that remits shortly after menses onset; the one discriminating feature is confinement to the luteal phase confirmed by **prospective daily rating over at least two cycles** (DSM-5-TR Criterion F), and the numbers to hold are **5 of 11** symptoms with at least one from the affective core.
- **Placement:** DSM-5 among the depressive disorders; ICD-11 gynaecological (GA34.41, Chapter 16) with a cross-listing into depressive disorders; SSRIs (continuous or luteal-phase dosing) are first-line, cross-referred to the Mood disorders: pharmacotherapy notes.

INDIA

PMDD is under-recognised in Indian practice because it usually presents first to gynaecology as "premenstrual tension" rather than to psychiatry, and the ICD-10 gynaecological framing many Indian services still work from does not demand prospective charting; the practical teaching point is to hand the woman a simple daily symptom chart across at least two cycles before committing to the diagnosis or starting an SSRI (Kaplan & Sadock 2024).

HOLD THIS

PMDD is a luteal-phase affective disorder confirmed by prospective daily rating over at least two cycles (not by retrospective history), needing 5 of 11 symptoms with at least one affective-core symptom; DSM-5 files it under depressive disorders, ICD-11 files it in the gynaecological chapter with a cross-listing, and SSRIs continuous or luteal-phase are first-line.

12 · Andrade construct, masked and mixed anxiety-depression

Why this matters. This is the small-print corner where depression stops looking like the textbook picture. Three ideas cluster here: the academic reframing of depression as a **syndrome** rather than a single disease, the everyday clinical reality that depression often arrives dressed as physical complaints, and the diagnostic no-man's-land where anxiety and low mood sit together but neither reaches threshold. Each is separately examinable, and each carries the same practical lesson: the mood component is often present but unspoken, and it is found only if you ask.

The raw descriptive definitions of the mood symptoms and the rating scales are owned by the Psychometry, Assessment and Descriptive Psychopathology notes; the full depressive-episode criteria live earlier in this chapter. Held here is the atypical presentation: how depression hides behind somatic symptoms, what the **depressive equivalents** are, and where sub-threshold mixed anxiety-depression sits in the nosology.

12.1 The Andrade construct: depression as a syndrome of depression

The Andrade construct, an Indian academic reframing associated with the term **syndrome of depression**, treats depression not as a single unitary disease but as a heterogeneous syndrome, a

final common presentation reachable by many routes, so that the clinical entity is better understood as a cluster of overlapping subtypes than as one disorder. This is the same conceptual move made across the field when depression is called an affective **spectrum** rather than a discrete illness, and it underpins why masked forms and depressive equivalents belong in the same discussion. The exact wording, scope and primary attribution of the Andrade **syndrome of depression** construct could not be confirmed against the parsed reference library, so it is named here and flagged rather than elaborated with invented detail; the trainee should hold the label and the core idea (depression as a syndrome, not a single disease) and verify the primary source before quoting specifics.

RULE **Read depression as a syndrome, not a single disease.** A common depressive surface is reached by many routes, which is exactly why it can present masked, somatised or blended with anxiety.

12.2 Masked depression and the somatic presentation

Masked depression describes a depressive disorder in which the depressive mood is not readily apparent and is hidden behind a **somatic presentation**: the patient complains of physical symptoms, and low mood is elicited only on direct enquiry (Shorter Oxford 2018). Older writers called it *depressio sine depressione* (depression without depression) or a **depressive equivalent**, but the concept was never officially endorsed by the classifications and appears in DSM-5-TR only informally, listed among the varied presentations of a depressive episode (Kaplan & Sadock 2024). The somatic complaints span chronic pain, insomnia, atypical facial pain, paraesthesias, fatigue and multiple unexplained bodily symptoms, and the picture is described as especially common in the elderly, where facial expression, vocal inflection and overall appearance may reveal the underlying mood the patient does not report (Kaplan & Sadock 2024). The depressive core can also be obscured by concurrent alcohol or drug misuse.

The examinable counterpoint is that the reasoning must run both ways. Just as a depressive disorder can be missed in a patient who does not spontaneously complain of low mood, so a depression should not be diagnosed merely because depressive symptoms are prominent, since those may belong to another disorder; and unexplained aches and pains must not be assumed to be depressive equivalents without excluding treatable physical illness such as hypothyroidism or anaemia (Shorter Oxford 2018).

WORKED EXAMPLE

A woman in her sixties attends repeatedly with chronic backache, poor sleep and vague paraesthesias; investigations are unremarkable and analgesics do little. On direct enquiry she describes weeks of anhedonia, early-morning waking, guilt and hopelessness that she had never volunteered because she came about her body, not her mood. The physical complaints were the mask; the depressive episode was found only because mood was asked about directly.

RULE **When a patient somatises, ask directly about mood.** Masked depression is common, and the depressive core is elicited on direct enquiry, not volunteered.

TRAP **Do not keep treating recurrent unexplained somatic complaints without screening for depression.** Repeated analgesics and investigations for a masked depression miss the treatable disorder underneath.

GOOD TO REMEMBER

- **Masked depression:** a depressive disorder hidden behind physical or somatic complaints, with the mood elicited only on direct enquiry; the one discriminator is that low mood is present but not volunteered; the label to hold is *depressio sine depressione*, and it was never officially endorsed by the classifications.
- **Somatic presentation:** the dominant complaints are physical, chronic pain, insomnia, atypical facial pain, paraesthesias, fatigue; classically described as most common in the elderly.
- **Depressive equivalents:** conditions comparable to, or on the affective spectrum with, depression (for example chronic pain, panic, agoraphobia, alcoholism, eating disorders) that are not part of the core depressive syndrome; hold that many respond to antidepressants but the concept is not an official diagnosis.

12.3 Mixed anxiety and depressive disorder

Mixed anxiety and depressive disorder, also written **mixed anxiety-depressive** disorder, describes the co-occurrence of sub-threshold anxiety and depressive symptoms together, causing distress or disability, where neither symptom set meets the full criteria for a specific anxiety disorder nor for a depressive disorder (Shorter Oxford 2018). Anxiety and depressive symptoms overlap most when they are mild and least when they are severe enough to reach a categorical diagnosis, so this residual category captures the milder, blended presentations that are common in primary care and medical outpatient settings and frequently go untreated in the community (Shorter Oxford 2018). In the English Adult Psychiatric Morbidity Survey it was the most common psychiatric syndrome in the community, with about **9%** of adults meeting the symptomatic criteria in the week before interview, commoner in women and in low-income households (McManus et al. 2009, in Shorter Oxford 2018).

Classification. The nosological placement is itself the exam point. ICD-10 contains a category of mixed anxiety and depressive disorder (F41.2), placed among the other anxiety disorders, whereas DSM-5 and DSM-5-TR deliberately do **not** include it as a diagnosis (Shorter Oxford 2018). In ICD-11 the category is retained but reconceptualised and moved into the depressive-disorders grouping as mixed depressive and anxiety disorder, a genuine shift from its ICD-10 home under the anxiety disorders (ICD-11 CDDR); the exact ICD-11 code is flagged under gaps as it could not be confirmed against the parsed library. For examinations that still use ICD-10, the point to reproduce is that ICD-10 has the category and DSM-5 does not.

TRAP **Do not reach for mixed anxiety and depressive disorder in DSM-5.** DSM-5 and DSM-5-TR have no such category; it is an ICD construct, placed under anxiety in ICD-10 and moved to the depressive grouping in ICD-11.

Prognosis. The prognostic significance is the second high-yield point: despite being sub-threshold, the outcome of mixed anxiety and depressive disorder appears to be **worse** than that of a specific anxiety disorder (Tyrer et al. 2004, in Shorter Oxford 2018), so the label is not

simply a mild or trivial residual state. Persistent anxiety more often precedes the onset of secondary depression than the reverse, and the two share predisposing factors including childhood adversity and probable common genetic mechanisms with generalised anxiety disorder (Shorter Oxford 2018).

about 9%	F41.2	sub-threshold
COMMUNITY WEEK-PREVALENCE (APMS)	ICD-10 CATEGORY (ABSENT IN DSM-5)	NEITHER SET MEETS FULL CRITERIA

INDIA

Masked depression with a predominant somatic presentation, and sub-threshold mixed anxiety-depression, are both familiar in Indian practice, where distress is frequently expressed through bodily complaints and first presents to general and medical outpatient departments rather than to psychiatry. The practical implication is the same as the rule: screen for mood directly in the patient who somatises, because the depressive core is common and treatable but is not volunteered.

GOOD TO REMEMBER

- **Mixed anxiety and depressive disorder:** sub-threshold anxiety and depressive symptoms together with neither meeting full criteria; the discriminating feature is that it is a residual category defined by what it does *not* reach; the codes to hold are ICD-10 F41.2 (present) versus DSM-5 (absent), with ICD-11 moving it to the depressive grouping.
- **Prognostic significance:** the one fact examiners want is that its outcome is *worse* than a specific anxiety disorder (Tyrer 2004), so it is not a benign residual label.
- **Epidemiology:** the number to hold is about **9%** community week-prevalence in the English APMS, the most common community psychiatric syndrome there, commoner in women.

HOLD THIS

Depression is a syndrome that often hides: masked depression presents through somatic complaints with the mood found only on direct enquiry, and mixed anxiety and depressive disorder is a sub-threshold ICD category (F41.2 in ICD-10, absent in DSM-5) whose outcome is worse than a specific anxiety disorder.

13 . Management of depressive disorders: guidelines-first

Managing a depressive disorder is a decision about three things in order: **where** to treat the patient, **what phase** of illness you are targeting, and **which mode** of treatment each guideline recommends first. The board answer is not a drug list, it is this structured, guideline-anchored plan. This topic teaches the plan at **guideline level**; the individual drug pharmacology, the dosing tables, the adverse-effect profiles and the treatment-resistant-depression algorithm are owned by, and cross-referred to, the Mood disorders: pharmacotherapy notes.

Lead with the CANMAT guidelines (CANMAT 2016 and its updates), then state what the Indian Psychiatric Society and NICE recommend. Throughout, the spine is LOCUS (where), FOCUS (which phase), MODUS (which mode). The single organising principle that the exam rewards: **treat to remission, then continue.**

13.1 LOCUS: where to treat, and when to admit

Outpatient is the default. Most depressive episodes are managed in the outpatient or the day care centre setting from the outset. Admission is reserved for a defined set of high-risk situations: **high suicide risk**, depression **with psychotic features**, severe **self-neglect** (not eating or drinking, dehydration), and the need for inpatient-level treatment such as ECT. The clinical suicide risk assessment and safety planning that decide the admission threshold are owned by the Somatic-symptom, sexual, impulse-control disorders and suicide notes. Across every locus, care is delivered as **measurement-based care**: CANMAT specifies regular, frequent monitoring of clinical and functional outcomes with a validated scale, not clinical impression alone (CANMAT 2016).

RULE **Admit for suicide risk, psychosis, severe self-neglect, or the need for ECT.** Everything else is outpatient with measurement-based follow-up.

13.2 FOCUS: the acute phase, aim remission

The acute-phase target is **remission**, not merely response. Review early and often: CANMAT and BAP both advise reviewing the patient every **1 to 2 weeks** after starting an antidepressant (BAP 2015). Response is judged on a trajectory: **lack of significant improvement by 2 to 4 weeks** substantially reduces the chance of eventual sustained response, so for a non-improver at 2 to 4 weeks you increase the dose if tolerated, or switch if tolerability is the problem (CANMAT 2016). BAP frames the same checkpoint as assessing response at 4 weeks and again at 6 to 8 weeks, switching or stepping up if there is no improvement trajectory by 4 weeks or only minimal improvement by 6 to 8 weeks (BAP 2015).

TRAP **Do not combine two antidepressants at initiation.** CANMAT states this explicitly; start one first-line agent, monitor, then optimise or switch.

13.3 FOCUS: the continuation phase, protect the remission

Once remission is achieved, do not stop. The **continuation** phase continues the antidepressant at the **acute treatment dose** (not a reduced "maintenance" dose) for **6 to 9 months** after symptomatic remission (CANMAT 2016). BAP frames the lower bound as at least 1 year for anyone with an increased relapse risk (BAP 2015). This is the phase most often failed in practice: the patient feels well at week 8 and stops, and the relapse that follows is a continuation-phase relapse, not a new episode.

13.4 FOCUS: the maintenance phase, prevent recurrence

For recurrent or high-risk illness, the plan extends into a **maintenance** phase. CANMAT extends antidepressant treatment to **2 years or more** for patients with risk factors for recurrence (CANMAT 2016); BAP names the higher-risk group as, for example, more than five lifetime episodes or two episodes in recent years, and recommends at least 2 years and often long-term (BAP 2015). The maintenance-phase psychological options are CBT or mindfulness-based cognitive therapy (MBCT) to prevent relapse (CANMAT 2016). When treatment is eventually

stopped, taper slowly over several weeks to limit discontinuation symptoms, which CANMAT summarises with the mnemonic FINISH.

MNEMONIC

FINISH

Antidepressant discontinuation symptoms: **F**lu-like symptoms, **I**nsomnia, **N**ausea, **I**mbalance, **S**ensory disturbances, **H**yperarousal (CANMAT 2016). Taper over several weeks; taper short half-life drugs more slowly.

13.5 MODUS: CANMAT first-line pharmacotherapy

The **first-line** pharmacological treatment is a **second-generation antidepressant**, individualised to patient and medication factors with measurement-based monitoring (CANMAT 2016). The first-line class as a group covers the SSRIs, the SNRIs, bupropion, mirtazapine, vortioxetine and agomelatine (with liver-function monitoring for agomelatine). CANMAT's caution at initiation is explicit: two antidepressants are not combined at the initiation of treatment. The deep pharmacology, the full dosing and the adverse-effect detail live in the Mood disorders: pharmacotherapy notes.

RULE **First-line = a second-generation antidepressant, one agent, individualised.** SSRIs and other newer agents are preferred for tolerability and overdose safety (BAP 2015).

13.6 MODUS: CANMAT first-line psychological treatments

The first-line psychological treatments for acute major depressive disorder are cognitive behavioural therapy (CBT), interpersonal therapy (IPT) and behavioural activation (BA) (CANMAT 2016). CANMAT's headline for combination is that, where feasible, combining a psychological treatment (CBT or IPT) with an antidepressant is superior to either alone. Combined medication-plus-therapy is therefore the preferred option for many patients, not a fallback. The raw descriptive definitions of the mood symptoms and the rating scales used to measure them are cross-referred to the Psychometry, Assessment and Descriptive Psychopathology notes.

13.7 MODUS: augmentation and the next step (guideline pointer)

For an inadequate response after an optimised first-line trial, the first-line augmentation agents are the atypical antipsychotics aripiprazole (2 to 15 mg/day), quetiapine (150 to 300 mg/day) and risperidone (1 to 3 mg/day), or adjunctive lithium to therapeutic serum levels with monitoring (CANMAT 2016; BAP 2015). This is a guideline-level pointer only: the full treatment-resistant-depression algorithm, the sequencing, the switch-versus-augment logic and the drug detail are owned by the Mood disorders: pharmacotherapy notes.

13.8 MODUS: neurostimulation and the psychotic-depression rule

Neurostimulation appears at guideline level in two places. rTMS, including intermittent theta burst stimulation (iTBS), is a **first-line** option that CANMAT positions alongside pharmacotherapy for acute depression (CANMAT 2016). ECT is reserved for severe, psychotic or

treatment-resistant depression; the ECT technique itself is owned by the ECT and neurostimulation notes. The **psychotic-depression rule** is a fixed board point: treat with an **antidepressant plus an antipsychotic** from the outset, in preference to either alone, or use ECT (BAP 2015). The mood-with-psychotic-features entity and the schizoaffective boundary are owned by the Other psychotic disorders, delusional syndromes and catatonia notes.

TRAP **Do not treat psychotic depression with an antidepressant alone.** The rule is antidepressant plus antipsychotic from the outset, or ECT.

13.9 The Indian Psychiatric Society and NICE positions

Beyond CANMAT, two further guideline positions are examinable. The Indian Psychiatric Society Clinical Practice Guideline for depression has been updated: the 2025 IPS depression update (IPS 2025, Tripathi et al., Indian J Psychiatry 2026;68:68-93) supersedes the 2017 Gautam guideline and is the current standard Indian reference cited in postgraduate examinations. It names the **SSRIs** as the first-line antidepressants on grounds of tolerability and overdose safety, with the other second-generation agents including vilazodone, vortioxetine and agomelatine as alternatives; it selects the initial treatment by severity (psychotherapy preferred for mild low-risk depression, pharmacotherapy or psychotherapy for moderate, combined pharmacotherapy and psychotherapy for severe without psychosis, an antidepressant plus an antipsychotic for severe with psychosis, and ECT with admission for life-threatening presentations); it reappraises the regimen if there is under a quarter improvement by about four weeks (optimise the dose, switch within or between class, augment, or add ECT); and it sets the treatment phases as acute 8 to 16 weeks, continuation 4 to 9 months and maintenance 6 to 24 months (long-term for recurrent depression), reserving ECT for severe, psychotic, suicidal or treatment-resistant depression (IPS 2025, Tripathi et al.). NICE organises depression management as **stepped care**: for less severe depression it favours a psychological or psychosocial intervention first, and for more severe depression it recommends an antidepressant combined with a psychological therapy. CANMAT, the IPS position (at the level of principle) and NICE therefore converge on the same spine: a second-generation antidepressant or an evidence-based psychotherapy first, combination for the more severe, and continuation after remission.

2 to 4 wk	6 to 9 mo	2 years+	1 to 2 wk
ACUTE NON-IMPROVER REVIEW	CONTINUATION AFTER REMISSION	MAINTENANCE IF RECURRENT	EARLY REVIEW INTERVAL

PHASE	TARGET	DURATION / CHECKPOINT	GUIDELINE-FIRST MODES
Locus decision	Choose the safest adequate setting	**Admit for suicide risk, psychosis, severe self-neglect or the need for ECT**	Outpatient default; measurement-based care throughout

PHASE	TARGET	DURATION / CHECKPOINT	GUIDELINE-FIRST MODES
Acute	Remission	**Review every 1 to 2 weeks; judge response by 2 to 4 weeks and switch or step up if no trajectory**	Second-generation antidepressant (one agent) and/or CBT, IPT or BA; combination superior for many (CANMAT 2016)
Continuation	Protect the remission	**Continue at the acute dose for 6 to 9 months after remission**	Same acute-phase agent at the same dose; do not down-titrate (CANMAT 2016)
Maintenance	Prevent recurrence	**Extend to 2 years or longer for recurrent or high-risk patients**	Continue antidepressant; CBT or MBCT to prevent relapse; taper slowly (FINISH) at stop (CANMAT 2016)
Inadequate response	Optimise, then augment or switch	Optimise dose first; reassess	First-line augmentation aripiprazole, quetiapine, risperidone or lithium; details in the pharmacotherapy notes
Neurostimulation	Severe or resistant illness	By severity and resistance	**First-line rTMS/iTBS; ECT for severe, psychotic or treatment-resistant depression**
Psychotic depression	Remission with psychosis control	From the outset	**Antidepressant plus antipsychotic, or ECT (BAP 2015)**

The phase-by-phase, guideline-first plan on the LOCUS to FOCUS to MODUS spine; the highlighted cell in each row is the fact the examiner tests. Drug detail is cross-referred to the Mood disorders: pharmacotherapy notes.

INDIA

In Indian practice, the full range of second-generation antidepressants (SSRIs, SNRIs, bupropion, mirtazapine, vortioxetine, agomelatine) is widely available, and the SSRIs are the usual first-line pharmacotherapy for depressive disorders. This chapter is generic and names no brand; drug branding, Indian brand first, belongs to the Mood disorders: pharmacotherapy notes. For severe, psychotic or treatment-resistant depression, ECT is widely available and heavily used across Indian teaching hospitals, and it remains a mainstream option for inpatient-level depression rather than a last resort. The current Indian Psychiatric Society guideline for depression is the 2025 update (IPS 2025, Tripathi et al.), which supersedes the 2017 Gautam guideline and is the one most likely to be named in Indian postgraduate examinations for depression management.

GOOD TO REMEMBER

- **LOCUS:** outpatient default; admit for suicide risk, psychosis, severe self-neglect or the need for ECT; measurement-based care throughout.
- **Acute phase:** aim remission; review every **1 to 2 weeks**; switch or step up if no improvement trajectory by **2 to 4 weeks** (CANMAT 2016).
- **Continuation phase:** continue at the acute dose for **6 to 9 months** after remission; do not down-titrate.
- **Maintenance phase:** extend to **2 years or longer** for recurrent or high-risk patients; CBT or MBCT prevents relapse.
- **CANMAT first-line:** a second-generation antidepressant (one agent, individualised) or CBT / IPT / behavioural activation; combination superior for many.
- **Do-not-combine rule:** two antidepressants are not combined at initiation (CANMAT 2016).
- **Psychotic depression:** antidepressant plus antipsychotic from the outset, or ECT (BAP 2015).
- **Convergence:** CANMAT leads; the Indian Psychiatric Society and NICE agree on stepped care and continuation after remission.

WORKED EXAMPLE

A 42-year-old woman with a first moderate depressive episode, no psychosis and no active suicidal plan, is managed as an outpatient. She is started on a single second-generation antidepressant with a shared decision about which agent, and offered CBT alongside because combination is superior to either alone. She is reviewed at 2 weeks, then at 4 weeks: there is a partial improvement trajectory, so the dose is optimised rather than switched. She reaches remission by month 3. The antidepressant is continued at the same acute dose for 6 to 9 months, not reduced, because stopping at response is the classic route to relapse. Because this is a first episode with no high-risk features, an open-ended maintenance phase is not mandated, but the recurrence-risk conversation is documented for the future.

PEARL

"Remission then continuation" is a single instruction, not two. The dose that achieved remission is the dose that maintains it: the continuation phase is the acute-phase drug at the acute-phase dose for 6 to 9 months. Reducing the dose once the patient feels well is a common and avoidable cause of relapse.

RULE **Treat to remission and continue at the acute dose; do not stop at response.** Continuation is 6 to 9 months at the same dose after remission (CANMAT 2016).

TRAP **Stopping the antidepressant as soon as the patient feels better.** Response is not remission, and remission is not the end point; early cessation invites relapse.

HOLD THIS

First-line is a second-generation antidepressant or an evidence-based psychotherapy, combination is superior for many, continuation runs 6 to 9 months at the acute dose after remission, and CANMAT leads while the Indian Psychiatric Society and NICE agree on stepped care.

Bipolar and related disorders

14 · Bipolar I disorder

Having walked the whole soft-bipolar spectrum, you now step onto its classic pole. **Bipolar I disorder** (written bipolar 1 in some notations) is the modern name for manic-depressive illness, and its definition is deceptively simple: it is the disorder in which a single **manic episode** has ever occurred. Everything else about the illness, the depressions that dominate the timeline, the recurrences, the suicide burden, follows from that one anchoring fact but is not needed to make the diagnosis (DSM-5-TR 2022; Kaplan & Sadock 2024). The exam rewards the resident who states the definition crisply, who knows the illness is mostly a depressive one over a lifetime despite being named for mania, and who never demands a depressive episode before diagnosing.

This topic stays at the disorder level: the definitional frame, the lifetime pattern, the course and its kindling logic, the comorbidity and burden. The phenomenology of the manic episode itself, the Criterion A and B symptoms, is the next topic; the full manic-episode and depressive-episode criteria live in this chapter's own episode topics, and the raw descriptive definitions of the mood symptoms sit in the Psychometry, Assessment and Descriptive Psychopathology notes. Nosology is given ICD-11-primary, DSM-5-TR cross-mapped.

	Bipolar I	Bipolar II	Cyclothymia
Defining episode	a manic (or mixed) episode	a hypomanic plus a major depressive episode	sub-threshold highs and lows
High pole	full mania	hypomania only, never mania	hypomanic symptoms only
Duration threshold	mania at least 1 week	hypomania at least 4 days (several days, ICD-11)	at least 2 years
Psychosis or admission	may occur	excludes hypomania	no
Tell it by	**one manic episode, ever**	**hypomania plus depression, no mania**	**chronic, 2 years, sub-threshold**

Fig 11.5 Bipolar I versus bipolar II versus cyclothymia. A single manic episode, ever, defines bipolar I. A hypomanic episode plus a major depressive episode, with no manic episode ever, defines bipolar II, and any marked impairment, psychosis or hospitalisation would make the high a mania instead. Cyclothymia is at least two years of sub-threshold highs and lows that never reach episode criteria.

14.1 The definition: one manic episode makes the diagnosis

A single lifetime mania is sufficient, and necessary. DSM-5-TR Criterion A for bipolar I disorder reads that criteria have been met for at least one manic episode, and the text is explicit that "the occurrence of at least one manic episode is necessary for the diagnosis of bipolar I disorder" (DSM-5-TR 2022). A manic episode required is therefore the whole gate: no manic episode, no bipolar I. Hypomanic and major depressive episodes usually occur across the lifetime and are the reason most patients present, but DSM-5-TR states plainly that they are "not essential to a diagnosis of bipolar I disorder" (DSM-5-TR 2022). ICD-11 mirrors this: bipolar type I disorder is defined by a history of at least one manic or mixed episode, and a manic episode

lasting **at least 1 week** (or any duration if hospitalisation is required) is the definitional event. The full manic-episode criteria are taught in this chapter's manic-episode topic.

RULE **One manic episode is enough for bipolar I, ever.** A single lifetime manic episode makes and fixes the diagnosis, however the patient looks today, and no depressive episode is required.

TRAP **Do not require a depressive episode.** Demanding a past major depression before diagnosing bipolar I is the classic error; depression is usual but never a diagnostic requirement, and a first-episode mania with no prior depression is already bipolar I.

14.2 The lifetime pattern: a recurring, mostly depressive illness

Named for mania, lived as depression. Bipolar I disorder is, in DSM-5-TR's phrasing, "characterized by a clinical course of recurring mood episodes (manic, depressive, and hypomanic)" (DSM-5-TR 2022). Onset can take several shapes: some patients begin with weeks or months of depression that then switches into a manic episode; others open with a severely psychotic manic episode with schizophreniform features whose affective nature is clarified only when a more classic mania follows; in a third group several depressive episodes precede the first mania (Kaplan & Sadock 2024). A "single manic episode" simply describes a patient in a first episode of mania; most such patients eventually develop depressive episodes, and more than **90%** of individuals who have a single manic episode go on to have recurrent mood episodes (DSM-5-TR 2022). Approximately **60%** of manic episodes occur immediately before a major depressive episode (DSM-5-TR 2022).

PEARL

Chart the course in colour over time (Kraepelin's method, developed into systematic science by Robert Post at the NIMH): red for manic, blue for depressive, violet for mixed, with hypomanic and cyclothymic periods on a smaller scale, and arrows for life events, stressors and treatment. A life chart makes the predominant polarity and the cycle pattern visible at a glance (Kaplan & Sadock 2024).

14.3 The course of bipolar I: episodic with inter-episode recovery

Episodes come and go against a baseline of relative recovery. The course of bipolar I disorder is classically episodic: discrete manic, depressive, hypomanic and mixed episodes separated by periods of inter-episode recovery in which the patient returns toward, though often not fully to, euthymia (Kaplan & Sadock 2024). The course is highly heterogeneous. Polarity of the first episode tends to predict the predominant polarity of future episodes, so a depressive onset is associated with a greater density of depressive episodes and more suicidal behaviour (DSM-5-TR 2022). About half of patients show a predominant polarity (relapse tending to be either depressive or manic); one international bipolar I cohort found 31.3% with predominant mania, 21.4% with predominant depression and 47.3% without polarity predominance (DSM-5-TR 2022). Inter-episode recovery is the norm early, but subthreshold symptoms and functional deficits frequently persist between full episodes.

14.4 More time is spent depressed than manic

The depressive pole dominates the lifetime clock. Despite the manic naming, patients with bipolar I disorder spend far more of their symptomatic time depressed than manic. NIMH Collaborative Depression Study data, using prospective life-charting of bipolar I cohorts followed for an average of **12 years**, showed patients were symptomatic for nearly **50%** of the weeks across the entire follow-up, with depression, especially its subthreshold variants, predominating over mania (Kaplan & Sadock 2024). This asymmetry is why bipolar depression, not mania, is the harder and more time-consuming management problem, and why an antidepressant given alone to a patient later found to be bipolar is such a common and costly error.

RULE **More time depressed than manic.** Over a lifetime the bipolar I patient is symptomatically depressed for far longer than manic; mania names the illness, depression fills its calendar.

WORKED EXAMPLE

A 24-year-old man is admitted with his first episode: three days of no sleep, grandiose plans to buy a hotel, pressured speech and reckless spending, requiring involuntary admission. He has never had a depressive episode. This is already bipolar I disorder, because a single manic episode is sufficient and no depression is required. Over the next decade, if his course runs true to form, he will have several more episodes and will spend more of his symptomatic time depressed than manic; his management therefore looks past this admission to long-term relapse prevention, not just to settling the mania.

14.5 Recurrence risk and the kindling / cycle-acceleration concept

Episodes beget episodes. Recurrence is the rule, not the exception: with the single-manic-episode patient having a greater than **90%** chance of recurrent mood episodes and a lifetime mean of around **8 to 9** major episodes in bipolar disorder (against five to six in recurrent unipolar depression), bipolar I is fundamentally a recurrent illness (DSM-5-TR 2022; Kaplan & Sadock 2024). The **kindling** and **cycle-acceleration** model, associated with Robert Post, proposes that early episodes are often triggered by identifiable psychosocial stressors, whereas later episodes arise more autonomously and the cycle length (the interval between episodes) tends to shorten over time, as if episodes progressively sensitise the brain to recur (Kaplan & Sadock 2024). The evidence is the observed shortening of well intervals across successive episodes and the analogy to electrophysiological kindling. The limitation: the model is a heuristic, not a settled mechanism; the human data are largely retrospective and confounded by treatment, adherence and ascertainment, and prospective cohorts have not uniformly reproduced a lawful progressive shortening. It motivates early and continued prophylaxis without being an established pathophysiology.

TRAP **Do not present kindling as proven mechanism.** Cycle acceleration is a clinically useful model with real retrospective support, but it is confounded and not consistently replicated prospectively; state it as a hypothesis, not a fact.

at least 1 wk	>90%	~50% of weeks	8 to 9
MANIC EPISODE (DEFINES BIPOLAR I)	RECURRENCE AFTER ONE MANIC EPISODE	SYMPTOMATIC OVER 12 YR FOLLOW-UP	MEAN LIFETIME MAJOR EPISODES

14.6 Comorbidity: anxiety and substance use are the rule

Pure bipolar I is uncommon. Co-occurring disorders are so frequent that their absence is notable. Anxiety disorders are the commonest comorbidity and, when present, are associated with a worse course of illness across both bipolar I and bipolar II (DSM-5-TR 2022). Substance use is the other dominant partner: nearly **half** of individuals whose symptoms meet criteria for bipolar disorder have an alcohol use disorder, and those with both are at greater risk of suicide attempt and suicide death (DSM-5-TR 2022). Across bipolar I and II the commonest substance comorbidities are alcohol use (**42%**) and cannabis use (**20%**) disorders, and cannabis in particular is associated with exacerbation of manic symptoms and with first onset of mania in the general population (DSM-5-TR 2022). Childhood adversity predisposes to earlier onset and a worse picture including comorbidity, suicide and psychotic features.

14.7 Functional and suicide burden

A high-mortality, high-disability illness. Bipolar I disorder carries significant decrements in quality of life and well-being even between episodes, and the suicide burden is severe: the lifetime risk of suicide in bipolar disorder is estimated at **20 to 30 times** that of the general population, and an estimated **5% to 6%** die by suicide (DSM-5-TR 2022). Suicide attempts are more frequent in women, but lethal suicide is more common in men; a past suicide attempt and the proportion of days spent depressed in the past year predict greater risk of attempts and completions (DSM-5-TR 2022). Mixed features add risk: depressive symptoms occur in some 35% of manic episodes, and mixed presentations carry a poorer prognosis, poorer lithium response and increased suicide attempts (DSM-5-TR 2022). Clinical suicide risk assessment and safety planning are taught in the Somatic-symptom, sexual, impulse-control disorders and suicide notes.

INDIA

In Indian practice the two comorbidity patterns that most change the bipolar I picture are alcohol use disorder (very common in men, and a driver of relapse, non-adherence and suicide) and cannabis use (a frequent precipitant and aggravator of manic episodes). Both are routinely screened at every review. Lithium, the long-standing prophylactic backbone, is widely available and affordable in India; the guideline-level management and its monitoring headline are covered in the bipolar-management topic below, and the deep pharmacology sits in the Mood disorders: pharmacotherapy notes.

14.8 One-line management pointer

Diagnosis reframes treatment from episode to lifetime. Because bipolar I is recurrent and mostly depressive over time, the management goal is not only to treat the presenting episode but to prevent the next one. Guideline-anchored management, led by CANMAT (with the Indian Psychiatric Society and NICE positions cross-mapped), is organised by phase (acute mania,

bipolar depression, maintenance) and leads with mood stabilisers, most classically lithium, rather than antidepressant monotherapy (CANMAT 2018; Kaplan & Sadock 2024). The full guideline plan is taught in the bipolar-management topic; the deep drug pharmacology, dosing and treatment-resistant algorithms are owned by the Mood disorders: pharmacotherapy notes.

MNEMONIC

ONE HIGH

ONE manic episode, ever, and it is bipolar I. Read it as the whole definition: you need exactly one lifetime "high" that reaches manic threshold, and you need nothing else, no depression, to diagnose.

HOLD THIS

One manic episode ever, lasting at least 1 week (or any duration if hospitalised), makes bipolar I; no depressive episode is required, yet the patient spends more lifetime time depressed than manic.

GOOD TO REMEMBER

- **Bipolar I disorder:** the disorder in which at least one lifetime manic episode has occurred; the one discriminator is a full manic episode (at least 1 week, or any duration if hospitalised); hold "one manic episode required."
- **Course of bipolar I:** episodic with inter-episode recovery but more time spent depressed than manic; the one discriminator is the depressive-predominant lifetime clock; hold "symptomatic ~50% of weeks over 12-year follow-up."
- **Recurrence:** the rule, not the exception; the one discriminator is that a single manic episode carries a greater than 90% chance of further mood episodes; hold ">90% recur; mean 8 to 9 lifetime episodes."
- **Kindling / cycle acceleration:** a hypothesis that cycles shorten and become more autonomous over time; the one discriminator is the retrospective narrowing of well intervals; hold "Post; heuristic, not proven, motivates early prophylaxis."
- **Comorbidity:** anxiety (commonest, worsens course) and substance use (nearly half have alcohol use disorder); the one discriminator is that pure bipolar I is uncommon; hold "alcohol 42%, cannabis 20%."
- **Suicide burden:** a high-mortality illness; the one discriminator is a lifetime suicide risk 20 to 30 times the general population; hold "5% to 6% die by suicide."

15 · The manic episode

Why this matters. The **manic episode** is the diagnostic keystone of bipolar type I disorder: a single lifetime manic episode is sufficient for the diagnosis, no depressive episode being required. This chapter is the canonical home of the manic-episode criteria, so they are taught here in full; the Other psychotic disorders, delusional syndromes and catatonia notes cross-refer here for the manic pole of schizoaffective disorder. The examiner tests three reflexes on **mania**: the exact criterion set (the mood-and-energy anchor, the duration floor, and the symptom count), the point at which the episode acquires **psychotic features**, and the discrimination from hypomania on which the whole bipolar-I-versus-bipolar-II split turns.

The structure to hold is a nesting mirrored from the depressive side: the manic episode is the atom of criteria; bipolar type I disorder is the disorder built from at least one such episode. Nosology is given ICD-11 primary with the DSM-5 (the DSM-5-TR) criteria cross-mapped, and ICD-10 (F30) flagged where Indian exams still cite it. The raw descriptive definitions of the individual manic symptoms, pressured speech and flight of ideas among them, are owned by the Psychometry, Assessment and Descriptive Psychopathology notes and cross-referenced here, not re-derived. The full drug pharmacology of the antimanic agents is owned by the Mood disorders: pharmacotherapy notes.

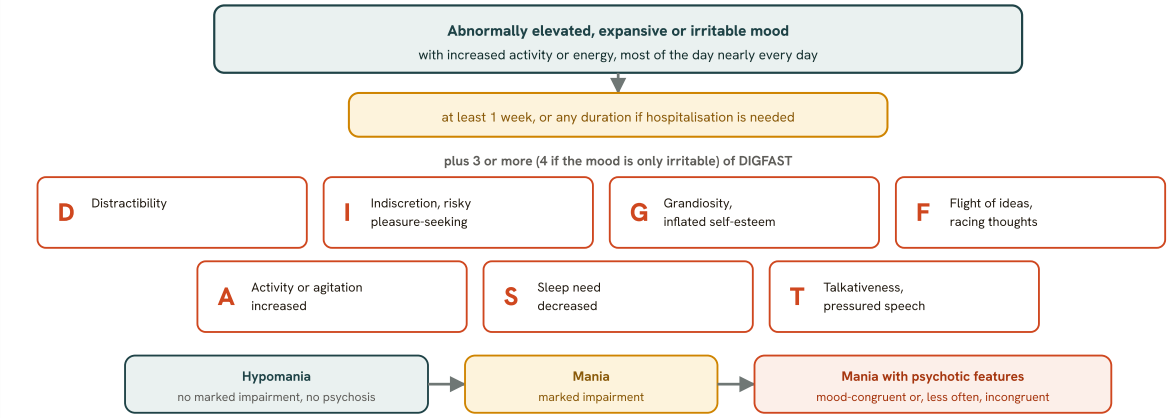


Fig 11.6 The manic episode. A distinct period of abnormally elevated, expansive or irritable mood with increased activity or energy, lasting at least one week (or any duration if hospitalisation is needed), plus three or more of the DIGFAST symptoms (four if the mood is only irritable), causing marked impairment. Severity runs from hypomania, which has no marked impairment and no psychosis, up to mania and mania with psychotic features.

15.1 The mood-and-energy anchor: the two-part gate criterion A

Every manic diagnosis opens on a two-part anchor, and the modern point is that both parts are mandatory. DSM-5-TR criterion A requires a distinct period of abnormally and persistently **elevated, expansive, or irritable mood** *and* abnormally and persistently increased activity or energy (DSM-5-TR). The steer for this topic uses **elevated or irritable** as the shorthand for the mood limb: mood may be euphoric and expansive or, especially when wishes are thwarted, purely irritable. The change from DSM-IV that the examiner rewards is that **increased activity or energy is now a required part of the gate, not merely an associated symptom**: euphoria alone, without the rise in goal-directed activity or energy, does not open the gate. ICD-11 phrases the same anchor as an extreme mood state of euphoria, irritability or expansiveness together with increased activity or a subjective experience of increased energy, both representing a significant change from the individual's typical state (ICD-11 CDDR).

RULE **Mania needs mood and energy together.** Abnormally elevated or irritable mood plus abnormally increased activity or energy is the two-part gate; euphoria without the energy rise does not qualify.

15.2 The duration floor: one week or hospitalisation

The anchor must hold for a fixed minimum. The mood-and-energy disturbance must last at least **one week** and be present most of the day, nearly every day, *or any duration if hospitalisation is necessary* (DSM-5-TR; ICD-11 CDDR). Two riders complete the duration rule. First, an episode that meets the full symptom requirements but is cut short below one week **because a treatment intervention truncated it** still counts as a manic episode (ICD-11 CDDR). Second, a fully syndromal manic episode that emerges during antidepressant treatment (medication, ECT, light therapy) and **persists beyond the physiological effect of the inducing agent** is sufficient for a manic episode and hence for bipolar I disorder (DSM-5-TR, criterion D). The **one week** floor is the single number that most cleanly separates mania from hypomania, whose floor is four days.

at least 1 wk	any duration	3 (or 4)	4 days
MANIC EPISODE	IF HOSPITALISATION NEEDED	DIGFAST SYMPTOMS REQUIRED	HYPOMANIA FLOOR (CONTRAST)

15.3 The symptom count and the DIGFAST set

Within the anchored window, DSM-5-TR criterion B requires **three or more** of a seven-symptom set to be present to a significant degree, rising to **four or more if the mood is only irritable** rather than elevated or expansive (DSM-5-TR). The seven, verbatim in substance, are: (1) inflated self-esteem or **grandiosity**; (2) decreased need for sleep (feeling rested after only about three hours); (3) more talkative than usual or pressure to keep talking; (4) flight of ideas or the subjective experience that thoughts are racing; (5) distractibility, attention too easily drawn to unimportant external stimuli; (6) increase in goal-directed activity or psychomotor agitation; and (7) excessive involvement in activities with a high potential for painful consequences (unrestrained buying, sexual indiscretions, foolish investments). The examiner's memory hook is **digfast**: **D**istractibility, **I**ndiscretion/impulsivity (irresponsibility), **G**randiosity, **F**light of ideas, **A**ctivity increase, **S**leep decrease (decreased need), **T**alkativeness/pressured speech. ICD-11 carries the same symptoms as a list from which "several" must be present, without DSM-5-TR's rigid arithmetic (ICD-11 CDDR).

MNEMONIC

DIGFAST

Distractibility, Indiscretion/impulsivity (irresponsibility), Grandiosity, Flight of ideas, Activity increase, Sleep decrease (decreased need for sleep), Talkativeness/pressured speech. Count three of these to a significant degree, or four if the mood is only irritable, over one week (or any duration if hospitalised), with the mood-and-energy anchor present.

TRAP **Do not read decreased need for sleep as insomnia.** In mania the person sleeps little yet feels rested and energised; insomnia is wanting to sleep but being unable to. Only the former counts toward DIGFAST.

15.4 Criterion C: marked impairment, hospitalisation, or psychosis

The final required criterion sets the severity floor that distinguishes mania from hypomania. DSM-5-TR criterion C is satisfied by **any one** of three conditions: the mood disturbance is severe enough to cause **marked impairment** in social or occupational functioning; it **necessitates hospitalisation** to prevent harm to self or others; or there are **psychotic features** (DSM-5-TR). By definition, the presence of psychotic features during the episode makes it manic, never hypomanic. ICD-11 phrases the same threshold as significant impairment, or the need for intensive treatment such as hospitalisation to prevent harm, or the presence of delusions or hallucinations (ICD-11 CDDR). Any one of these three, on its own, lifts a candidate episode above the hypomania line.

WORKED EXAMPLE

A 26-year-old man is brought in after nine days of barely sleeping, talking non-stop, spending his savings on a business he cannot explain, and telling relatives he has been chosen to reform the country. Count it: the mood is expansive with grandiosity, and there is a clear rise in goal-directed activity (the two-part anchor); over more than one week he shows grandiosity, decreased need for sleep, pressured speech, and reckless spending, which is four DIGFAST symptoms; and the financial ruin plus the need for admission satisfy criterion C. This is a manic episode. Because the grandiosity has reached the belief of a special mission, screen for psychotic features: if it is held with delusional conviction, the episode is manic with psychotic features.

15.5 Severity and the psychotic features of mania

Mania is graded from a syndrome that just clears threshold to a life-threatening state. When present, **psychotic features** are most often **mood-congruent**: grandiose delusions consonant with the elevated mood, such as beliefs of special powers, a divine mission, exceptional wealth or a special relationship to a famous person (ICD-11 CDDR; Kaplan & Sadock 2024). Less often the psychosis is **mood-incongruent**, carrying persecutory, self-referential, or passivity and thought-interference phenomena (thought insertion, withdrawal or broadcast) whose content does not fit the elevated mood; the incongruent pattern is the harder one and points toward the schizoaffective boundary (ICD-11 CDDR). Hallucinations are less frequent than delusions and usually accompany the delusional theme. The fuller handling of mood with psychotic features and the schizoaffective boundary is cross-referenced to the Other psychotic disorders, delusional syndromes and catatonia notes.

RULE **Manic psychosis is grandiose until proven otherwise.** The default psychotic feature of mania is a mood-congruent grandiose delusion; mood-incongruent or first-rank content should prompt a look toward the schizoaffective boundary.

15.6 Delirious (Bell's) mania: the extreme

At the severe extreme sits delirious mania, also called Bell's mania after Luther Bell, who described it in 1849 (Kaplan & Sadock 2024). It is a rapidly escalating triad of manic excitement, psychosis and a clouded, delirium-like disturbance of consciousness with disorientation, and it frequently overlaps with catatonic features. It is a psychiatric emergency: exhaustion,

hyperthermia and dehydration threaten life, and it is classically responsive to ECT. The catatonia entity itself and the ECT technique are cross-referenced to the Other psychotic disorders, delusional syndromes and catatonia notes and the ECT and neurostimulation notes respectively; what to hold here is that the most severe manic presentation carries clouding of consciousness and demands urgent treatment.

INDIA

Severe and psychotic manic and delirious-mania presentations are a recognised indication for ECT in Indian practice, where ECT is widely available in teaching hospitals and is used for treatment-refractory, catatonic or life-threatening mania; the technique itself is owned by the ECT and neurostimulation notes.

15.7 The differential from hypomania, and a management pointer

The single most examined discrimination is manic episode versus hypomanic episode, and it turns on four axes: **duration** (one week versus four days), **severity/impairment** (marked impairment in mania, no marked impairment in hypomania), **psychosis** (its presence defines the episode as manic and excludes hypomania), and **hospitalisation** (needing admission defines mania). Hypomania is, in essence, the same symptom picture at a shorter duration and a lower severity that stops short of marked impairment, psychosis or admission; the detailed hypomania criteria are the subject of the next topic (DSM-5-TR; ICD-11 CDDR). For management, the one-line pointer: a confirmed manic episode is treated with a mood stabiliser or an atypical antipsychotic first-line (lithium, quetiapine, divalproex, aripiprazole and others), any antidepressant is discontinued, and the acute and maintenance detail is owned by the bipolar-management topic and the Mood disorders: pharmacotherapy notes (CANMAT 2018).

AXIS	MANIC EPISODE	HYPOMANIC EPISODE
Minimum duration	**At least one week (or any duration if hospitalised)**	At least four consecutive days
Impairment	**Marked impairment in social or occupational functioning**	Observable change, but no marked impairment
Psychotic features	**May be present; if present, the episode is by definition manic**	Absent (any psychosis makes it manic)
Hospitalisation	**May require admission; need for admission defines mania**	Does not require admission
Symptom count	3 or more DIGFAST (4 if mood only irritable)	Same set, same count

The manic-versus-hypomanic grid: the four discriminators (duration, impairment, psychosis, hospitalisation) that lift an episode from hypomania to mania; the highlighted cells are the mania-defining features.

TRAP **Do not call an impairing, psychotic or hospitalised episode "hypomania".** Marked impairment, any psychotic feature, or the need for admission each independently makes the episode manic; hypomania has none of these.

PEARL

Think of the four "mania makers", each sufficient on its own to exclude hypomania: a full week's duration, marked impairment, psychosis, and hospitalisation. If any one is present, the episode is manic, and a single lifetime manic episode is enough to diagnose bipolar type I disorder.

GOOD TO REMEMBER

- **Manic episode:** abnormally elevated or irritable mood plus increased activity/energy (the two-part gate), lasting at least **one week** (or any duration if hospitalisation is needed), with three or more DIGFAST symptoms (four if mood only irritable) and marked impairment, hospitalisation, or psychosis; one lifetime episode diagnoses bipolar type I.
- **DIGFAST:** Distractibility, Indiscretion/impulsivity, Grandiosity, Flight of ideas, Activity increase, Sleep decrease, Talkativeness; the count to hold is 3, or 4 if irritable-only.
- **Psychotic features of mania:** most often mood-congruent grandiose delusions; less often mood-incongruent; their presence makes the episode manic, never hypomanic.
- **Delirious (Bell's) mania:** manic excitement plus psychosis plus clouded consciousness/delirium, often with catatonia; the eponym is Luther Bell (1849), and it is an ECT-responsive emergency.

HOLD THIS

One week (or hospitalisation), the two-part mood-and-energy gate, three DIGFAST symptoms (four if irritable-only), and marked impairment or psychosis: any one of impairment, psychosis or admission makes it mania, not hypomania.

16 · Bipolar II and hypomania

Why this matters. **bipolar ii** disorder is the diagnosis the exam loves because it is the one most easily missed at the bedside and most easily faked on paper. The patient almost always arrives depressed, the highs are quiet and ego-syntonic, and the whole diagnosis rests on documenting a single genuine **hypomanic episode** that the patient and often the last three clinicians never noticed. Two reflexes are tested: the precise definition of the disorder (at least one hypomanic episode and at least one major depressive episode, and never a manic episode), and the exact **hypomania** threshold, the same symptom set as mania but at a shorter duration and, decisively, under the impairment, psychosis and hospitalisation ceilings that separate it from mania.

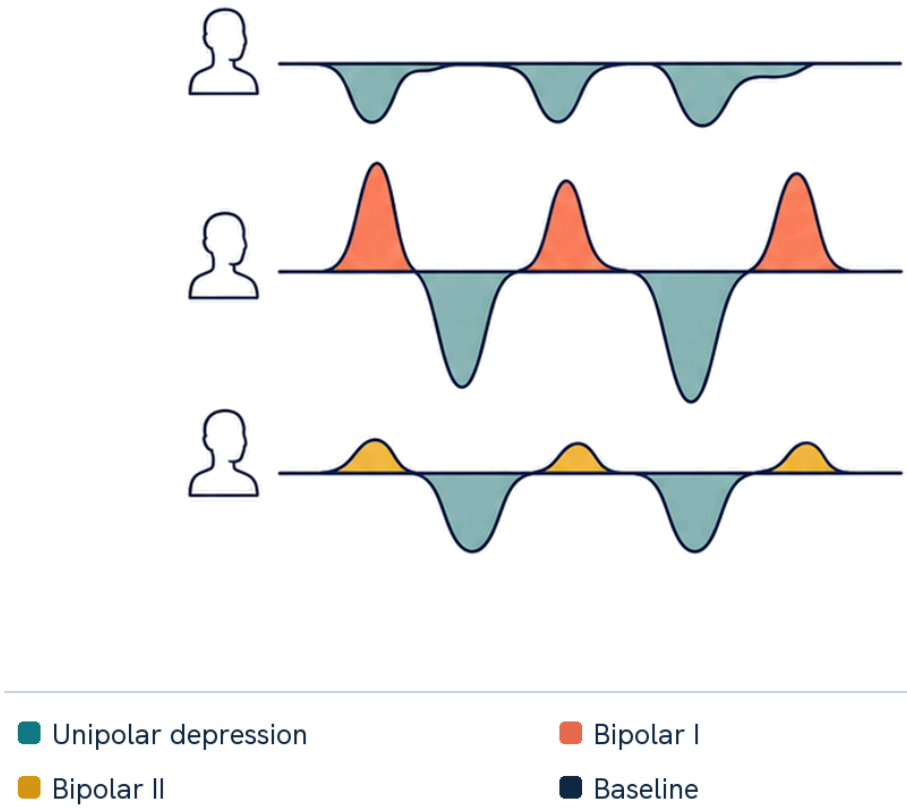


Fig 11.7 Longitudinal course distinguishes recurrent unipolar depression from bipolar I, with full manic peaks, and bipolar II, with hypomanic peaks plus major depressive episodes.



Fig 11.8 Mania, hypomania and depression differ in activation, symptom intensity, duration and functional consequence; hypomania is not merely a milder visual version of mania but lacks marked impairment or psychosis.

This topic teaches the disorder-level definition and the hypomanic-episode criteria in full, since the manic-episode and depressive-episode criteria are taught in this chapter's own episode topics and the raw descriptive definitions of the individual mood symptoms sit in the Psychometry, Assessment and Descriptive Psychopathology notes. Nosology is given ICD-11 primary, DSM-5-TR cross-mapped, with ICD-10 (F31) flagged where the exams still cite it. The deep drug pharmacology of bipolar depression is owned by the Mood disorders: pharmacotherapy notes and only pointed to here.

16.1 The definition: a hypomania and a depression, but never a mania

Two episodes required, one episode forbidden. DSM-5-TR Criterion A for bipolar II disorder requires that criteria have been met for at least one hypomanic episode (Criteria A to F under Hypomanic Episode) *and* at least one major depressive episode (Criteria A to C under Major Depressive Episode); Criterion B states plainly that **there has never been a manic episode** (DSM-5-TR 2022). The presence of even one lifetime manic episode instantly re-diagnoses the

patient as bipolar I disorder and excludes bipolar II. ICD-11 mirrors this exactly: bipolar type II disorder (6A61) requires a history of at least one hypomanic episode and at least one depressive episode, with **no history of manic or mixed episodes** (ICD-11 CDDR). The disorder is therefore defined by a specific pair plus an absolute exclusion: a hypomania, a depression, and never a mania.

RULE **bipolar ii needs a hypomania and an MDE, never a mania.** At least one hypomanic episode plus at least one major depressive episode, with no lifetime manic episode, is the whole definition; one mania makes it bipolar I.

TRAP **Do not diagnose bipolar II without a documented hypomanic episode.** A recurrent, early, atypical depression *suggests* bipolarity, but the label requires a genuine hypomanic episode on the record, not a temperament, a family history or a hunch.

16.2 The hypomania threshold: the same symptoms as mania, for four days

Mania's symptom set at a lower altitude. DSM-5-TR Criterion A for a hypomanic episode requires a distinct period of abnormally and persistently elevated, expansive, or irritable mood *and* abnormally and persistently increased activity or energy, lasting at least **four consecutive days** and present most of the day, nearly every day (DSM-5-TR 2022). Within that window, Criterion B requires **three or more** of the seven-symptom set (the same DIGFAST set as mania), rising to **four or more if the mood is only irritable**: inflated self-esteem or grandiosity, decreased need for sleep, more talkative than usual, flight of ideas, distractibility, increase in goal-directed activity or psychomotor agitation, and excessive involvement in activities with a high potential for painful consequences (DSM-5-TR 2022). The single number that separates hypomania from mania is the duration floor: **four days** for hypomania against **at least one week** for mania. ICD-11 keeps the same symptom picture but does not fix a day-count, requiring only that the disturbance persist for **at least several days** (ICD-11 CDDR); when the exam wants a number, quote the DSM-5-TR four days.

RULE **Hypomania is at least four days and under the ceilings.** The DSM-5-TR duration floor is four consecutive days (ICD-11 says at least several days), and the episode must stay below marked impairment, psychosis and hospitalisation.

16.3 The three ceilings: observable change without marked impairment, psychosis or admission

What is present, and what must be absent. Two things must be positively present. DSM-5-TR Criterion C requires that the episode is associated with an **unequivocal change in functioning that is uncharacteristic** of the individual when not symptomatic, and Criterion D requires that the disturbance in mood and the change in functioning are **observable by others** (DSM-5-TR 2022). Three things must be absent, and they are the crux. DSM-5-TR Criterion E states the episode is **not severe enough to cause marked impairment** in social or occupational functioning or to necessitate hospitalisation, and that **if there are psychotic features, the episode is, by definition, manic** (DSM-5-TR 2022). So hypomania is defined **without marked impairment**, without psychotic features and without hospitalisation. Any one of impairment, psychosis or

hospitalisation, on its own, converts the episode from hypomania into mania, and therefore the patient from bipolar II into bipolar I. ICD-11 phrases the same ceilings: the mood disturbance is not sufficiently severe to result in marked impairment or to require intensive treatment such as hospitalisation, and is not accompanied by delusions or hallucinations (ICD-11 CDDR).

at least four days	at least several days	3 (or 4)	at least 2 wk
HYPOMANIC EPISODE (DSM-5-TR)	HYPOMANIC EPISODE (ICD-11)	DIGFAST SYMPTOMS, 4 IF IRRITABLE-ONLY	THE REQUIRED MAJOR DEPRESSIVE EPISODE

TRAP **Do not upgrade an impairing episode to "hypomania".** If the high caused marked impairment, needed admission, or carried any psychotic feature, it was a manic episode; calling it hypomania to fit a bipolar II label is the classic error.

WORKED EXAMPLE

A 27-year-old woman presents with her fourth episode of low mood since age 20: each time she sleeps eleven hours, feels leaden and craves carbohydrate. She denies ever being "manic". On careful behavioural-activation screening she recalls two distinct spells, each lasting five to six days, of needing only four hours of sleep, redecorating the flat overnight, talking so fast that friends teased her and feeling unusually confident, changes her sister clearly noticed. There was no marked impairment, no admission and no psychosis. Count it: elevated mood plus increased activity, over four days, with decreased need for sleep, pressured speech, grandiosity and goal-directed activity (four DIGFAST symptoms), observable by others and under all three ceilings. That is a hypomanic episode, and with recurrent major depression the diagnosis is bipolar II disorder. An antidepressant alone would have been the wrong first move.

16.4 The clinical reality: presents depressed, hypomania under-recognised, and a heavy burden

The illness you meet is depression; the diagnosis you make is bipolar. Individuals with bipolar II disorder **typically present to a clinician during a major depressive episode** and are unlikely to complain of hypomania, because they either do not recognise its symptoms or consider the state desirable (DSM-5-TR 2022). Hypomania by definition does not cause significant impairment, so the impairment, and hence the presentation, comes from the depressive episodes or from the persistent, unpredictable mood instability; collateral history from family is often what establishes the diagnosis (DSM-5-TR 2022). Critically, DSM-5-TR is explicit that bipolar II disorder **is not a "milder form" of bipolar I disorder**: compared with bipolar I, patients have greater chronicity of illness and spend, on average, **more time in the depressive phase**, which can be severe and disabling, and the overall bipolar suicide burden is high (DSM-5-TR 2022). The one-line management pointer: because the presenting state is bipolar depression, the treatment is guideline-anchored and phase-based, led by mood-stabilising and atypical-antipsychotic agents rather than an antidepressant alone, and the full plan is taught in the bipolar-management topic and the Mood disorders: pharmacotherapy notes (CANMAT 2018).

COMMON TRAP

Treating the depressive presentation of bipolar II as unipolar major depression and starting an antidepressant alone. The switch, cycling and mixed-state risks, and the guideline-preferred bipolar-depression agents, sit in the Mood disorders: pharmacotherapy notes and the bipolar-management topic; the reflex to hold here is to screen every depression for a past hypomanic episode before committing.

16.5 Nosology: ICD-11 gives bipolar II its own category, ICD-10 does not

A coding difference the exam can probe. DSM-5-TR and ICD-11 both recognise bipolar II as a discrete disorder: DSM-5-TR codes it F31.81, and ICD-11 gives it code 6A61 with the essential features stated above (DSM-5-TR 2022; ICD-11 CDDR). ICD-10, by contrast, has **no separate bipolar II category**: bipolar affective disorder is coded under F31 on a history of discrete episodes of mania, hypomania and depression, so a bipolar II picture maps onto F31 (for example F31.0 for a current hypomanic episode, or F31.3 to F31.5 for the depressive episodes) rather than to a dedicated code (ICD-11 CDDR mapping table). For the exam: name bipolar II as its own disorder in DSM-5-TR (F31.81) and ICD-11 (6A61), and flag that ICD-10 folds it under F31 without a standalone bipolar II label.

PEARL

Bipolar II is defined by the softest high and the heaviest lows: the hypomania is quiet and often welcomed, but the depressions are more chronic and occupy more of the lifetime clock than in bipolar I. That asymmetry, not "mild mania", is why bipolar II is a serious diagnosis and never a lesser one (DSM-5-TR 2022).

FEATURE	HYPOMANIC EPISODE	MANIC EPISODE
Minimum duration	At least four consecutive days (ICD-11: at least several days)	**At least one week (or any duration if hospitalised)**
Symptom set and count	Same DIGFAST set, three or more (four if irritable-only)	Same DIGFAST set, three or more (four if irritable-only)
Change in functioning	Unequivocal, uncharacteristic, observable by others	Present, but reaching marked impairment
Marked impairment	**Absent (without marked impairment)**	Present (marked social/occupational impairment)
Psychotic features	**Absent (any psychosis makes it manic)**	May be present; if present, the episode is manic
Hospitalisation	**Not required**	May be required; need for admission defines mania
Diagnosis it defines (with MDE)	Bipolar II disorder	Bipolar I disorder

The hypomania-versus-mania grid: identical symptom set and count, but hypomania is shorter and stays under the three ceilings (impairment, psychosis, admission); the highlighted cells are the features that keep the episode hypomanic rather than manic.

MNEMONIC

FOUR DAYS, NO CEILING BROKEN

Read it as the whole hypomania test: at least FOUR DAYS of the manic symptom set, with NO CEILING BROKEN, no marked impairment, no psychosis, no hospitalisation. Break any one ceiling and it is mania; pair the intact hypomania with a major depression and it is bipolar II.

HOLD THIS

Hypomania is the manic symptom set for at least four days (ICD-11: at least several days), observable, without marked impairment, without psychosis and without hospitalisation; bipolar II needs one such hypomanic episode plus one major depressive episode and never a manic episode, and it presents depressed with the hypomania missed.

GOOD TO REMEMBER

- **Hypomanic episode:** the manic symptom set (three or more DIGFAST, four if irritable-only) lasting at least four days, with an observable, uncharacteristic change in functioning but *without marked impairment*, without psychotic features and without hospitalisation; hold "at least four days (DSM-5-TR), at least several days (ICD-11), and no ceiling broken."
- **Bipolar II disorder:** at least one hypomanic episode and at least one major depressive episode, with no lifetime manic episode; the one discriminator is a documented genuine hypomanic episode plus an intact "never a mania"; hold the code F31.81 (DSM-5-TR) / 6A61 (ICD-11).
- **The three mania-makers (excluded in hypomania):** marked impairment, any psychotic feature, or the need for hospitalisation; the one discriminator is that any single one converts hypomania to mania and bipolar II to bipolar I; hold "any one makes it mania, not hypomania."
- **Clinical reality and burden:** presents in the depressive phase with the hypomania under-recognised, not a milder illness, with more lifetime time spent depressed than in bipolar I and a high suicide risk; the one discriminator is the depressive-predominant, quiet-high profile; hold "presents depressed, screen every depression for a past hypomanic episode."
- **Nosology:** a discrete disorder in DSM-5-TR (F31.81) and ICD-11 (6A61), but ICD-10 has no separate bipolar II and folds it under F31; hold "ICD-11 6A61 primary, ICD-10 F31 (no standalone bipolar II)."

17 · Cyclothymia

Why this matters. **Cyclothymia** is the chronic, sub-threshold floor of the bipolar spectrum: numerous ups and downs, neither of which is ever severe or long enough to become a full hypomanic or a full major depressive episode. The examiner tests it because it is doubly easy to get wrong, over-read as ordinary moodiness or a personality problem, or under-read and missed as a bipolar diathesis that will later declare itself. The single reflex to build is that **cyclothymic disorder** is **chronic sub-threshold bipolarity**, defined by duration and persistence rather than the depth of any one swing, and that it sits on a continuum with the **cyclothymic temperament** at one end and bipolar I or bipolar II at the other (Kaplan & Sadock 2024; Akiskal 2007).

Nosology is given ICD-11 primary (the ICD-11 CDDR term is cyclothymic disorder), with the DSM-5 (the DSM-5-TR) cross-mapped and ICD-10 flagged where Indian exams still cite it (ICD-10 uses the bare term cyclothymia, F34.0). The raw descriptive definitions of the individual hypomanic and depressive symptoms are owned by the Psychometry, Assessment and

Descriptive Psychopathology notes and cross-referenced here, not re-derived; the deep drug pharmacology, dosing and treatment-resistance algorithms belong to the Mood disorders: pharmacotherapy notes; and the full soft-bipolar spectrum is laid out in this chapter's unipolar-versus-bipolar-spectrum topic, of which cyclothymia is one rung.

17.1 The core criteria: two years of sub-threshold ups and downs

The defining criterion of cyclothymic disorder is **at least two years** (**at least 1 year in children and adolescents**) of numerous periods of hypomanic symptoms that do **not** meet the threshold for a hypomanic episode and numerous periods of depressive symptoms that do **not** meet the threshold for a major depressive episode (DSM-5-TR Criterion A; ICD-11 CDDR). Over that span the symptoms must be present for at least **half the time** (ICD-11 CDDR phrases this as "more days than not"), and the patient must never have been symptom-free for more than **two months** at a time (DSM-5-TR Criterion B). Crucially, criteria for a major depressive, manic, or hypomanic episode must **never** have been met (DSM-5-TR Criterion C), and the pattern must cause clinically significant distress or impairment (DSM-5-TR Criterion F). It is the "never symptom-free for more than two months" clause plus the "never a full episode" clause together that fix cyclothymia as chronic and sub-threshold rather than as an early bipolar disorder.

RULE **Cyclothymia is chronic sub-threshold bipolarity.** At least two years (one year in youth) of numerous hypomanic and depressive symptoms, present at least half the time, never symptom-free for more than two months, and never once reaching full episode threshold.

17.2 The exclusions and the conversion rule

The remaining criteria are exclusions and a conversion clause. The mood swings must not be better explained by a schizophrenia spectrum or other psychotic disorder (DSM-5-TR Criterion D), and must not be attributable to a substance or medication (especially stimulants, including withdrawal) or another medical condition such as hyperthyroidism (DSM-5-TR Criterion E; ICD-11 CDDR). The conversion rule is the high-yield twist: if, **after** the initial two years (one year in youth), the patient goes on to experience a full major depressive, manic, or hypomanic episode, the diagnosis **changes** to major depressive disorder, bipolar I disorder, or a bipolar II or other specified bipolar and related disorder respectively, and the cyclothymic disorder label is dropped (DSM-5-TR; ICD-11 CDDR). ICD-11 adds that during the first two years there must never have been a two-week period meeting depressive-episode requirements, and that individuals with cyclothymic disorder do not typically show psychotic symptoms (ICD-11 CDDR).

CRITERION	DSM-5-TR (CYCLOTHYMIC DISORDER)	ICD-11 CDDR (CYCLOTHYMIC DISORDER)
Duration	**At least 2 years; at least 1 year in children and adolescents**	**At least 2 years; a briefer initial period (about 1 year) may suffice in children**
Content	Numerous periods of hypomanic symptoms and of depressive symptoms, both sub-threshold	Numerous hypomanic and depressive periods; depressed mood may present as irritability in youth

CRITERION	DSM-5-TR (CYCLOTHYMIC DISORDER)	ICD-11 CDDR (CYCLOTHYMIC DISORDER)
Persistence	**Symptoms present at least half the time; never symptom-free for more than 2 months**	**Present more days than not; no prolonged (2 months or more) symptom-free period since onset**
Episode ceiling	Full major depressive, manic, or hypomanic episode never met	**No history of manic or mixed episodes; no depressive-episode-level 2-week period in the first 2 years**
Exclusions	Not a psychotic disorder; not a substance, medication, or medical condition (e.g. hyperthyroidism)	Not a substance, medication (e.g. stimulants), or medical condition; psychosis atypical
Impact	Clinically significant distress or impairment in functioning	Significant distress about the mood instability, or impairment sustained only through extra effort

DSM-5-TR and ICD-11 CDDR agree closely: the highlighted cells are the load-bearing discriminators, the two-year floor, the at-least-half-the-time persistence with no two-month gap, and the never-a-full-episode ceiling.

TRAP **Do not keep the cyclothymia label once a full episode appears.** A subsequent manic episode makes it bipolar I; a depressive episode with a past hypomanic episode makes it bipolar II; the cyclothymic disorder diagnosis is then dropped.

17.3 Position on the bipolar spectrum, temperament, and progression risk

Cyclothymia is one of the attenuated, temperamental variants at the mild end of the bipolar spectrum, the "soft bipolar" territory Kraepelin and Kretschmer described as predisposing substrates and Akiskal formalised (Kaplan & Sadock 2024; Akiskal 2007). Two related ideas sit here. First, the cyclothymic temperament is the trait-level, lifelong version, biphasic mood lability that is a habitual baseline rather than a disorder, and it shades into cyclothymic disorder when it produces distress or impairment; the disorder is often "considered to reflect a temperamental predisposition" to the other bipolar disorders (DSM-5-TR). Second, in Akiskal's numbered spectrum, cyclothymic depressions define **bipolar two-and-a-half**, depressive episodes arising on a cyclothymic base, positioned between bipolar II and the antidepressant-associated bipolar III (Akiskal 2007; see this chapter's unipolar-versus-bipolar-spectrum topic). On progression, DSM-5-TR gives a **15% to 50%** risk that a person with cyclothymic disorder will subsequently develop bipolar I or bipolar II disorder, with higher conversion rates in youth than in adults (DSM-5-TR); ICD-11 concurs that these individuals are at high risk of converting, while noting that in children the most common trajectory is actually remission (ICD-11 CDDR).

at least 2 years DURATION (1 YEAR IN YOUTH)	**at least half the time** SYMPTOMS PRESENT	**15% to 50%** PROGRESSION TO BIPOLAR I OR II	**0.4% to 2.5%** LIFETIME PREVALENCE

17.4 Epidemiology and onset

The lifetime prevalence of cyclothymic disorder in the United States and Europe is approximately **0.4% to 2.5%**, rising to around **3% to 5%** in mood-disorder clinic samples (DSM-5-TR). In the general population it is about equally common in males and females, although in clinical settings females may present for treatment more often (DSM-5-TR). Onset is typically insidious, in adolescence or early adult life, and the course is persistent; in children the onset of mood symptoms is usually **before age 10**, with irritability and sleep disturbance the prominent presenting features, and cyclothymic disorder is thought to be under-diagnosed in this age group despite being more common there than bipolar I or bipolar II (DSM-5-TR; ICD-11 CDDR). First-degree relatives show raised rates of major depressive disorder, bipolar I and bipolar II disorder, and of substance-related disorders, and cyclothymic disorder itself is more common among the relatives of people with bipolar I disorder (DSM-5-TR).

INDIA

Cyclothymic disorder is rarely a stand-alone presenting complaint in Indian practice: the sub-threshold swings are commonly brought to attention only when a full episode supervenes or when comorbid substance use surfaces, and the label is easily missed against a backdrop of "moody temperament". ICD-10 (F34.0, cyclothymia) remains in day-to-day coding use, so the resident should be able to map the ICD-11 cyclothymic disorder criteria onto the older category. No India-specific brand name is relevant here; drug brands belong to the Mood disorders: pharmacotherapy notes.

17.5 The differential: cyclothymia versus borderline personality disorder

The classic trap is mistaking cyclothymia for the emotional instability of a borderline personality disorder, and the two can genuinely co-occur, so the discrimination is on quality and content of the affective shifts rather than their mere presence (DSM-5-TR; Kaplan & Sadock 2024). In borderline personality disorder the mood instability sits in the domains of **anxiety, irritability, and sadness**, usually reactive to interpersonal triggers (rejection, abandonment), and **elation, euphoria, and increased energy are not characteristic**; there is enduring disturbance of self-image and unstable, idealising-then-devaluing relationships (DSM-5-TR). In cyclothymia the shifts are into genuine hypomanic territory, elevated mood, increased energy, decreased need for sleep, and they are episodic and often lack an adequate precipitant (endoreactive), without the fixed self-functioning and interpersonal pathology that define a personality disorder (Kaplan & Sadock 2024; ICD-11 CDDR). ICD-11 makes the operational point: assess personality outside a mood episode, and assign both diagnoses only if each set of requirements is independently met (ICD-11 CDDR).

FEATURE	CYCLOTHYMIC DISORDER	BORDERLINE PERSONALITY DISORDER
Poles of instability	**Hypomanic (elation, energy, reduced sleep) alternating with sub-threshold depression**	**Anxiety, irritability, sadness; elation and euphoria not characteristic**
Trigger	Often endoreactive, lacking an adequate precipitant; episodic	Typically reactive to interpersonal events (rejection, abandonment)
Core disturbance	An affective (mood) diathesis; self-image intact between swings	**Enduring identity disturbance and unstable idealise-devalue relationships**
Time frame	Sub-threshold mood periods over at least 2 years, no full episode	Pervasive trait pattern from adolescence, across contexts

The discriminator is the up-pole and the core disturbance: true hypomanic colour and an intact between-swing self point to cyclothymia; anxiety-irritability-sadness swings with identity disturbance point to borderline personality disorder.

17.6 Management pointer: mood stabiliser, and caution with antidepressants

Management is a one-line pointer here, with the detailed agents, dosing and algorithms owned by the Mood disorders: pharmacotherapy notes. There are no firm guideline recommendations specific to cyclothymic disorder, and no clear consensus on the most effective pharmacotherapy (Tasman). The pragmatic stance is to treat it as attenuated bipolarity: favour a **mood stabiliser** over an antidepressant, with some evidence that lamotrigine stabilises some of the symptoms of cyclothymia (Manning et al. 2005, cited in Tasman), and structured psychotherapy has support, a sequential CBT-plus-well-being-therapy programme outperformed routine care in a controlled trial with gains maintained at two years (Fava et al. 2011). The **caution with antidepressants** is the examinable point: antidepressants can mobilise hypomania and can aggravate a cycling course in a bipolar-spectrum patient, so an antidepressant used alone, without mood-stabiliser cover, risks switching or destabilisation (Kaplan & Sadock 2024).

TRAP **Do not start an antidepressant alone in cyclothymia.** It can mobilise hypomania and worsen cycling; the mood-stabiliser-first logic of the bipolar spectrum applies to its sub-threshold floor too.

MNEMONIC

TWO-TWO-NEVER

Two years of sub-threshold swings (one in youth), present at least half the time and never symptom-free for more than two months, and never once a full episode: the three numbers that lock cyclothymic disorder.

GOOD TO REMEMBER

- **Cyclothymia (cyclothymic disorder):** chronic sub-threshold bipolarity, **at least two years** (one year in youth) of numerous hypomanic and depressive symptoms that never meet full episode threshold, present at least half the time, never symptom-free for more than **two months**, causing distress or impairment; ICD-11 primary, DSM-5-TR cross-mapped, ICD-10 F34.0.
- **Progression:** a **15% to 50%** lifetime risk of converting to bipolar I or bipolar II disorder (higher in youth), the one number to hold; a full episode reclassifies and drops the diagnosis.
- **Cyclothymic temperament:** the lifelong trait-level version, the habitual biphasic-labile baseline that shades into the disorder when it causes distress; Akiskal's cyclothymic depressions define bipolar two-and-a-half.
- **Management:** mood stabiliser preferred (lamotrigine has some evidence; Manning et al. 2005) with structured psychotherapy (Fava et al. 2011); caution with antidepressants, which can mobilise hypomania.

PEARL

Screen every apparently "unipolar" chronic depression and every "moody personality" for the cyclothymic pattern: a history of numerous short, endoreactive highs with reduced sleep need and elevated energy, alongside sub-threshold lows over years, is chronic sub-threshold bipolarity, and it changes the treatment logic from antidepressant-first to mood-stabiliser-first.

HOLD THIS

Cyclothymia is chronic sub-threshold bipolarity: at least two years (one in youth) of numerous hypomanic and depressive symptoms, present at least half the time, never symptom-free for more than two months and never a full episode, carrying a 15% to 50% risk of progression to bipolar I or II; treat with a mood stabiliser, be cautious with antidepressants, and do not mistake it for the emotional instability of a personality disorder.

18 · Mixed features and mixed affective states

Why this matters. A **mixed affective** presentation is where opposite-pole symptoms co-occur inside one mood episode: depressive symptoms intruding on a manic or hypomanic picture, or manic symptoms intruding on a depressive one. The examiner rewards three moves here. First, the nosological shift from a self-standing **mixed episode** in ICD-10 to a **mixed-features qualifier** attached to an episode in DSM-5, with ICD-11 sitting between the two. Second, the two classic clinical pictures, **dysphoric mania** and agitated (mixed) depression, and their Kraepelinian ancestry. Third, and most testable, the clinical weight: mixed features flag underlying bipolarity, predict a worse course and a higher suicide risk, and blunt the antidepressant response, so they change what you prescribe.

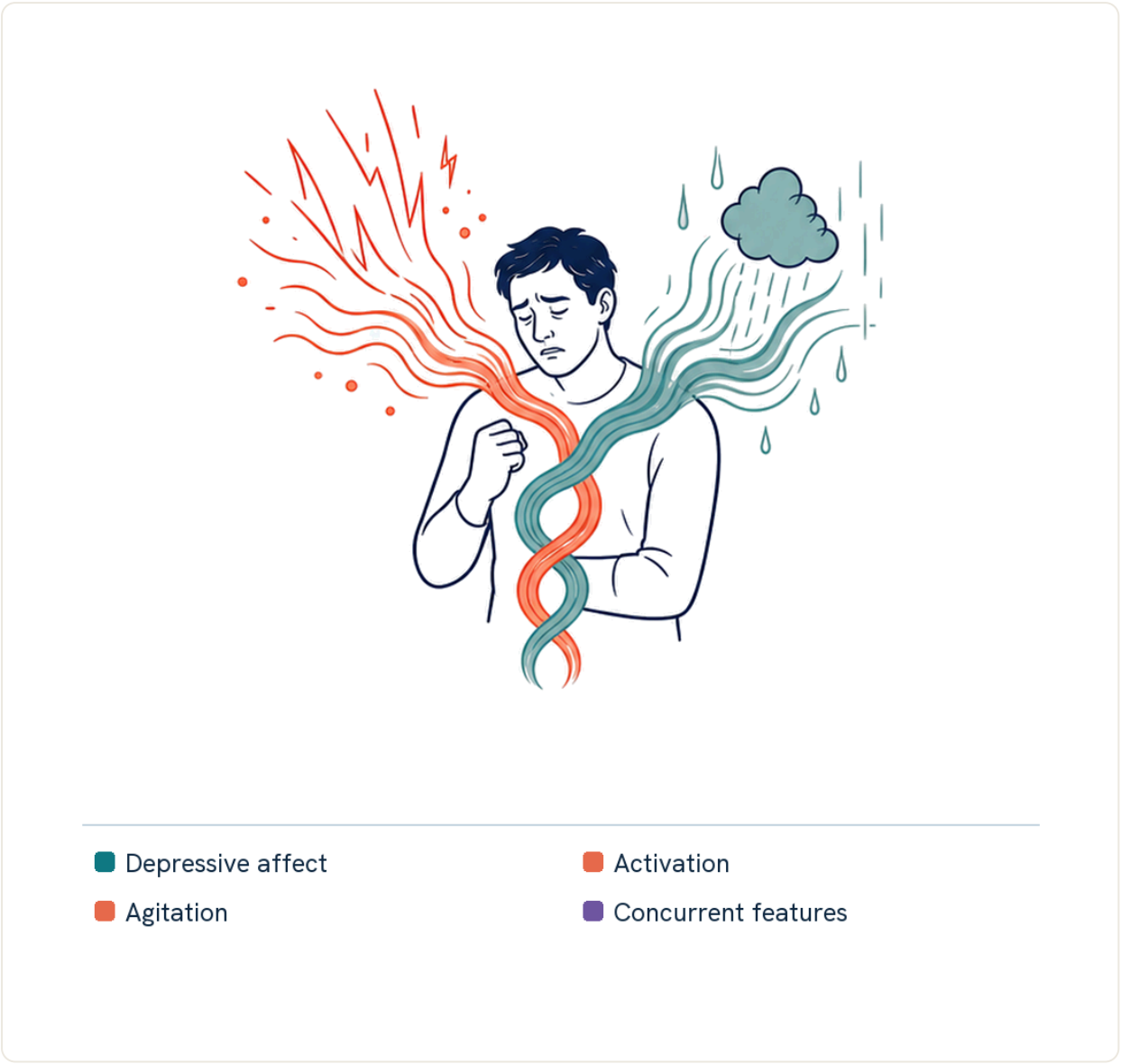


Fig 11.9 Mixed features combine elements from the opposite mood pole in the same episode, for example depressive affect with increased activation or agitation, rather than simple sequential switching.

Nosology is given ICD-11 primary, with the DSM-5 (the DSM-5-TR) rule cross-mapped and ICD-10 flagged because Indian exams still cite its mixed episode (F38.00 in the mood-disorders block, and F31.6 for bipolar affective disorder, current episode mixed). The full manic-episode and major-depressive-episode criteria on which this rests are the canonical property of the manic-episode and MDD topics; the raw descriptive definitions of the individual mood symptoms belong to the Psychometry, Assessment and Descriptive Psychopathology notes. The deep pharmacology of the antimanic and antidepressant agents is owned by the Mood disorders: pharmacotherapy notes, and the guideline-level management of a mixed presentation is owned by the bipolar-management topic; what is taught here is the concept, the criteria for the qualifier, and the discrimination.

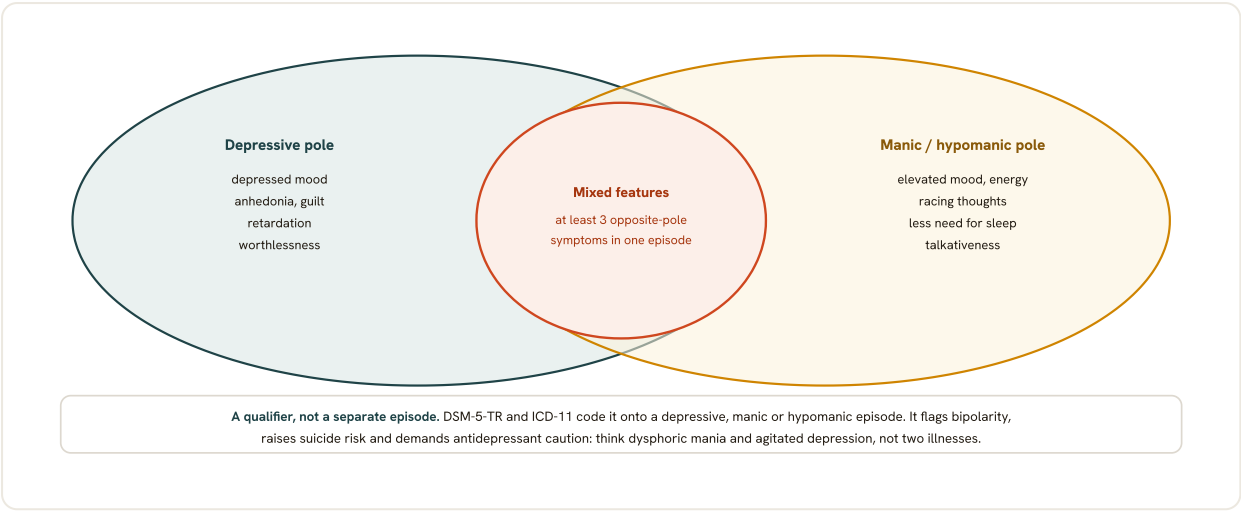


Fig 11.10 Mixed features: opposite-pole symptoms co-occurring within one episode. The DSM-5-TR "with mixed features" specifier needs at least three non-overlapping symptoms of the opposite pole and attaches to a depressive, manic or hypomanic episode rather than standing alone. The overlap is what separates true mixed features from a purely agitated depression or a straightforward dysphoric mania, and it flags bipolarity, a higher suicide risk and the need to avoid an antidepressant alone.

18.1 The core concept: opposite-pole symptoms inside one episode

A **mixed affective** state is defined by the simultaneous or rapidly alternating presence of symptoms of both mood poles within a single episode (Kaplan & Sadock 2024). The manic (or hypomanic) and the depressive symptoms are not sequenced across separate episodes but braided together in the same window: a patient may be flooded with racing thoughts, pressured speech and goal-directed overactivity while at the same time carrying dysphoric mood, hopelessness and active suicidal ideation. The clinical texture is one of internal contradiction, high energy driving a black mood, and it is this coupling of drive to despair that makes the state so dangerous. Transient tearfulness at the height of mania, or a few racing thoughts in a depression, is not a mixed state; the threshold is that *several* prominent contrapolar symptoms co-occur (ICD-11 CDDR).

RULE **Mixed means both poles, at once, in one episode.** Several prominent symptoms of the opposite pole must co-occur or alternate rapidly within a single episode; momentary lability at a pole-transition does not qualify.

18.2 From the ICD-10 mixed episode to the DSM-5 and ICD-11 qualifier

The nosology has moved from an episode to a specifier. ICD-10 classified a **mixed affective episode** as a distinct episode type: either a mixture, or a rapid alternation (within a few hours), of manic and depressive symptoms lasting at least two weeks. DSM-5 abolished the standalone DSM-IV "mixed episode" (which had required full criteria for both mania and depression nearly every day for a week) and replaced it with a **with mixed features qualifier** that is appended to a manic, hypomanic or major depressive episode (DSM-5-TR). ICD-11 takes an intermediate route: it keeps a named **mixed episode** as one of its mood-episode descriptions inside bipolar type I disorder (6A60), rather than reducing it to a pure specifier, defining it by several prominent manic symptoms occurring simultaneously or alternating rapidly with several prominent depressive symptoms across at least two weeks (ICD-11 CDDR). The single point to hold is the

direction of travel: the entity has migrated from a rare, all-or-none episode toward a dimensional feature that is far more commonly detected.

SYSTEM	HOW A MIXED PRESENTATION IS CODED	THRESHOLD
ICD-10	Mixed affective episode: a self-standing episode type (F38.00; bipolar current episode mixed F31.6)	**Mixture or rapid alternation of manic and depressive symptoms for at least 2 weeks**
DSM-IV	Mixed episode: a self-standing episode type	Full criteria for both mania and depression, nearly every day, for at least 1 week
DSM-5-TR	**"With mixed features" qualifier on a manic, hypomanic or depressive episode**	At least 3 non-overlapping opposite-pole symptoms on most days of the episode
ICD-11	Mixed episode retained as a mood-episode description within bipolar type I (6A60)	Several prominent manic and several prominent depressive symptoms, simultaneous or rapidly alternating, for at least 2 weeks

The migration of the mixed presentation across systems: from a standalone episode (ICD-10, DSM-IV) to a specifier (DSM-5-TR), with ICD-11 keeping a named mixed episode; the highlighted cells carry the modern thresholds.

TRAP **Do not expect DSM-5 to have a "mixed episode".** DSM-5-TR deleted the standalone mixed episode and replaced it with a "with mixed features" specifier; only ICD-10, DSM-IV and (as a retained description) ICD-11 name a mixed episode.

18.3 The DSM-5 rule: three non-overlapping opposite-pole symptoms

The DSM-5-TR **with mixed features** specifier applies when full criteria are met for one episode and **at least three** symptoms of the opposite pole are present on the majority of days of the episode (DSM-5-TR). The design is deliberately restrictive: the contrapolar symptom list is trimmed to the symptoms that are **non-overlapping** between the two poles. For a **depressive episode with mixed features**, the three-plus manic symptoms drawn on are elevated/expansive mood, grandiosity, talkativeness/pressured speech, flight of ideas or racing thoughts, increased energy or goal-directed activity, involvement in risky pleasurable activity, and decreased need for sleep. For a **manic or hypomanic episode with mixed features**, the three-plus depressive symptoms are dysphoria or depressed mood, anhedonia, psychomotor retardation, fatigue, worthlessness or guilt, and recurrent thoughts of death or suicidality. Critically, symptoms that are *shared* across both poles, namely irritability, distractibility, psychomotor agitation and insomnia, are excluded from the counting because they cannot discriminate the opposite pole (DSM-5-TR). If full criteria for both mania and depression are met simultaneously, the episode is coded as manic with mixed features, mania winning on severity (DSM-5-TR).

at least 3	most days	at least 2 wk	non-overlapping
OPPOSITE-POLE SYMPTOMS (DSM-5-TR)	OF THE EPISODE	ICD-11 MIXED EPISODE	IRRITABILITY/AGITATION EXCLUDED

COMMON TRAP

Counting irritability, distractibility, agitation or insomnia toward a DSM-5-TR mixed-features specifier. These four are common to both poles and are deliberately excluded; only the non-overlapping opposite-pole symptoms count. This is the single most tested detail of the specifier.

18.4 Dysphoric mania: the classic mixed manic picture

The prototype mixed manic state is dysphoric mania, also called mixed mania. It is a manic syndrome carrying a dysphorically excited mood, so the drive of mania is yoked to the misery of depression: irritability, anger, panic, pressured speech, agitation, severe insomnia, grandiosity, hypersexuality, and, ominously, suicidal ideation and persecutory ideas can all coexist (Kaplan & Sadock 2024). Two to four depressive symptoms (depressed mood, helplessness, hopelessness, fatigue, anhedonia, guilt, or suicidal ideation) arising in the setting of a manic syndrome are enough to define the mixed manic state, and such states occur in around **50%** of bipolar patients at some point in the illness, though full-blown co-occurrence of mania and complete depression (true "dysphoric mania" in the strict sense) is relatively uncommon (Kaplan & Sadock 2024). Mixed mania is over-represented in women, often arising as mania intruding on a depressive or dysthymic baseline; in men it more often arises through comorbid substance or alcohol use (Kaplan & Sadock 2024). A severely psychotic mixed state, with hallucinations and Schneiderian symptoms, can be genuinely hard to separate from schizoaffective disorder, which is cross-referenced to the Other psychotic disorders, delusional syndromes and catatonia notes.

GOOD TO REMEMBER

- **Dysphoric (mixed) mania:** a manic syndrome with a dysphoric, irritable, agitated mood and depressive admixtures; the one to hold is that suicidal ideation can co-occur with full manic drive. Roughly **50%** of bipolar patients have a mixed state at some point (Kaplan & Sadock 2024).

18.5 Agitated and mixed depression: the depressive-pole picture

The mirror picture is the depressive episode carrying manic admixtures: an **agitated, mixed depression**. Here the depressive syndrome runs with intrusions of the opposite pole, racing or crowded thoughts, inner tension and restlessness, psychomotor activation, pressured speech, and, at the severe end, sexual arousal and increased energy despite the depressed mood (Kaplan & Sadock 2024). This is the "depression with increased energy or irritability" that patients themselves may not label as anything but a bad depression (DSM-5-TR). Depressive mixed states are strikingly common on the bipolar side of the ledger: they occur in as much as **60%** of bipolar II depressions and in around **30%** of ostensibly "unipolar" major depressions, a finding that repositions a substantial slice of "unipolar" depression as latently bipolar (Kaplan & Sadock 2024). The agitated, mixed depression is the presentation most dangerous to mismanage, because the reflex to reach for an antidepressant is exactly wrong (see 18.7).

GOOD TO REMEMBER

- **Agitated/mixed depression:** a depressive episode with racing thoughts, inner tension, activation and pressured speech; the discriminating feature is manic admixture inside a depression. It appears in up to **60%** of bipolar II and about **30%** of "unipolar" depressions (Kaplan & Sadock 2024).

18.6 The Kraepelinian mixed states: the historical scaffold

The concept is Kraepelinian in origin. Emil Kraepelin held that manic-depressive illness was one disease whose surface state was set by three independent axes, mood, thought or ideation, and psychomotor activity, each of which could run high (manic) or low (depressive). When the three axes did not move together, so that, for instance, mood was depressed while thought and activity were accelerated, the result was a **mixed state** rather than a pure mania or depression (Kaplan & Sadock 2024). This cross-combination of the three axes is the historical scaffold behind the modern qualifier, and it explains why mixed states are best thought of dimensionally rather than as a single stereotyped picture; the pure "excited depression" and "depressive or anxious mania" of the classic descriptions are simply particular settings of the three dials. The examiner point is the framework, that Kraepelin generated the mixed states by dissociating mood, thought and psychomotor activity, not any single memorised list.

PEARL

Kraepelin's insight was that mania and depression are not opposite ends of one dial but the joint state of three separate dials (mood, thought, psychomotricity); a mixed state is simply any setting where those dials disagree. Modern "mixed features" is that idea made operational.

18.7 Why it matters: bipolarity, worse course, suicide, antidepressant caution

Mixed features are not a curiosity; they carry heavy prognostic and management freight. Four consequences are examinable. First, **they flag bipolarity**: mixed features in a major depressive episode are a recognised risk factor for the later emergence of bipolar I or bipolar II disorder, so their presence should shift the diagnostic bet toward the bipolar spectrum (DSM-5-TR). Second, **a worse course**: the presence of mixed features in an episode is associated with a poorer prognosis and a poorer lithium response (DSM-5-TR; Kaplan & Sadock 2024). Third, **a higher suicide risk**: mixed features are associated with increased suicide attempts, the coupling of depressive hopelessness to manic drive and impulsivity being the lethal combination (DSM-5-TR); the clinical assessment of that risk is owned by the Somatic-symptom, sexual, impulse-control disorders and suicide notes. Fourth, **a poorer antidepressant response and a real hazard**: an antidepressant given alone into a mixed depression can worsen the mixed and manic pole and destabilise the illness, so the management pivots away from antidepressant monotherapy toward mood stabilisers or atypical antipsychotics (Kaplan & Sadock 2024). The guideline-level detail of that management is the property of the bipolar-management topic and the Mood disorders: pharmacotherapy notes.

RULE **Mixed features flag bipolarity and raise suicide risk.** Contrapolar symptoms in a depression predict a bipolar course, a poorer lithium response and more suicide attempts, and they change management.

TRAP **Do not treat an agitated, mixed depression with an antidepressant alone.** Antidepressant monotherapy into a mixed depression can worsen the mixed/manic pole; screen every activated depression for mixed features and past hypomania first.

INDIA

In Indian practice, where many bipolar presentations first reach care during a depressive phase, an agitated, mixed depression is a frequent and easily missed presentation; the working caution is to screen every depression for a past hypomanic episode and for current contrapolar symptoms before committing to an antidepressant. Severe, psychotic or life-threatening mixed states are a recognised indication for ECT, which is widely available in Indian teaching hospitals; the technique itself is owned by the ECT and neurostimulation notes.

GOOD TO REMEMBER

- **Mixed features (the concept):** opposite-pole symptoms co-occurring within one episode; now a qualifier, not a separate episode (DSM-5-TR), with ICD-11 retaining a named mixed episode.
- **The DSM-5 rule:** at least three non-overlapping opposite-pole symptoms on most days; irritability, distractibility, agitation and insomnia are excluded from the count.
- **Clinical weight:** mixed features predict bipolarity, a worse course, a poorer lithium response, and a higher suicide risk, and mandate antidepressant caution.
- **Kraepelin:** mixed states arise when mood, thought and psychomotor activity dissociate; the historical origin of the modern specifier.

HOLD THIS

Mixed features = at least three non-overlapping opposite-pole symptoms inside one episode (a DSM-5-TR qualifier, an ICD-11 mixed episode); they flag bipolarity, worsen course, raise suicide risk, and forbid an antidepressant alone in a mixed depression.

19 · Rapid cycling bipolar disorder

Why this matters. **Rapid cycling** is not a separate diagnosis but a **course specifier** applied to bipolar I or bipolar II disorder, and it is examined because it changes both the prognosis and the treatment logic. The single reflex to build is that rapid cycling means **four or more episodes** of any polarity in a twelve-month window, that it is disproportionately driven by **antidepressant exposure** and by **hypothyroidism**, and that the correct response to a worsening cycle is usually to withdraw the antidepressant rather than to add another one (Maudsley 2021).

Nosology is given ICD-11 primary, where a rapid cycling qualifier can be added to bipolar type I and bipolar type II disorder, with the DSM-5 (the DSM-5-TR) "with rapid cycling" specifier cross-mapped and ICD-10 flagged where Indian exams still cite it. The raw descriptive definitions of the individual manic, hypomanic and depressive symptoms are owned by the Psychometry, Assessment and Descriptive Psychopathology notes and cross-referenced here; the full soft-

bipolar spectrum, the manic-episode criteria and the bipolar II hypomania threshold are laid out elsewhere in this chapter; and the deep drug pharmacology, dosing and treatment-resistance algorithms belong to the Mood disorders: pharmacotherapy notes.

19.1 The definition: four or more episodes in twelve months

Rapid cycling is defined as bipolar disorder in which **four or more episodes** of a mood disturbance occur within a twelve-month period (Maudsley 2021; Kaplan & Sadock 2024). Three points make the definition examinable. First, the episodes may be of **any polarity**, depressive, manic, hypomanic or mixed, counted in any combination, so four depressive episodes, or two manic plus two depressive, or four clear switches in polarity, all qualify (Maudsley 2021). Second, each counted episode must **meet the duration and symptom criteria for a full episode** of its type (a major depressive episode, a manic, a hypomanic or a mixed episode), so a merely labile mood does not count. Third, the episodes must be **demarcated** from one another, either by a period of partial or full remission of at least **two months**, or by a switch to an episode of the opposite polarity (DSM-5-TR). It is the counting of *episodes*, not the counting of mood swings, that residents most often get wrong.

RULE **Rapid cycling is four or more episodes in twelve months and is often antidepressant-driven.** Four or more full episodes of any polarity within twelve months, each demarcated by a two-month remission or a switch of polarity, applied as a specifier to bipolar I or bipolar II.

four or more episodes	at least 2 months	commoner in women
IN TWELVE MONTHS	REMISSION DEMARCATING EPISODES	RAPID-CYCLING SEX DISTRIBUTION (DSM-5-TR)

19.2 The ultra-rapid and ultradian variants

Beyond the twelve-month definition sit two faster, non-official descriptors used in the literature and worth naming (Kaplan & Sadock 2024). Ultra-rapid cycling denotes phases of mania and depression that alternate very rapidly, in the order of days to weeks (described as "in a matter of hours or days"). Ultra-ultra-rapid cycling, also called ultradian cycling, denotes distinct mood shifts occurring within a twenty-four-hour period, that is, within one day; it is described particularly in paediatric-onset bipolar disorder, where children characteristically exhibit ultradian cycling, irritability and explosive temper outbursts rather than the discrete episodes seen in adults (Kaplan & Sadock 2024). These variants are not separate diagnoses and lack formal operational criteria; treat them as descriptive intensifiers of the rapid cycling course.

TERM	FREQUENCY OF SWITCHING	STATUS
Rapid cycling	**Four or more full episodes in 12 months**	Formal specifier (DSM-5-TR; ICD-11 qualifier)
Ultra-rapid cycling	**Switches over days to weeks**	Descriptive, non-official
Ultra-ultra-rapid (ultradian) cycling	**Distinct shifts within a single 24-hour day**	Descriptive, non-official; typical of paediatric-onset

The formal boundary is the twelve-month, four-episode line; ultra-rapid and ultradian are progressively faster descriptive labels without their own criteria.

19.3 Associations and precipitants: women, bipolar II, thyroid, antidepressants

Rapid cycling clusters with a recognisable set of associations that the examiner expects listed (Maudsley 2021). It is **commoner in women**, although the guidelines give no precise sex ratio (DSM-5-TR), and it is **well recognised in bipolar II** as well as in bipolar I. It is associated with **hypothyroidism** and low thyroxine states, and rapid cycling has been linked to the presence of antithyroid antibodies even where overt thyroid dysfunction is absent (Gan et al. 2019, cited in Maudsley 2021). The most examinable precipitant is **antidepressant exposure**, especially the tricyclic antidepressants, which can accelerate the cycle (Maudsley 2021). Rapid cyclers also carry more depressive morbidity, higher rates of anxiety disorders, substance use and borderline personality disorder, and greater functional impairment than non-rapid cyclers (Maudsley 2021).

MNEMONIC

WATCH the cycle: Women, Antidepressants, Thyroid (low), bipolar-two, Chronic morbidity

The five things that drive or mark rapid cycling: female sex (a female preponderance, with no precise ratio given), antidepressant exposure (especially tricyclics), hypothyroidism or antithyroid antibodies, a bipolar II diathesis, and a heavier depressive and comorbid burden.

19.4 Prognosis: a poorer-outcome, harder-to-treat course

Rapid cycling carries a **poorer prognosis** than a non-rapid cycling course. It is generally held to be **less responsive to drug treatment**, entails considerable depressive morbidity and suicide risk, and is associated with poorer functioning, more obesity, and the need to be treated with more drugs and at somewhat higher doses (Maudsley 2021). Importantly, lithium is **less likely to be effective** in rapid cycling than in non-rapid cycling illness (Maudsley 2021), a point that shapes the management pointer below. Rapid cycling is not necessarily permanent: it may come and go, and spontaneous or treatment-related remission of the rapid cycling pattern occurs in around a third of rapid cyclers (Maudsley 2021).

19.5 Management principles: withdraw the antidepressant, treat the thyroid, combine stabilisers

Detailed agents, doses and algorithms are owned by the Mood disorders: pharmacotherapy notes; the principles here are a guideline-level pointer. There is **no formal first-choice agent or combination** for rapid cycling, and NICE concluded that there is no evidence to support managing a rapid cycling illness any differently from a more conventional bipolar course (NICE, cited in Maudsley 2021). The pragmatic staged strategy is: first, **review and often withdraw antidepressants** in all patients, since antidepressants are implicated in driving and sustaining the cycle; second, **evaluate and treat precipitants**, in particular thyroid dysfunction (including antithyroid antibodies), alcohol and external stressors; and third, **optimise and consider combining mood stabilisers**, using plasma levels, favouring combinations such as lithium plus valproate, lithium plus lamotrigine, or valproate plus carbamazepine, with adjunctive atypical antipsychotics (for example quetiapine, olanzapine or aripiprazole) where needed (Maudsley 2021). Because lithium is less effective here, valproate and lamotrigine-containing combinations

often carry the weight, and lamotrigine is favoured where the burden is predominantly depressive.

TRAP **Chasing each low with more antidepressant accelerates the cycling.** Adding an antidepressant to treat every depressive dip in a rapid cycler tends to speed the cycle rather than settle it; the corrective move is to withdraw the antidepressant and optimise mood-stabiliser cover.

WORKED EXAMPLE

A woman with bipolar II disorder, treated with an SSRI for recurrent depression, presents with five distinct mood episodes over the past year, brief hypomanias alternating with fuller depressions. She is now cycling faster on a recently increased antidepressant dose. The examinable move is not to add a second antidepressant but to recognise antidepressant-driven rapid cycling: check thyroid function, review and taper the antidepressant, and optimise or combine mood stabilisers (Maudsley 2021).

INDIA

In Indian practice the tricyclic antidepressants remain in wide use, so antidepressant-driven acceleration of cycling is a real and preventable scenario; screening thyroid function is inexpensive and worthwhile in any bipolar patient whose course speeds up. Coding still frequently uses ICD-10, where rapid cycling is not a discrete category, so the resident should be able to map the ICD-11 rapid cycling qualifier and the DSM-5-TR "with rapid cycling" specifier onto the older bipolar affective disorder codes. Drug brand names belong to the Mood disorders: pharmacotherapy notes.

19.6 Nosological mapping: ICD-11, DSM-5-TR and ICD-10

The three systems handle rapid cycling as a course modifier, not a stand-alone illness. ICD-11 allows a rapid cycling qualifier to be added to bipolar type I disorder and bipolar type II disorder. The DSM-5-TR carries an explicit **"with rapid cycling"** specifier defined by at least four mood episodes in the previous twelve months that meet criteria for a major depressive, manic, hypomanic or mixed-features episode and are demarcated by at least two months of partial or full remission or by a switch to the opposite polarity (DSM-5-TR). ICD-10 has no discrete rapid cycling category, so the pattern is captured descriptively under bipolar affective disorder. Whatever the system, the operational content is identical: four or more full episodes, any polarity, in twelve months.

PEARL

Rapid cycling is a red flag to re-audit the drug chart before escalating: an unrecognised antidepressant or an untreated hypothyroid state is frequently the engine of the cycle, and removing the driver often does more than adding a further agent (Maudsley 2021).

GOOD TO REMEMBER

- **Rapid cycling bipolar disorder:** a course specifier on bipolar I or bipolar II, defined by **four or more episodes** of any polarity (depressive, manic, hypomanic or mixed) within twelve months, each meeting full-episode criteria and demarcated by a **two-month** remission or a polarity switch; the one number to hold is four episodes in a year.
- **Ultra-rapid and ultradian variants:** ultra-rapid cycling switches over days to weeks; ultra-ultra-rapid (ultradian) cycling switches within a single 24-hour day and is typical of paediatric-onset bipolar disorder; both are descriptive, not formal diagnoses.
- **Associations and drivers:** commoner in women and well recognised in bipolar II; hypothyroidism and antithyroid antibodies, and antidepressant exposure (especially tricyclics), drive it; the course is poorer and lithium is less effective.
- **Management pointer:** withdraw antidepressants, treat the thyroid and other precipitants, and favour lithium, lamotrigine or valproate combinations; no formal first-choice agent exists (Maudsley 2021). Details in the Mood disorders: pharmacotherapy notes.

HOLD THIS

Rapid cycling is four or more full episodes of any polarity in twelve months, a specifier on bipolar I or II that is commoner in women and bipolar II and is often driven by antidepressants and by hypothyroidism; the corrective move is to withdraw the antidepressant, treat the thyroid, and combine mood stabilisers (lithium, lamotrigine, valproate) rather than to chase each low with more antidepressant.

20 · Course, prognosis and outcome of bipolar disorder

Why this matters. Bipolar disorder is the paradigm **recurrent, lifelong mood illness**. The single fact that reorganises everything downstream is that it is a disorder of **recurrence, not of one-off episodes**: most patients recover symptomatically from any given episode, yet the great majority relapse, carry **sub-syndromal symptoms** and cognitive and functional impairment between episodes, and lose years of life to suicide and to cardiovascular and metabolic disease (Kaplan & Sadock 2024; Shorter Oxford 2018). The examinable reflex is to read every bipolar presentation as a point on a long trajectory and to think maintenance from the outset.

Nosology is given ICD-11 primary, with the DSM-5-TR cross-mapped and ICD-10 flagged where Indian exams still cite it; the raw descriptive definitions of the individual mood symptoms and the rating scales are owned by the Psychometry, Assessment and Descriptive Psychopathology notes. The manic-episode and depressive-episode criteria, the soft-bipolar spectrum and the rapid cycling specifier are laid out elsewhere in this chapter. Guideline-level maintenance drug choices, dosing and treatment-resistance algorithms belong to the Mood disorders: pharmacotherapy notes and are only pointed to here; clinical suicide risk assessment and safety planning belong to the Somatic-symptom, sexual, impulse-control disorders and suicide notes.

20.1 The natural history: recurrence with inter-episode recovery but residual impairment

The defining shape of the **course** is Kraepelinian: acute episodes end and a temporary recovery occurs, unlike schizophrenia where acute exacerbations merge into a chronic deficit state, so it is **recurrence, not permanent chronicity**, that is the essential feature (New Oxford 2020). **Nearly all patients recover from the acute episode**, yet **at least 90% experience further episodes** of

major mood disturbance over follow-up (Shorter Oxford 2018; Kaplan & Sadock 2024). The recovery is, however, incomplete: over long-term follow-up patients are symptomatic with mood disturbance of varying severity for about **one-third** of the time, and in bipolar I disorder syndromal or sub-syndromal symptoms are present an average of about **50%** of the time (Shorter Oxford 2018; Kaplan & Sadock 2024). In both bipolar I and bipolar II this residual burden is **predominantly depressive**: bipolar I patients spend depressive to manic symptom-time in a ratio of about **3:1**, and in bipolar II the average patient spends roughly **37 times** more days depressed than hypomanic (Kaplan & Sadock 2024, from the Judd cohorts). These inter-episode sub-syndromal symptoms are not benign: they themselves increase the risk of a full-blown mood episode, and multiple episodes track with cognitive impairment, structural brain change and functional decline (Kaplan & Sadock 2024).

RULE **Bipolar is a recurrent, lifelong illness even between episodes, so think maintenance early.** At least 90% relapse, the inter-episode state carries sub-syndromal (mostly depressive) symptoms and cognitive and functional impairment, so long-term prophylaxis is planned from the outset, not after the third admission.

TRAP **Treating bipolar as a series of unrelated one-off episodes.** Managing each mania or depression as a self-limiting event, stopping treatment on recovery, ignores that over 90% recur and that euthymia is rarely symptom-free; it is the commonest structural error in bipolar management.

20.2 Episode frequency over the lifetime and the tendency to shortening cycles

The **episode frequency** accumulates across the lifespan. Bipolar disorder usually begins as depression, with the first manic episode manifesting on average about **5 years** later, and the average length of a manic episode, treated or untreated, is about **6 months** (Shorter Oxford 2018). Over a 25-year follow-up bipolar patients experience, on average, about **10 further episodes** of major mood disturbance (Shorter Oxford 2018). Crucially, in some patients the illness is not stationary: the **interval between episodes becomes progressively shorter with both age and the number of episodes**, a pattern captured by the kindling or neuroprogressive (staging) model, in which repeated episodes lower the threshold for the next, reduce the likelihood of remission and worsen cognitive and neurologic function (Shorter Oxford 2018; Kaplan & Sadock 2024). Frequent episodes also alter the response to treatment: patients with many prior episodes are less likely to respond to acute treatment and to prophylaxis (Kaplan & Sadock 2024). Kindling is a heuristic model, not an established mechanism, and the shortening-cycle pattern is seen in only a subset rather than universally; it is best held as a rationale for early, sustained prophylaxis rather than as a proven law of the illness.

at least 90%	about 10	about one-third
RECUR (FURTHER MOOD EPISODE)	FURTHER EPISODES OVER 25 YEARS	OF TIME SYMPTOMATIC LONG-TERM

20.3 Predictors of poorer outcome and of better outcome

The **prognosis** is stratified by a recognisable set of predictors that the examiner expects listed against each other (Kaplan & Sadock 2024; Shorter Oxford 2018). Markers of a **poorer outcome** include **early age of onset**, a **mixed** and **rapid-cycling** course, the presence of **psychotic**

features, comorbid **substance use**, and **poor adherence** to treatment, together with a greater number and severity of prior episodes, comorbid anxiety, and persistent cognitive deficits and mood instability. A **better outcome** is associated with the mirror image: later and clearly episodic onset, a classical euphoric-mania course with full inter-episode euthymia, absence of psychosis and of substance comorbidity, good treatment adherence, and preserved cognition; bipolar II disorder as a whole carries a somewhat better functional outcome than bipolar I (Shorter Oxford 2018). Even so, the long-term prognosis is sobering: fewer than **20%** of bipolar patients achieve a 5-year period of clinical stability with good social and occupational performance (Shorter Oxford 2018).

DOMAIN	PREDICTS POORER OUTCOME	PREDICTS BETTER OUTCOME
Age of onset	**Early onset**	Later, clearly episodic onset
Episode type/course	**Mixed features; rapid-cycling course**	Classical euphoric mania; full inter-episode euthymia
Psychosis	**Psychotic features present**	No psychosis
Comorbidity	**Substance use; anxiety comorbidity**	No substance or anxiety comorbidity
Adherence	**Poor adherence**	Good treatment adherence
Episode burden	**Many/severe prior episodes; persistent cognitive deficits**	Few episodes; preserved cognition
Subtype	Bipolar I (greater manic morbidity)	Bipolar II somewhat better functional outcome

Predictors of outcome in bipolar disorder; the discriminating markers of a worse course are early onset, a mixed or rapid-cycling pattern, psychosis, substance use and poor adherence.

MNEMONIC

The worse course is EMPS-A: Early onset, Mixed/rapid-cycling, Psychosis, Substance use, poor Adherence

The five high-yield predictors of a poorer bipolar outcome: Early onset, a Mixed and rapid-cycling course, Psychotic features, Substance use, and poor Adherence. Their mirror image predicts a better outcome.

20.4 Mortality: the elevated suicide risk

Bipolar disorder carries one of the highest suicide risks in psychiatry. The standardized mortality ratios for suicide in bipolar disorder range from about **10 to 30**, meaning bipolar patients are roughly 10 to 30 times more likely to die by suicide than the general population (Kaplan & Sadock 2024). Over a 40-year follow-up of hospitalised patients, about **8% of men and 5% of women** died by suicide (Nordentoft et al. 2011, in Shorter Oxford 2018). The risk is **front-loaded and state-dependent**: it is higher **early in the course** of the illness, during acute mood episodes (especially with mixed features), during and around hospitalisation, and within **4 to 12 weeks** of discharge (Kaplan & Sadock 2024). Established risk markers, from the ISBD Task Force,

include a depressive or mixed first and current episode, greater number and severity of episodes, rapid cycling, anxiety, atypical features, hopelessness, a first-degree family history of mood disorder or suicide, and prior suicide attempts (Schaffer et al. 2015, in Kaplan & Sadock 2024). The detailed clinical risk assessment and safety planning belong to the Somatic-symptom, sexual, impulse-control disorders and suicide notes.

TRAP **Assuming the danger is only during depression, and only in established illness.** Suicide risk is highest early in the course, in mixed states, and in the weeks around discharge, so vigilance cannot be relaxed once the acute low lifts.

20.5 Mortality: excess cardiovascular and metabolic death and the life-years lost

The excess mortality of bipolar disorder is **not accounted for by suicide alone**. The high mortality is driven also by general medical conditions, above all **cardiovascular disease**, and by the secondary consequences of comorbid substance misuse and smoking, compounded by the metabolic effects of long-term psychotropic, particularly antipsychotic, treatment (Shorter Oxford 2018; Goodwin et al. 2016). In a large Danish cohort, bipolar disorder was associated with a reduction in life expectancy of about **13 years in men and 9 years in women**, and about **two-thirds of this reduction was accounted for by natural causes** (chiefly cardiovascular disease), with the remainder due to suicide and accidents (Kessing et al. 2015, in Shorter Oxford 2018). The clinical corollary is that maintenance of a bipolar patient is not only mood-episode prophylaxis but active attention to cardiometabolic risk: weight, glucose, lipids, smoking and blood pressure. The specific monitoring schedules for individual mood stabilisers and antipsychotics belong to the Mood disorders: pharmacotherapy notes.

10 to 30	about 13 y / 9 y	about two-thirds
SMR FOR SUICIDE	LIFE-YEARS LOST, MEN / WOMEN	OF LIFE-YEARS LOST FROM NATURAL CAUSES

INDIA

In Indian practice the same recurrent, lifelong logic holds, and the cardiometabolic burden is amplified by the high background prevalence of diabetes and cardiovascular disease and by the widespread use of tricyclic antidepressants, which can destabilise the course. The National Mental Health Survey of India (2015 to 2016) established mood disorders as a substantial and largely untreated burden with a wide treatment gap, which makes early recognition and sustained maintenance, rather than episode-by-episode crisis care, the practical priority. Coding still frequently uses ICD-10, where bipolar affective disorder is a single category without the ICD-11 bipolar type I and type II split; the resident should be able to map between them. Drug brand names belong to the Mood disorders: pharmacotherapy notes.

20.6 Putting the outcome together: what "outcome of bipolar" means for management

The **outcome of bipolar** disorder is best summarised as a favourable *episode* outcome sitting on top of an unfavourable *illness* outcome. Acute episodes almost always remit, but across the lifespan the illness recurs in more than 90%, leaves residual mostly depressive symptomatology for about a third of the time, erodes cognition and function, and shortens life. This is why the

guideline consensus, led by the CANMAT/ISBD framework and echoed by NICE, is that long-term prophylaxis should be planned early, in bipolar I typically after the first manic episode, and why psychosocial adjuncts (psychoeducation, IPSRT, family-focused therapy and CBT) are added to reduce relapse and improve adherence (Kaplan & Sadock 2024). The specific first-line and next-line maintenance agents, the phase-by-phase drug logic and the treatment-resistance pathways are owned by the Mood disorders: pharmacotherapy notes; the point to carry from the course and prognosis is the indication for that maintenance, not the drug list itself.

PEARL

The prognostic asymmetry is the teaching point: nearly everyone recovers from the acute episode (good episode outcome) yet fewer than one in five achieves 5 years of stable good functioning (poor illness outcome). It is that gap, filled by sub-syndromal symptoms, cognitive drift and cardiometabolic risk, that maintenance treatment exists to close (Shorter Oxford 2018).

GOOD TO REMEMBER

- **Natural history:** a **recurrent** illness with inter-episode recovery in most, but residual (mostly depressive) sub-syndromal symptoms and cognitive and functional impairment persist between episodes; at least **90%** recur and patients are symptomatic about **one-third** of the time.
- **Episode frequency and kindling:** about **10** further episodes over 25 years, first mania roughly **5 years** after depression onset; in some the cycle shortens with age and episode number (kindling, a model not a proven law).
- **Predictors of worse outcome:** early onset, a mixed and rapid-cycling course, psychosis, substance use and poor adherence; the mirror predicts better outcome, and fewer than **20%** reach 5 years of stable good functioning.
- **Suicide mortality:** standardized mortality ratio for suicide about **10 to 30**; risk highest early, in mixed states and within **4 to 12 weeks** of discharge.
- **Cardiometabolic mortality and life-years:** excess death from cardiovascular and metabolic disease as well as suicide, with life expectancy reduced about **13 years (men) and 9 years (women)**, two-thirds from natural causes (Kessing et al. 2015).

HOLD THIS

Bipolar disorder is a recurrent, lifelong illness in which acute episodes remit but over 90% relapse, the inter-episode state carries residual mostly depressive symptoms and cognitive and functional impairment, mixed and rapid-cycling courses (with early onset, psychosis, substance use and poor adherence) predict a worse outcome, and mortality is high from both suicide (SMR about 10 to 30) and cardiovascular and metabolic disease (about 13 years of life lost in men, 9 in women): so plan maintenance from the outset rather than treating episodes as unrelated one-offs.

21 · Bipolar disorder in special populations

Bipolar disorder does not read the textbook the same way at every age or in every physiological state. Three **special populations** bend the diagnosis and the safe management enough to earn their own topic: the child, the older adult, and the woman in the peripartum. Each carries a signature examiner-favourite error, and each error is a mirror image of the same underlying principle, that bipolar disorder is defined by discrete **episodes** and that a "manic" presentation must always be interrogated for a non-affective cause before it is owned as primary bipolarity.

This topic teaches the discrimination in each population, not the deep drug pharmacology: the full agent-level detail, dosing and treatment-resistant algorithms belong to the Mood disorders: pharmacotherapy notes, and the wider perinatal frame is developed in the Perinatal/women's mental health and emergency psychiatry notes. The full manic-episode and depressive-episode criteria live in this chapter's own episode topics; here we apply them at the extremes of the lifespan. Nosology is given ICD-11-primary, DSM-5-TR cross-mapped.

21.1 Paediatric bipolar disorder: the diagnostic controversy

An overdiagnosis debate, resolved by insisting on episodicity. **Paediatric bipolar** disorder became one of the most contested diagnoses in child psychiatry after a sharp late-twentieth-century rise in the rate at which clinicians, mostly in the United States, applied the bipolar label to children. DSM-5-TR is explicit that this increase "appears to be attributable to clinicians combining at least two clinical presentations into a single category," namely classic episodic mania and non-episodic severe irritability, both of which were being called bipolar disorder in children (DSM-5-TR 2022). The correction was twofold: DSM-5 reserved the term bipolar disorder for episodic presentations, and it created a new home for the chronically irritable child. Both DSM-IV and DSM-5-TR require that children, exactly as adults, show distinct episodes of mania or hypomania to qualify for bipolar I or bipolar II (DSM-5-TR 2022; Kaplan & Sadock 2024).

RULE **Require clear episodicity before diagnosing paediatric bipolar.** There must be a distinct time period, of the required duration, in which mood and behaviour were markedly and unmistakably different from the child's own baseline.

21.2 The distinction from disruptive mood dysregulation disorder

Episodic mania versus chronic, non-episodic irritability. Disruptive mood dysregulation disorder was added to DSM-5 precisely to capture the chronically irritable child who is not bipolar. Its core is chronic, severe, persistent irritability with two manifestations: frequent temper outbursts, on average **three or more times per week**, grossly out of proportion to provocation, and a persistently irritable or angry mood present between outbursts, most of the day nearly every day, noticeable to others (DSM-5-TR 2022). The outbursts must run for **at least 1 year** in **at least two settings**; onset is before **age 10** years; the diagnosis is not applied below a developmental age of 6 and is validated for the **6 to 18** year range (DSM-5-TR 2022). The single discriminating feature is longitudinal course: bipolar disorders are episodic, disruptive mood dysregulation disorder is not.

WORKED EXAMPLE

A 9-year-old boy has raged three to four times a week for eighteen months, at home and at school, and is sullen and touchy in between. He has never shown a distinct several-day stretch of elated or expansive mood, decreased need for sleep or grandiosity that stood out from his usual self. This is chronic irritability, and the correct diagnosis is disruptive mood dysregulation disorder, not paediatric bipolar disorder. Elevated or expansive mood and grandiosity, common in mania, are not characteristic of disruptive mood dysregulation disorder, and their absence here is diagnostic (DSM-5-TR 2022).

FEATURE	PAEDIATRIC BIPOLAR DISORDER	DISRUPTIVE MOOD DYSREGULATION DISORDER
Course	**Episodic: discrete episodes distinct from baseline**	**Chronic, non-episodic, persistent irritability**
Hallmark mood	Elevated / expansive mood, grandiosity present	Irritable / angry mood; elation and grandiosity absent
Temper outbursts	Within an episode	3 or more per week, over 1 year, in 2 or more settings
Onset criterion	Any age, but rare pre-adolescence	Before age 10; validated for 6 to 18 years
Longitudinal outcome	Recurrent bipolar illness	**Unipolar depressive / anxiety disorders, not bipolar**
Exclusion	Excludes if criteria for another cause met	Cannot coexist with, or follow, any manic/hypomanic episode

The one discriminator is episodicity: a manic or hypomanic episode ever, even one lasting more than one day, forbids disruptive mood dysregulation disorder (DSM-5-TR 2022).

TRAP **Do not diagnose bipolar from chronic irritability alone in a child.** Non-episodic severe irritability is disruptive mood dysregulation disorder and predicts unipolar depression and anxiety, not bipolar disorder; conversion to bipolar disorder is very low.

GOOD TO REMEMBER

- **Paediatric bipolar disorder:** bipolar disorder in a child, requiring the same episodic mania/hypomania as adults; the one discriminator is a distinct episode markedly different from the child's baseline; hold "episodicity is mandatory; rare pre-adolescence."
- **Disruptive mood dysregulation disorder:** chronic non-episodic severe irritability with frequent outbursts; the one discriminator is that it is never episodic and elation/grandiosity are absent; hold "3+ outbursts/week, over 1 year, onset before age 10, validated 6 to 18 years."

21.3 Elderly bipolar disorder: later-onset ("secondary" or vascular) mania

New mania in later life is organic until proven otherwise. **Elderly bipolar** disorder splits into two populations: those with typical younger onset who have aged, and those with a genuinely later age of onset, usually at **40 or 50 years or older** (Tasman 2015). The later-onset group is enriched with identifiable medical, particularly neurological, factors that may be causing the mania: such factors are found in **12 to 38%** of later-onset cases (Tasman 2015). This is the

domain of secondary mania, conceptualised by Krauthammer and Klerman (1978) as mania occurring close on the heels of a specific physiological insult: stroke, head trauma, dementia, brain tumours and metastases, and endocrine or drug-induced states (Tasman 2015). Where cerebrovascular disease drives it, the term **vascular mania** is used, the manic analogue of vascular depression.

RULE **Exclude an organic cause in new late-life mania.** First-onset mania in an older adult mandates neurological and medical workup for a secondary cause before it is called primary bipolar disorder.

21.4 Elderly bipolar disorder: the organic differential and drug sensitivity

A wider differential and a narrower therapeutic window. Because the organic yield is high, the older adult with new mania carries a heavier burden of causes to exclude than the young adult: stroke and other cerebrovascular disease, space-occupying lesions, dementia, delirium, hyperthyroidism, and drug or steroid effects all sit in the differential (Tasman 2015; Kaplan & Sadock 2024). Management is then constrained by age-related pharmacokinetics: reduced renal clearance, greater sensitivity to central nervous system effects, and more interacting comorbid medication all narrow the safe dosing range, lithium especially. Guideline-anchored practice reflects this: CANMAT advises that in older adults lithium be started at a low dose, for example **150 mg** nightly, targeting a lower serum level of **0.4 to 0.8 mEq/L**, with lithium level and renal function monitored every **3 to 6 months** and 5 to 7 days after any dose or interacting-drug change (CANMAT 2018). The agent-level detail sits in the Mood disorders: pharmacotherapy notes; the catatonia and organic-psychosis boundaries are developed in the Other psychotic disorders, delusional syndromes and catatonia notes.

TRAP **Do not miss a vascular or organic mania in an older adult.** Anchoring on primary bipolar disorder and skipping the neurological and metabolic workup misses stroke, tumour, dementia and endocrine causes, and risks lithium toxicity from age-reduced clearance.

40 to 50+ yr	12 to 38%	0.4 to 0.8 mEq/L
TYPICAL LATER-ONSET AGE	LATER-ONSET CASES WITH NEUROLOGICAL FACTORS	LITHIUM TARGET IN OLDER ADULTS (CANMAT)

INDIA

In Indian geriatric practice the high organic yield of late-life mania is a live concern: cerebrovascular disease and untreated endocrine disorder are common, and a first manic presentation after 50 routinely prompts neuroimaging and thyroid and metabolic screening before a primary bipolar label is accepted. Lithium remains affordable and widely available, but the same age-reduced renal clearance applies, so lower starting doses, lower target levels and closer renal monitoring are standard.

GOOD TO REMEMBER

- **Elderly bipolar disorder (later-onset):** new bipolar disorder arising at 40 to 50 years or older; the one discriminator is the high load of identifiable organic cause; hold "neurological factors in 12 to 38%; workup before diagnosis."
- **Secondary / vascular mania:** mania on the heels of a physiological insult (Krauthammer and Klerman) or driven by cerebrovascular disease; the one discriminator is a demonstrable medical cause; hold "stroke, tumour, dementia, endocrine; exclude before calling it primary."
- **Drug sensitivity in the elderly:** age-reduced renal clearance and CNS sensitivity narrow the window; the one discriminator is lower dosing and lower targets; hold "lithium start 150 mg nightly, target 0.4 to 0.8 mEq/L (CANMAT)."

21.5 Bipolar in pregnancy: the peripartum relapse risk

The postpartum is the single highest-risk window in the illness. **Bipolar in pregnancy** and the peripartum is defined less by pregnancy itself than by the puerperium: the BAP guidance states plainly that the postpartum period "carries very high relapse risk for bipolar disorder" and that focus of care planning should be increased in women of childbearing potential for this reason (BAP, in _MGMT-GUIDELINES). Postnatal bipolar recurrences, and new-onset bipolar and other affective postpartum psychoses, are to be treated as psychiatric emergencies: they tend to commence suddenly in the first few days after delivery, progress rapidly, and be severe (BAP, in _MGMT-GUIDELINES). Pregnancy does not protect against recurrence, and discontinuing prophylactic mood stabilisers near conception roughly **doubles** the recurrence risk, shortens the time to recurrence and increases time spent ill during pregnancy (BAP, in _MGMT-GUIDELINES). The wider perinatal frame, including puerperal psychosis and maternity blues, is developed in the Perinatal/women's mental health and emergency psychiatry notes.

RULE **Treat postpartum bipolar recurrence as an emergency.** New-onset or recurrent bipolar and affective postpartum psychosis begins abruptly in the first days after delivery, escalates fast, and warrants urgent assessment and admission.

21.6 Bipolar in pregnancy: the teratogenicity trade-offs

Avoid valproate in women of childbearing potential. The dominant teratogenicity rule is that valproate is avoided in women of childbearing potential: CANMAT advises avoiding divalproex in pregnancy due to teratogenicity, using monotherapy at the minimum effective dose, supplementing high-dose folic acid at **5 mg/day**, and monitoring with foetal ultrasound where lithium is used in the first trimester (CANMAT 2018). BAP goes further on the practical mechanics: if a woman planning pregnancy is already on valproate, withdraw it gradually over at least 4 weeks while she uses effective contraception (BAP, in _MGMT-GUIDELINES). Antipsychotics generally form the mainstay of perinatal bipolar treatment because they have a better risk-benefit ratio than valproate and carbamazepine and a larger reproductive evidence base; if lithium is used, plasma levels are measured monthly until 36 weeks then weekly until delivery, with the dose suspended around delivery to avoid toxicity (BAP, in _MGMT-GUIDELINES). This topic gives the direction of travel only; the agent-by-agent teratogenic detail is a pointer to the Mood disorders: pharmacotherapy notes and to the perinatal notes.

TRAP **Do not start or continue valproate in a woman of childbearing potential.** Valproate is the highest-teratogenicity mood stabiliser; the guideline default in this group is to avoid it and to prefer an antipsychotic, with folic acid supplementation where an anticonvulsant is unavoidable.

PEARL

The peripartum management problem is a scheduling problem as much as a drug problem: relapse risk peaks in the first postpartum days, so a plan made in pregnancy that specifies what to restart, and when, on the first day after childbirth (for example restarting a previously effective antipsychotic such as quetiapine or olanzapine) can pre-empt an early relapse (BAP, in _MGMT-GUIDELINES). Sleep protection and mood self-monitoring are part of the same relapse-prevention scaffold.

GOOD TO REMEMBER

- **Bipolar in pregnancy / peripartum:** a high-relapse state dominated by the postpartum window; the one discriminator is that the puerperium, not pregnancy, is the danger zone; hold "postpartum recurrence is an emergency; discontinuing prophylaxis near conception roughly doubles recurrence risk."
- **Valproate in women of childbearing potential:** the highest-teratogenicity mood stabiliser, to be avoided; the one discriminator is the teratogenic default to avoid; hold "avoid valproate; prefer antipsychotic; folic acid 5 mg/day if an anticonvulsant is unavoidable (CANMAT)."

21.7 The unifying principle across all three populations

Episodicity and exclusion, applied at both ends of the lifespan. The three special populations rehearse the same two disciplines. In the child, insist on a discrete episode before diagnosing bipolar disorder, and route chronic irritability to disruptive mood dysregulation disorder. In the older adult, insist on excluding an organic or vascular cause before owning a new mania as primary. In the peripartum woman, insist on relapse-prevention planning and on avoiding the teratogenic agent. Each is a specific instance of the general rule that bipolar disorder is an episodic illness whose "manic" presentations must always be tested for a non-affective explanation, and whose treatment must be tuned to the physiology of the person in front of you.

MNEMONIC

CHILD, ELDER, MOTHER

CHILD: demand episodicity (else it is disruptive mood dysregulation disorder). ELDER: exclude organic/vascular cause. MOTHER: postpartum emergency, avoid valproate. Three populations, three signature errors, one principle: episodes and exclusion.

HOLD THIS

Require clear episodicity before diagnosing paediatric bipolar disorder (else it is disruptive mood dysregulation disorder), exclude an organic or vascular cause in new late-life mania, and in the peripartum treat postpartum recurrence as an emergency while avoiding valproate in women of childbearing potential.

22 . Management of bipolar disorder: guidelines-first

Bipolar disorder is a lifelong, phasic illness, and its management is organised not by a single drug list but by **phase**: the drug that quiets an acute mania is not the drug that lifts a bipolar depression, and neither is automatically the drug you keep for maintenance. The board answer is a guideline answer. This note builds the plan on a **LOCUS to FOCUS to MODUS** spine: **LOCUS** (where you treat and how you keep the patient safe), **FOCUS** (the phase you are treating), and **MODUS** (the first-line and next modalities each guideline recommends). We LEAD with CANMAT (the CANMAT and ISBD 2018 bipolar guidelines, Yatham et al.), then state where the Indian Psychiatric Society and NICE sit.

The deep drug pharmacology, the full dosing tables, the adverse-effect profiles and the treatment-resistant-mania algorithm are not taught here: they are owned by, and cross-referred to, the Mood disorders: pharmacotherapy notes. This note stays at guideline level: which agent is first-line, in which phase, and the single monitoring headline. The manic-episode and depressive-episode criteria themselves are taught in full elsewhere in this chapter; the restraint and de-escalation technique is cross-referred to the Perinatal/women's mental health and emergency psychiatry notes.

22.1 LOCUS: where to treat, and the safety base

Admit for acute mania with risk. The default LOCUS for a florid **acute mania** is inpatient when there is risk to self or others, psychotic features, severe functional collapse, exhaustion or dehydration, or when the patient is non-adherent and cannot be safely held at home (CANMAT 2018, Kaplan & Sadock 2024). Maintenance, by contrast, is an outpatient enterprise: stable, adherent euthymic patients are followed in the clinic. The universal base under every phase is the same: a written safety and risk plan, a **mood diary** for early-warning-sign monitoring, sleep and routine stabilisation, and structured psychoeducation for the patient and, wherever possible, the family.

Suicide risk is elevated across the illness and formal risk assessment is cross-referred to the Somatic-symptom, sexual, impulse-control disorders and suicide notes; the clinical suicide-risk detail lives there.

RULE **Admit the risky mania.** Acute mania with risk, psychosis or non-adherence is an inpatient problem; maintenance is an outpatient one.

22.2 LOCUS: the crisis, severe agitation and the first-line intramuscular options

When an acutely manic patient is severely agitated and oral therapy is refused or unsafe, verbal de-escalation comes first, but if pharmacological control is needed CANMAT names a first-line parenteral set: intramuscular aripiprazole, intramuscular lorazepam, inhaled loxapine, or intramuscular olanzapine (CANMAT 2018). A practical caution repeated across guidelines: do not give intramuscular olanzapine and parenteral benzodiazepine together closely because of the risk of excessive sedation and cardiorespiratory depression. This is behavioural control of the crisis, not the definitive mood treatment, which is chosen in 22.3.

WORKED EXAMPLE

A man is brought in floridly manic, has not slept for four nights, is threatening staff and spits out oral medication. LOCUS: admit. Crisis MODUS: de-escalate, then offer a first-line intramuscular option (IM aripiprazole, IM lorazepam, inhaled loxapine or IM olanzapine). FOCUS once settled: an acute-mania first-line agent per 22.3, and stop any antidepressant he arrived on.

22.3 FOCUS: acute mania, the CANMAT first-line plan

For **acute mania**, CANMAT (CANMAT 2018) sets a clear first-line tier. First-line **monotherapy** is lithium, quetiapine, divalproex, asenapine, aripiprazole, paliperidone, risperidone or cariprazine. First-line **combination**, favoured in severe mania, is an atypical antipsychotic (quetiapine, aripiprazole, risperidone or asenapine) plus lithium or divalproex. The single most important co-prescribing move: **discontinue any antidepressant** the patient is on when they present with mania (CANMAT 2018). Second-line options (olanzapine, carbamazepine, ziprasidone or haloperidol) belong to the pharmacotherapy notes.

The minimal serum-level pointer. When lithium is used for the acute phase, the target is a serum level of **0.8 to 1.2 mEq/L** (CANMAT 2018); divalproex targets roughly **350 to 700 micromol/L**. Full titration, loading and monitoring detail is cross-referred to the Mood disorders: pharmacotherapy notes. Antipsychotics act faster than a mood stabiliser started alone, but lithium retains a distinct anti-suicidal and mood-stabilising signature (the Lithium Handbook 2023), which is why the severe presentation gets both.

RULE **Stop the antidepressant, start lithium, valproate or an atypical.** Acute mania: monotherapy with a first-line agent, or an atypical plus lithium/divalproex if severe.

TRAP **Continuing the antidepressant.** Leaving an antidepressant running in a manic patient fuels the episode; discontinue it and reassess the diagnosis in a first presentation.

22.4 FOCUS: bipolar depression, the CANMAT first-line plan

For **bipolar depression** (acute bipolar I depression), CANMAT first-line is quetiapine monotherapy (target about 300 mg/day), lurasidone (as monotherapy or adjunctive to lithium or divalproex), lithium monotherapy, and lamotrigine (monotherapy or adjunctive, target at least 200 mg/day with slow titration) (CANMAT 2018). The governing principle is that **antidepressant monotherapy is avoided**: if any antidepressant is used at all it is only adjunctive to a mood stabiliser or antipsychotic, and only in pure, non-mixed depression.

The two cautions. In **mixed features** and in **rapid cycling**, antidepressants are best avoided altogether because they can worsen the mixed state or accelerate the cycling; CANMAT reserves any antidepressant use for pure non-mixed bipolar II depression as a second-line option (CANMAT 2018). This is the highest-yield discrimination in the whole note.

RULE **Reach for quetiapine, lurasidone or lamotrigine and a mood stabiliser, not an antidepressant alone.** That is the first-line bipolar depression answer.

TRAP **Antidepressant monotherapy in bipolar depression.** It risks a switch into mania or hypomania and can precipitate rapid cycling; never give an antidepressant alone in a bipolar depression.

22.5 FOCUS: maintenance, the CANMAT first-line plan and the monitoring headline

For **maintenance**, CANMAT first-line monotherapy is lithium, quetiapine, divalproex, lamotrigine, asenapine or aripiprazole (CANMAT 2018). Adjunctive structured psychoeducation (for example the Barcelona or Life Goals programmes, at least five sessions) is itself a first-line relapse-prevention intervention in euthymic patients. For the non-adherent patient, offer a long-acting injectable antipsychotic (risperidone LAI two-weekly or aripiprazole once-monthly) to prevent relapse. A memory hook: lamotrigine is the depression-pole protector, aripiprazole prevents manic but not depressive episodes, and lithium leads because it covers both poles and lowers suicide risk.

The monitoring headline. Maintenance lithium is run to a serum level of **0.6 to 1.0 mEq/L**, with baseline and periodic **renal and thyroid function** (thyroid, renal function and plasma calcium at six months then at least annually) (CANMAT 2018). Full monitoring schedules for every agent are in the Mood disorders: pharmacotherapy notes.

0.8 to 1.2 mEq/L	0.6 to 1.0 mEq/L	at least 200 mg/day
LITHIUM, ACUTE PHASE	LITHIUM, MAINTENANCE	LAMOTRIGINE TARGET, BIPOLAR DEPRESSION

22.6 The first-line map by phase

The whole plan collapses into one grid. This is the table to hold.

PHASE (FOCUS)	FIRST-LINE MONOTHERAPY (CANMAT)	THE ONE MOVE
Acute mania	Lithium, quetiapine, divalproex, asenapine, aripiprazole, paliperidone, risperidone or cariprazine	**Discontinue any antidepressant; add atypical + lithium/divalproex if severe**
Acute mania, severe agitation (crisis)	IM aripiprazole, IM lorazepam, inhaled loxapine or IM olanzapine	**Behavioural control first, then a mood agent**
Bipolar depression	Quetiapine, lurasidone (mono or adjunctive to lithium/divalproex), lithium, lamotrigine (adjunctive)	**No antidepressant monotherapy; caution in mixed features and rapid cycling**
Maintenance	Lithium, quetiapine, divalproex, lamotrigine, asenapine or aripiprazole	**Add psychoeducation; LAI if non-adherent; lithium leads**

CANMAT/ISBD 2018 first-line options by bipolar phase; deeper dosing and second-line agents are in the Mood disorders: pharmacotherapy notes.

22.7 MODUS across guidelines: IPS and NICE alongside CANMAT

The Indian Psychiatric Society. The **indian psychiatric society** guideline for bipolar disorder has been updated: the 2025 IPS bipolar update (IPS 2025, Menon et al., Indian J Psychiatry

2026;68:8-43) supersedes the 2017 Shah guideline. For acute mania the 2025 update names lithium, divalproex, risperidone, quetiapine, aripiprazole, asenapine and cariprazine as first-line monotherapy (with the indigenous protein-kinase-C inhibitor endoxifen, 8 mg/day, as an additional Indian option), adds an antipsychotic to lithium or divalproex for severe or psychotic mania, and discontinues any antidepressant; for acute bipolar depression it names the olanzapine-fluoxetine combination, quetiapine, lurasidone and cariprazine as first-line and does not recommend unopposed antidepressant monotherapy; for maintenance it is lithium-led, with lamotrigine for the depression-pole prophylaxis; and it adds a separate section for bipolar II disorder, given its high Indian prevalence. It notes that sublingual dexmedetomidine, approved abroad for bipolar agitation, is not yet available in India. The IPS therefore agrees with CANMAT on the phase-based spine and differs mainly in emphasising lithium and valproate as the practical Indian first-line (IPS 2025, Menon et al.).

NICE. NICE (CG185) recommends an antipsychotic (for example haloperidol, olanzapine, quetiapine or risperidone) first-line for acute mania, switching to an alternative antipsychotic and then adding lithium, or valproate if lithium is unsuitable, if response is inadequate; for bipolar depression NICE favours a psychological intervention plus quetiapine, or olanzapine (with or without fluoxetine) or lamotrigine, and it positions lithium first-line for long-term maintenance with valproate or olanzapine as alternatives. Valproate is not to be offered to women of childbearing potential.

HOLD THIS

Phase decides the drug: acute mania stop the antidepressant and give lithium, valproate or an atypical; bipolar depression give quetiapine, lurasidone or lamotrigine (never an antidepressant alone); maintenance lithium leads.

22.8 India: lithium, ECT and the acute behavioural disturbance

INDIA

Lithium remains a workhorse first-line and maintenance mood stabiliser in Indian practice: it is inexpensive, widely available and well suited to a resource-limited, high-treatment-gap setting (the treatment gap for mental disorders in India runs about 70% to 92%) (Kaplan & Sadock 2024). Newer agents such as lurasidone, vortioxetine and cariprazine see minimal Indian use, mainly on cost grounds, so the practical first-line set skews to lithium, valproate and the older atypicals. ECT is widely used in India and is a genuine option for severe, psychotic, catatonic or treatment-resistant mania and for life-threatening presentations where a rapid response is needed; the ECT technique itself is cross-referred to the ECT and neurostimulation notes.

For acute behavioural disturbance in Indian inpatient settings, de-escalation and the least-restrictive approach come first, with parenteral options (an intramuscular antipsychotic or lorazepam) if needed; physical restraint is a last resort governed by the Mental Healthcare Act 2017 and must be time-limited and documented. The restraint and de-escalation detail is cross-referred to the Perinatal/women's mental health and emergency psychiatry notes.

GOOD TO REMEMBER

- **Acute mania (CANMAT first-line):** lithium, quetiapine, divalproex, asenapine, aripiprazole, paliperidone, risperidone or cariprazine; the one move is stop the antidepressant, and add an atypical plus lithium/divalproex if severe. Lithium acute level 0.8 to 1.2 mEq/L.
- **Severe agitation, crisis (CANMAT first-line IM):** intramuscular aripiprazole, intramuscular lorazepam, inhaled loxapine or intramuscular olanzapine; this is behavioural control, not the mood treatment.
- **Bipolar depression (CANMAT first-line):** quetiapine, lurasidone, lithium or adjunctive lamotrigine; the discriminator is never an antidepressant alone, and caution in mixed features and rapid cycling. Lamotrigine target at least 200 mg/day.
- **Maintenance (CANMAT first-line):** lithium, quetiapine, divalproex, lamotrigine, asenapine or aripiprazole, plus psychoeducation, plus an LAI if non-adherent; lithium leads. Maintenance level 0.6 to 1.0 mEq/L with renal and thyroid monitoring.
- **Indian Psychiatric Society:** the 2025 IPS bipolar update (Menon et al., superseding Shah 2017); first-line mania is lithium, divalproex, risperidone, quetiapine, aripiprazole, asenapine or cariprazine (add an antipsychotic if severe, stop the antidepressant; endoxifen an Indian option), bipolar depression is the olanzapine-fluoxetine combination, quetiapine, lurasidone or cariprazine (no unopposed antidepressant), maintenance is lithium-led with lamotrigine for the depressive pole, and a separate bipolar II section is added.
- **NICE (CG185):** antipsychotic first-line for acute mania, quetiapine/olanzapine-fluoxetine/lamotrigine for bipolar depression, lithium first-line for maintenance; no valproate in women of childbearing potential.

PEARL

The board question almost always turns on the phase and the antidepressant. Name the phase, and the first-line list follows; in mania you stop the antidepressant, and in bipolar depression you never start one alone.

23 · Differentiate: the mood-disorder interleaved differential

Why this matters. The mood disorders share a small pool of cross-sectional symptoms, so the examiner rarely tests whether a patient is depressed; the marks are in telling apart two entities that look identical on the day of assessment. This is the discrimination step: one interleaved **differential** that lays the mood syndromes side by side and, for each pairing, names the single feature that separates them. Hold the whole grid as a set of one-line discriminators rather than a mass of overlapping criteria, and the viva becomes a lookup.

The organising principle across the entire family is **polarity**. Almost every mood pairing collapses to one question: has there ever been a hypomanic or manic episode. Get that reflex right and the unipolar-versus-bipolar split, the bipolar-subtype split and the mixed-state count all fall into place; the depressive criteria and the manic-episode criteria themselves are taught in full elsewhere in these mood notes and are only invoked here as the yardsticks the differential measures against. The raw descriptive definitions of the individual mood symptoms and the rating scales are owned by the Psychometry, Assessment and Descriptive Psychopathology notes.

23.1 Unipolar versus bipolar depression: the same cross-section, told apart by history

The hardest and highest-yield pairing is **unipolar versus bipolar** depression, because the depressive episode in front of you can be phenomenologically identical in the two illnesses. A bipolar patient in the depressed phase meets exactly the same depressive-episode criteria as a unipolar patient; the two cannot be reliably separated on current symptomatology alone (Stahl 2021). What **distinguishes** them is not the cross-section but the longitudinal history: bipolar disorder requires at least one past hypomanic or manic episode, and unipolar major depressive disorder requires that no such episode has ever occurred. This is why the single most important move in every depression is to **screen for a past hypomanic** episode before the label is written. The failure is common and costly: over a third of patients diagnosed unipolar are eventually re-diagnosed bipolar, and as many as 60% of bipolar II patients are first labelled unipolar, because past hypomania is often pleasant and unreported and because bipolar patients usually present in the depressed phase (Stahl 2021).

Because the current picture will not settle it, the clinician leans on soft **pointers to bipolarity** that raise suspicion without being diagnostic (Stahl 2021; Akiskal 2007): an **early age of onset** (classically before 25 years); **atypical features** (hypersomnia, hyperphagia, leaden paralysis) or **psychotic features** in the depression; a **postpartum onset**, which carries a strong bipolar association; a **family history** of bipolar disorder; an **antidepressant-induced switch** into hypomania or mania on treatment; and a course of shorter but more frequent depressive episodes. None of these confirms bipolarity, but each should trigger a deeper hypomania screen. The definitive item, however, is always the same: a documented past hypomanic or manic episode.

RULE **Polarity is the master discriminator across the mood disorders.** A single past hypomanic or manic episode converts a unipolar depression into a bipolar one and changes first-line treatment; so screen every depression for a past hypomanic episode before the diagnosis is written.

TRAP **Letting a cross-sectional depression hide an underlying bipolarity.** The depressive episode looks the same in both illnesses; skip the lifetime hypomania screen and a bipolar depression is mislabelled unipolar and mistreated with an antidepressant alone.

23.2 MDD versus persistent depressive disorder versus adjustment disorder: duration, threshold and the stressor

Three depressive-spectrum diagnoses are separated on the axes of **duration**, **symptom threshold** and the **relationship to a stressor**, and they are constantly confused. Major depressive disorder is a full-threshold episode of **at least two weeks**: the whole five-of-nine cluster, most of the day nearly every day. Persistent depressive disorder (DSM-5-TR; the ICD-11 relative is dysthymic disorder) is a low-grade but chronic depression lasting **at least two years** (at least one year in children and adolescents), sub-threshold or threshold in intensity, with symptom-free intervals never exceeding two months. Adjustment disorder with depressed mood is the odd one out: it is defined by its tie to an identifiable psychosocial **stressor**, with symptoms arising within three months of the stressor and, once the stressor and its consequences resolve, remitting within six months (DSM-5-TR), and crucially it does **not** meet the full criteria for a major depressive

episode. So the discrimination is threefold: MDD on the two-week full-threshold episode, persistent depressive disorder on the two-year chronic floor, and adjustment disorder on the proportionate, stressor-locked, sub-threshold reaction. The pivotal test between adjustment disorder and MDD is whether the full episode threshold is met: if it is, a stressor does not downgrade the diagnosis to adjustment disorder.

at least 2 wk	at least 2 yr	within 3 mo	within 6 mo
MDD EPISODE FLOOR	PERSISTENT DEPRESSIVE DISORDER	ADJUSTMENT-DISORDER ONSET AFTER STRESSOR	ADJUSTMENT RESOLVES AFTER STRESSOR ENDS

23.3 The depressive subtypes against each other: melancholic versus atypical on mood reactivity

Within a confirmed depressive episode, the two classic subtypes are told apart by a single axis, **mood reactivity**, and the examiner rewards that one word. Melancholic depression is anchored on the **loss** of reactivity: the mood does not lift even transiently in response to normally pleasurable events, and it carries the reverse of the atypical vegetative pattern, namely early-morning awakening, a diurnal variation with mood worst in the morning, marked psychomotor change, anorexia and weight loss, and profound non-reactive despair (DSM-5-TR; Kaplan & Sadock 2024). Atypical depression is defined by **preserved mood reactivity** (the mood brightens in response to positive events) plus reverse-vegetative signs, at least two of hyperphagia or weight gain, hypersomnia, leaden paralysis, and long-standing interpersonal rejection sensitivity (DSM-5-TR). The single discriminator to hold is therefore mood reactivity: absent in melancholia, present in atypical depression; and because the atypical, reverse-vegetative pattern carries an affinity with the bipolar spectrum, atypicality should itself prompt a bipolar screen (Akiskal 2007).

23.4 Bipolar I versus II versus cyclothymia: mania versus hypomania versus sub-threshold

The bipolar subtypes are stratified purely on the **height of the highest pole ever reached**. Bipolar I disorder requires at least one full manic episode, defined by elevated or irritable mood and increased activity or energy lasting **at least one week** (or any duration if hospitalisation is needed), with marked functional impairment, and psychosis is permitted (its presence forces the manic rather than hypomanic label); a depressive episode is not even required for the diagnosis (DSM-5-TR). Bipolar II disorder requires at least one hypomanic episode, the same symptom picture lasting **at least four days**, but by definition **without** marked impairment, without hospitalisation and **without psychosis** (any psychotic feature makes the episode manic, not hypomanic), plus at least one major depressive episode (DSM-5-TR). Cyclothymic disorder is the sub-threshold floor: numerous periods of hypomanic and depressive symptoms over **at least two years** (one year in youth) that never at any point meet full criteria for a hypomanic, manic or major depressive episode (DSM-5-TR). The ladder is clean: full mania to bipolar I, hypomania plus depression to bipolar II, sub-threshold oscillation to cyclothymia. The distinction that decides bipolar I versus II is the mania-versus-hypomania boundary (the one-week, impairment, hospitalisation and psychosis markers), and diagnosing bipolar II without a documented hypomanic episode is the classic error.

COMMON TRAP

Calling a hypomania a mania (or the reverse). The hypomanic and manic pictures share their symptom list; the split is on duration (four days versus one week), severity (no marked impairment versus marked impairment), setting (no hospitalisation versus hospitalisation) and psychosis (absent in hypomania, since any psychotic feature upgrades the episode to manic). Get the boundary wrong and bipolar II is mislabelled bipolar I, or a genuine mania is under-treated as a hypomania.

23.5 Mixed features versus agitated depression versus dysphoric mania: the count of opposite-pole symptoms

The mixed-state pairings are separated by **how many opposite-pole symptoms are counted, and against which base episode.** A DSM-5-TR mixed features specifier attaches to a full episode of one pole carrying **at least three** non-overlapping symptoms of the opposite pole on most days; the shared symptoms, irritability, distractibility, psychomotor agitation and insomnia, are deliberately excluded from the count because they cannot discriminate the opposite pole (DSM-5-TR). This is exactly what **distinguishes** mixed features from a merely **agitated depression**: an agitated depression is a depressive episode whose restlessness and agitation are non-specific arousal, not counted manic symptoms, so with fewer than three genuine opposite-pole (manic) items it stays a plain unipolar-type depression with no mixed specifier. Dysphoric mania is the converse base episode: a full manic syndrome carrying three or more depressive symptoms, so the depression is intruding on a mania rather than the reverse. The single discriminator across all three is therefore the count and provenance of the opposite-pole symptoms: three or more true contrapolar symptoms earn the mixed specifier, and the base pole (depressive versus manic) decides whether the mixed picture is a depression with mixed features or a dysphoric mania. The deeper mixed-state phenomenology and its Kraepelinian roots are developed in the mixed-features topic of these notes.

PAIRING	WHAT LOOKS THE SAME	THE ONE DISCRIMINATOR
Unipolar versus bipolar depression	The cross-sectional depressive episode is identical in both	**A past hypomanic or manic episode (present = bipolar); pointers = early onset, atypical/psychotic features, postpartum onset, family history, antidepressant-induced switch**
MDD versus persistent depressive disorder	Both are depressive, low-mood states	**Duration and threshold: MDD = full episode at least 2 weeks; persistent depressive disorder = chronic sub/threshold at least 2 years**

PAIRING	WHAT LOOKS THE SAME	THE ONE DISCRIMINATOR
MDD versus adjustment disorder	Low mood after life events in both	**Adjustment disorder is stressor-locked and does NOT meet the full episode threshold; onset within 3 months, resolves within 6 months of the stressor ending**
Melancholic versus atypical depression	Both are subtypes of a depressive episode	**Mood reactivity: absent (non-reactive) in melancholic, preserved (reactive) in atypical**
Bipolar I versus bipolar II	Both have depressive and elevated-mood episodes	**Mania versus hypomania: at least 1 week with impairment/hospitalisation/psychosis-permitted (I) versus at least 4 days, no marked impairment, no psychosis (II)**
Bipolar II versus cyclothymia	Both are non-manic bipolar-spectrum states	**A full hypomanic AND a full major depressive episode (II) versus numerous sub-threshold periods over at least 2 years never meeting an episode (cyclothymia)**
Mixed features versus agitated depression	A restless, distressed depressive picture in both	**At least 3 non-overlapping manic symptoms counted (mixed) versus non-specific agitation with too few true manic items (plain depression)**
Mixed features versus dysphoric mania	Opposite-pole symptoms co-occur in both	**The base episode: depression carrying 3 or more manic symptoms (depression with mixed features) versus mania carrying 3 or more depressive symptoms (dysphoric mania)**

The interleaved mood differential: each pairing shares a cross-section but splits on one discriminator (the highlighted cell). Polarity, a past hypomania or mania, is the discriminator that recurs across the whole grid.

GOOD TO REMEMBER

- **Unipolar versus bipolar depression:** identical cross-section; the discriminator is a past hypomanic or manic episode, so screen every depression for a past hypomania; the number to hold is onset before **25 years** as a bipolar pointer.
- **MDD versus persistent depressive disorder:** full episode **at least two weeks** versus chronic sub/threshold depression **at least two years** (one year in youth).
- **MDD versus adjustment disorder:** the stressor-locked reaction that does not meet the full episode threshold; onset **within three months**, resolves **within six months** of the stressor ending (DSM-5-TR).
- **Melancholic versus atypical:** the one discriminator is **mood reactivity**, absent in melancholic, preserved in atypical.
- **Bipolar I versus II:** mania (**at least one week**, impairment, hospitalisation, psychosis permitted) versus hypomania (**at least four days**, no marked impairment, no psychosis).
- **Bipolar II versus cyclothymia:** a full hypomanic plus a full depressive episode versus numerous sub-threshold periods over **at least two years** never meeting an episode.
- **Mixed features versus agitated depression versus dysphoric mania:** the count and base pole, **at least three** non-overlapping opposite-pole symptoms earn the specifier; base depression = depression with mixed features, base mania = dysphoric mania.

MNEMONIC

FAST FAP

The pointers to bipolarity in a depression: **F**amily history of bipolar disorder, **A**typical (or psychotic) features, **S**witch on antidepressant, **T**iming of onset early (before 25 years), **F**requent but shorter episodes, **A**fter delivery (postpartum onset). Any of these should trigger a deeper past-hypomania screen; none of them replaces finding the episode itself.

HOLD THIS

Every mood-disorder differential resolves to one question first, has there ever been a hypomanic or manic episode; screen it in every depression, because a past hypomania is the single feature that separates unipolar from bipolar and reorders the whole grid.

Mood disorders: neurobiology and aetiology

24 · The monoamine hypothesis and its limitations

Why this matters. The **monoamine hypothesis** is the historical spine of biological psychiatry and the one neurochemical model every examiner expects a resident to state, defend and then puncture. It is taught here in the mood-neurobiology band under a strict rule: never as a settled cause, always as a mechanism handed straight to its own limitation. The high-yield move is to give the hypothesis, cite the two classes of evidence that built it (the pharmacological and the depletion evidence), and then produce the therapeutic-lag problem and the failure of acute depletion in healthy controls as the two facts that break it. The synaptic mechanics and the pathway anatomy of the monoamines are owned by the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the mood application is taught here.

The frame to carry: this is the oldest of the mood-neurobiology hypotheses and, in its original strong form, now regarded as obsolete (Kaplan & Sadock 2024). What survives is a refined version in which the monoamine change is a trigger for slower adaptive changes downstream (receptor sensitivity, second-messenger and neurotrophic signalling, neuroplasticity), not the primary lesion. Teaching it well means teaching the arc from a chemistry story to a plasticity story.

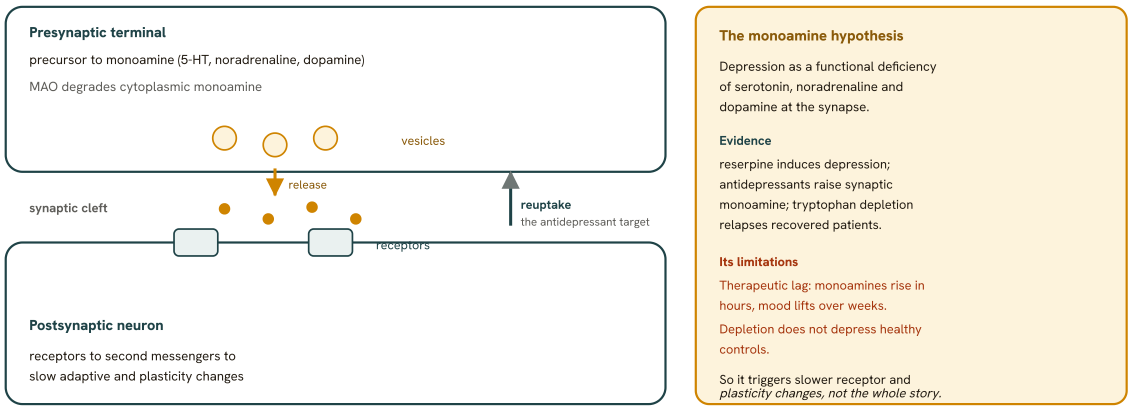


Fig 11.11 The monoamine hypothesis at the synapse, taught with its limits. A monoamine is synthesised, packaged, released into the cleft, and cleared by the reuptake transporter (the target of most antidepressants) and by MAO; the hypothesis holds that depression is a functional deficiency of serotonin, noradrenaline and dopamine. Its own evidence and its limitations sit side by side: the therapeutic lag and the failure of depletion to depress healthy controls are why the monoamine change is now read as the trigger for slower receptor and plasticity adaptations rather than the whole cause.

24.1 The hypothesis: a functional deficiency of synaptic monoamines

The **monoamine hypothesis** proposes that depressive disorder arises from a functional deficiency of one or more **monoamine** neurotransmitters at synapses in the brain (Shorter Oxford 2018; Kaplan & Sadock 2024). Three transmitters are implicated: serotonin (5-HT), noradrenaline (NA), and dopamine (DA), the latter two being catecholamines. In its early form the hypothesis pointed to a simple reduced provision of the amine at the synapse; more recent elaborations restate it as altered provision, turnover or receptor function rather than a bare fall in concentration (Shorter Oxford 2018). Schildkraut's original catecholamine hypothesis of 1965 framed depression as a deficiency, and mania as an excess, of catecholamines (chiefly noradrenaline) at functionally important adrenergic receptor sites, with a parallel serotonin ("indoleamine") hypothesis following (Kaplan & Sadock 2024). The examinable core is one line: depression as a functional deficiency of serotonin, noradrenaline and dopamine at the synapse.

RULE **Teach the monoamine hypothesis with the therapeutic-lag limitation attached.** The hypothesis is depression as a synaptic deficiency of 5-HT, NA and DA; the same breath must state that monoamines rise in hours while mood recovers over weeks.

24.2 The pharmacological evidence: reserpine and the antidepressants

The first pillar is pharmacological, and it runs in two directions that neatly bracket the hypothesis (Kaplan & Sadock 2024). Downwards: reserpine, an antihypertensive alkaloid of *Rauwolfia serpentina* that depletes monoamines by blocking their vesicular storage (VMAT2), was observed to precipitate depression as a side effect during the treatment of hypertension. Upwards: the antidepressants of the era, the tricyclic antidepressants and the monoamine oxidase inhibitors, were known to increase the amount of neurotransmitter available at monoamine synapses, the tricyclics by blocking reuptake and the MAOIs by blocking enzymatic breakdown. A supporting observation completed the picture: potent noradrenergic and dopaminergic agonists such as amphetamine and cocaine induce euphoria and activation, followed by a depression-like withdrawal crash (Kaplan & Sadock 2024). The logic is a bidirectional inference: drugs that lower synaptic monoamines depress, drugs that raise them treat depression, so a monoamine deficiency must underlie the illness.

PEARL

Reserpine is the reference toxin of the whole model: an antihypertensive that empties monoamine vesicles and, in a minority of exposed patients, precipitates a depressive syndrome. It is the single drug the examiner links to the monoamine hypothesis, and its Indian pedigree is genuine, the Rauwolfia snakeroot of Ayurvedic tradition.

24.3 The depletion evidence: tryptophan depletion relapses recovered patients

The second pillar is the tryptophan depletion paradigm, the most direct experimental test of the serotonin limb (Companion 2010; Shorter Oxford 2018). Serotonin synthesis depends on its dietary precursor amino acid, L-tryptophan; loading a subject with a mixture of large neutral amino acids that both competes with tryptophan for the brain transporter and accelerates peripheral tryptophan metabolism drives brain tryptophan, and therefore 5-HT synthesis and release, to very low levels. The striking finding is not in the well but in the recovered: in patients who have recovered from a depressive episode on a serotonin-selective reuptake inhibitor, acute tryptophan depletion produces a transient but clear-cut return of severe depressive symptoms (Delgado 1999; Companion 2010). The specificity is instructive, patients maintained on a noradrenaline-reuptake inhibitor such as desipramine do not relapse to tryptophan depletion, and the mirror manoeuvre for catecholamines, catecholamine depletion with alpha-methyl-para-tyrosine (AMPT), preferentially relapses noradrenergically-treated patients (Companion 2010; Shorter Oxford 2018). This double dissociation directly implicates the monoamines in the maintenance of recovery.

WORKED EXAMPLE

A euthymic patient, well for a year on an SSRI, is enrolled in a challenge study and given a tryptophan-free amino-acid drink. Within hours their plasma tryptophan falls and, over the same day, low mood, retardation and cognitive gloom return in a stereotyped replay of their prior episode; the state resolves as tryptophan is restored. The same patient had they been maintained on desipramine would very likely not have relapsed to tryptophan depletion. The lesson the examiner wants: depletion relapses the recovered along the transmitter axis of their treatment, which supports a monoamine role in relapse but, crucially, does not show that a deficiency caused the first episode.

24.4 The first limitation: the therapeutic-lag problem

The most powerful objection is a timing mismatch, the therapeutic-lag problem, and it is the single limitation to hold (Kaplan & Sadock 2024). Monoamine-enhancing antidepressants raise synaptic monoamine availability essentially at once: reuptake blockade elevates brain monoamines within **hours**, directly registered by in vivo microdialysis in animal models. Yet the clinical antidepressant response is delayed and measured in **weeks**, classically two to four weeks or longer before mood lifts. If a bare synaptic deficiency were the lesion, correcting it in hours should relieve the illness in hours. It does not. The therapeutic lag is therefore the fact that forces the model to change: the acute rise in monoamines cannot itself be the therapeutic event, and something slower, adaptive and downstream of the transporter must be doing the work. This is the **limitations of the monoamine** hypothesis in one clean argument.

hours	weeks	3
SYNAPTIC MONOAMINE RISE	CLINICAL ANTIDEPRESSANT RESPONSE	MONOAMINES: 5-HT, NA, DA

HOLD THIS

Antidepressants raise synaptic monoamines within hours, but mood recovers only over weeks: this therapeutic lag is the key limitation and the reason the monoamine change is read as a trigger for slower plasticity, not the lesion itself.

24.5 The second limitation: acute depletion does not depress healthy controls

The second decisive limitation belongs to the depletion experiments themselves (Companion 2010; Shorter Oxford 2018). Acute monoamine depletion, whether of serotonin by tryptophan depletion or of catecholamines by AMPT, does not reliably produce a depressive episode in healthy controls with no personal or family history of mood disorder. Where any effect is seen in the unaffected it is mild, transient and partial, and it clusters in vulnerable subgroups: a mood-lowering effect in women and in men with a family history of affective disorder, rather than a full syndrome in the general population (Companion 2010). The interpretation is exactly the one that undoes the strong hypothesis: lowering brain monoamines is not sufficient to cause depression. Depletion unmasks a latent vulnerability in those already predisposed or in remission from illness; it does not manufacture the disorder de novo. A deficiency that cannot induce the illness in a healthy brain cannot be its simple cause.

TRAP **Do not present "a chemical imbalance" as the settled cause of depression.** Acute monoamine depletion does not depress healthy controls and CSF and GWAS studies find no consistent monoamine deficit; the imbalance line is a patient-facing oversimplification, not the pathophysiology.

24.6 The wider limitations: the biochemical evidence never converged

Beyond timing and depletion, the direct biochemical search for a monoamine deficit largely failed, and these are the **limitations** that the examiner rewards a candidate for naming (Kaplan & Sadock 2024; Shorter Oxford 2018). Meta-analyses comparing CSF levels of the noradrenaline metabolite MHPG and the serotonin metabolite 5-HIAA found no consistent difference between depressed patients and controls; pharmacological "probe" studies found roughly 40% of patients with no measurable aberration of NA or 5-HT signalling; and genome-wide association studies found no evidence implicating monoamine-related genes in the aetiology of major depressive disorder (Kaplan & Sadock 2024). Low CSF 5-HIAA, where found, tracks impulsive and aggressive behaviour across diagnoses rather than depression specifically (Shorter Oxford 2018). Several studies in fact report elevated, not reduced, monoamine metabolites in untreated patients that normalise on recovery, consistent with altered monoamine signalling being a compensatory or secondary phenomenon rather than the primary lesion (Kaplan & Sadock 2024). The original monoamine hypotheses are therefore now viewed as obsolete in their strong form, with monoamine systems reconceived as broad neuromodulatory systems whose disturbance may be secondary or epiphenomenal.

24.7 The refinement: monoamines as the trigger for downstream plasticity

The resolution is not to discard the monoamines but to demote them from lesion to trigger (Kaplan & Sadock 2024; Shorter Oxford 2018). The refined account reads the acute rise in synaptic monoamines as the first step in a slower cascade: sustained transporter blockade drives adaptive receptor changes (down-regulation and desensitisation of, for example, post-synaptic and autoreceptor targets), engages second-messenger and gene-transcription signalling, and over weeks recruits neurotrophic and neuroplastic mechanisms, notably up-regulation of BDNF, increased synaptogenesis and hippocampal neurogenesis (Kaplan & Sadock 2024; Shorter Oxford 2018). This timescale of adaptation, measured in weeks, matches the therapeutic lag that the bare deficiency model could not explain. On this view the monoamine changes are the starting point, not the whole story: they set in motion the receptor-sensitivity, downstream-signalling and neuroplasticity changes that constitute the actual antidepressant mechanism. The synaptic mechanics and the pathway anatomy underlying this cascade are cross-referenced to the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the neurotrophic and HPA hypotheses that extend it are taught in the neighbouring mood-neurobiology topics; and the deep pharmacology of the individual agents is owned by the Mood disorders: pharmacotherapy notes.

STRAND	THE CLAIM	THE LIMITATION TO ATTACH
Pharmacological evidence	Reserpine depletes monoamines and depresses; TCAs and MAOIs raise synaptic monoamines and treat	**Reserpine depression is a minority effect; correlation of drug action with mood does not prove a deficiency lesion**
Depletion evidence	Tryptophan depletion relapses recovered SSRI-treated patients; AMPT relapses noradrenergically-treated patients	**Does not depress healthy controls with no vulnerability; unmasks latent risk rather than causing illness**
The therapeutic lag	Monoamines predict the transmitter target of antidepressants	**Monoamines rise in hours, mood improves over weeks: the acute rise is not the therapeutic event**
Direct biochemistry	A measurable monoamine deficit should mark the depressed brain	**CSF metabolites, probe studies and GWAS show no consistent monoamine deficit**
The refinement	Monoamine change is the trigger for slower adaptive changes	Receptor down-regulation, second-messenger and neurotrophic (BDNF) signalling and neuroplasticity, on the weeks timescale, do the therapeutic work

The monoamine hypothesis taught mechanism-with-limitation: each evidential strand paired with the fact that breaks the strong form and drives the shift to a downstream-plasticity account; highlighted cells are the limitations the examiner tests.

MNEMONIC

SNAP: Synapse deficiency, No lag fit, Amine depletion spares the healthy, Plasticity downstream

Synapse: the claim is a functional deficiency of 5-HT, NA and DA at the synapse. **N**o lag fit: monoamines rise in hours, mood in weeks. **A**mine depletion spares the healthy: acute depletion does not depress controls, only relapses the vulnerable. **P**lasticity downstream: the refinement, monoamine change triggers receptor and neurotrophic adaptation.

INDIA

Reserpine, the cornerstone of the pharmacological evidence, is an alkaloid of *Rauwolfia serpentina*, the Indian snakeroot used in Ayurvedic and traditional practice long before its twentieth-century use as an antihypertensive and early antipsychotic; its depressogenic reputation is the origin of the whole monoamine story (Kaplan & Sadock 2024; Maudsley). This chapter is otherwise generic on drug detail, which belongs to the Mood disorders: pharmacotherapy notes.

GOOD TO REMEMBER

- **Monoamine hypothesis:** depression as a functional deficiency of serotonin (5-HT), noradrenaline (NA) and dopamine at the synapse; three amines, catecholamines being NA and DA (Schildkraut 1965).
- **Pharmacological evidence:** reserpine depletes monoamines and depresses; TCAs and MAOIs raise synaptic monoamines and treat depression.
- **Depletion evidence:** tryptophan depletion transiently relapses recovered SSRI-treated patients (not desipramine-treated); the one eponym is Delgado.
- **The key limitation (therapeutic lag):** monoamines rise within **hours** but mood improves over **weeks**, so the acute rise cannot be the therapeutic event.
- **Second limitation:** acute monoamine depletion does not depress healthy controls, it only unmasks latent vulnerability.
- **The refinement:** the monoamine change is a trigger for slower adaptive changes (receptor down-regulation, second-messenger and neurotrophic BDNF signalling, neuroplasticity); a starting point, not the whole story.

25 · The HPA axis, cortisol, the DST and stress models

Why this matters. After the monoamine story, the **hpa axis** is the second pillar of mood neurobiology, and it carries the single most durable biological finding in the field: hyperactivity of the hypothalamic-pituitary-adrenal axis in major depression is, in the words of the standard text, one of the most consistent findings in biological psychiatry (Kaplan & Sadock 2024). This topic is taught the same way as its neighbour, mechanism handed straight to its limitation. The examinable arc is three-part: raised **cortisol** with blunted feedback in depression; the **dexamethasone suppression** test as the classic putative biological marker that failed to become a clinical test because of poor specificity; and the **stress**-diathesis and glucocorticoid-cascade models that link early adversity, chronic cortisol and hippocampal damage.

The frame to carry: the HPA changes are a robust *state* abnormality (they largely normalise on recovery), the DST is a real neuroendocrine window but never a diagnostic test, and chronic cortisol is neurotoxic to the hippocampus, which ties this topic to the neurotrophic and neuroimaging accounts. The axis mechanics themselves, the anatomy of the CRH-ACTH-cortisol loop and the receptor biology, are owned by the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the mood application is taught here.

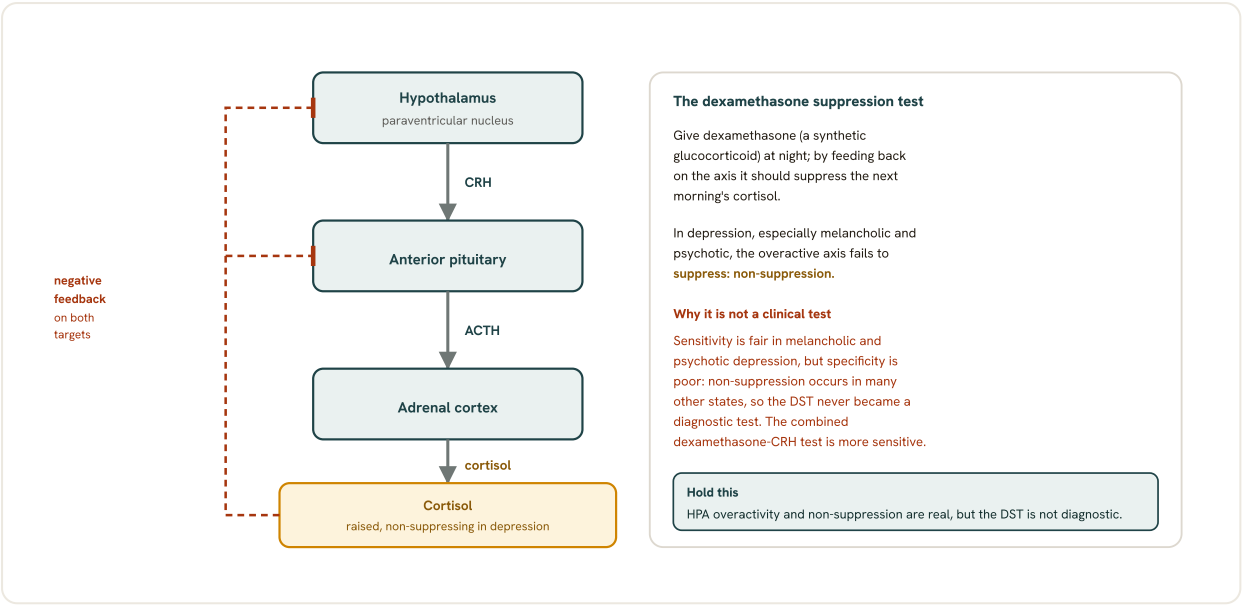


Fig 11.12 The HPA axis and the dexamethasone suppression test. CRH drives ACTH drives cortisol down the spine, and cortisol feeds back negatively on both the pituitary and the hypothalamus to switch the axis off. In depression the axis is overactive and the feedback is blunted, so dexamethasone fails to suppress the morning cortisol. The DST shows real HPA dysregulation but its poor specificity is why it never became a clinical diagnostic test.

25.1 HPA-axis overactivity in depression: the robust finding

The core. Hyperactivity of the HPA axis in major depression is one of the most consistent findings in biological psychiatry, recognised for over fifty years (Kaplan & Sadock 2024). The reported abnormalities cluster into five: **hypercortisolaemia** (raised plasma, urinary-free and CSF cortisol), resistance to dexamethasone suppression of cortisol (a measure of impaired negative feedback), a blunted ACTH response to intravenous CRH challenge, an increased cortisol response in the combined dexamethasone/CRH test, and elevated CSF CRH concentrations (Kaplan & Sadock 2024). A significant proportion of depressed patients hypersecrete cortisol, and this tends to normalise on recovery (Companion 2010). The most characteristic pattern is loss of the normal evening nadir, so cortisol is elevated near sleep onset and on first awakening; raised cortisol at these times has been shown to predict increased risk of future depression (Kaplan & Sadock 2024; Companion 2010).

RULE **HPA overactivity in depression is a state marker, not a trait or a cause.** Hypercortisolaemia, dexamethasone non-suppression and raised CSF CRH are the robust findings, and they largely remit when the patient recovers.

25.2 Blunted feedback and the glucocorticoid-receptor account

Impaired negative feedback. Cortisol release is held in check by a negative-feedback loop acting through low-affinity glucocorticoid receptors (GRs) and high-affinity mineralocorticoid receptors (MRs), with the hippocampus, rich in both, an important feedback site (Kaplan & Sadock 2024). In depression this brake is weakened: there is decreased sensitivity to glucocorticoid fast feedback as well as altered slow feedback, so a normally suppressive signal fails to shut the axis down (Kaplan & Sadock 2024). The diminished responsivity to dexamethasone seen in depressed patients gave rise to the glucocorticoid-receptor hypothesis of depression, in which HPA

dysfunction and the depressive syndrome are linked to genetic or acquired defects of glucocorticoid receptors (Shorter Oxford 2018). This account has a therapeutic hook: different classes of antidepressant increase glucocorticoid-receptor expression in animal studies, so one mechanism of antidepressant action may be to normalise excessive HPA activity by restoring feedback (Shorter Oxford 2018).

25.3 Adrenal and pituitary changes

End-organ correlates. Sustained central drive leaves structural and functional traces on the gland. Alterations in HPA function in depression include increased adrenal size and increased adrenal sensitivity to ACTH, alongside the blunted ACTH response to CRH (Kaplan & Sadock 2024). The picture fits a driven axis: hypothalamic CRH hypersecretion downregulates pituitary CRH receptors (the leading explanation for the blunted ACTH response), while the adrenal, chronically stimulated, enlarges and becomes hyper-responsive to ACTH so that cortisol output is high even when the pituitary signal is blunted (Kaplan & Sadock 2024). These are the end-organ counterparts of the central overactivity, and like the hormonal findings they behave as state markers that track the episode.

25.4 The link to melancholic and psychotic depression

Where the signal is strongest. HPA overactivity is not evenly distributed across depression: it concentrates in the more biological subtypes. Dexamethasone non-suppression is more common in depressed patients with melancholia, though it has not been reliably tied to any single symptom (Shorter Oxford 2018). The association is strongest of all in psychotic depression: some features of psychotic depression in particular appear to be mediated by hypercortisolaemia (Kaplan & Sadock 2024). Mechanistic support comes from treatment: mifepristone (RU-486), a glucocorticoid-receptor antagonist, has been reported to alleviate psychosis and depression in psychotic depression not associated with Cushing syndrome, and psychotic depression is explicitly described as a condition associated with HPA-axis dysregulation and glucocorticoid-receptor abnormalities (Kaplan & Sadock 2024). The clinical read is that the deeper the melancholic or psychotic colouring, the more likely the HPA axis is dysregulated. Mood-with-psychotic-features as a diagnostic entity is developed in the Other psychotic disorders, delusional syndromes and catatonia notes.

WORKED EXAMPLE

A severely retarded, guilt-ridden inpatient with nihilistic delusions has a morning cortisol at the upper limit and fails to suppress on an overnight 1 mg dexamethasone test. The temptation is to read the non-suppression as confirming the depression. It does not: non-suppression marks HPA dysregulation, which is genuinely more likely in this melancholic, psychotic presentation, but it is neither necessary nor sufficient for the diagnosis, which remains clinical. The finding is a correlate of severity and subtype, not a diagnostic ticket.

25.5 The dexamethasone suppression test: the principle

How the test works. The dexamethasone suppression test (DST) probes the integrity of glucocorticoid negative feedback (Companion 2010; Shorter Oxford 2018). A dose of the

synthetic corticosteroid dexamethasone, classically **1 mg** given overnight, acts at pituitary glucocorticoid receptors to suppress ACTH release and therefore endogenous cortisol; plasma cortisol is measured the next day. In a normally sensitive axis cortisol is suppressed. *Non-suppression*, a failure of cortisol to fall (or an early escape from suppression), indicates that feedback is impaired, implying either reduced sensitivity of the receptor-mediated brake and/or enhanced central drive to release cortisol (Companion 2010). About **50%** of depressed inpatients fail to show the normal suppression, and non-suppression reflects the underlying hypercortisolaemia (Shorter Oxford 2018; Companion 2010). This is the one-line principle: dexamethasone normally suppresses cortisol, and non-suppression indicates impaired feedback.

25.6 The DST as a putative biological marker, and why it failed

The historical hope. In the early 1980s the DST was proposed as a diagnostic biological marker for melancholic (endogenous) depression. The founding study reported that the 1 mg DST had high specificity, about **96%**, and sensitivity around **67%** for melancholia (Carroll et al 1981; Companion 2010). The problem, and the examinable core of this topic, is that the high specificity held only against normal controls and collapsed once other patient groups were included, and the result proved difficult to replicate (Companion 2010). Non-suppression is not confined to mood disorders: it also occurs in mania, chronic schizophrenia and dementia, and can be produced by weight loss or altered dexamethasone metabolism (Shorter Oxford 2018; Companion 2010). This lack of diagnostic specificity is exactly what killed the early hope that dexamethasone non-suppression could serve as a diagnostic marker of melancholic depression (Shorter Oxford 2018). The DST therefore never became a clinical diagnostic test: sensitivity is reasonable in melancholic and psychotic depression, but specificity is poor.

TRAP **Do not quote the DST as a clinical test to diagnose depression.** Non-suppression also occurs in mania, chronic schizophrenia and dementia; its poor specificity is precisely why it never entered clinical diagnostic use.

1 mg	~50%	~96% / ~67%
OVERNIGHT DEXAMETHASONE DOSE	DEPRESSED INPATIENTS NON-SUPPRESS	SPECIFICITY / SENSITIVITY, MELANCHOLIA (CARROLL 1981, POORLY REPLICATED)

25.7 The combined dexamethasone-CRH test: a more sensitive refinement

The refinement. The limits of the bare DST prompted a more sensitive probe, the combined dexamethasone/CRH test (Kaplan & Sadock 2024). It uses two opposing stimuli: dexamethasone to inhibit and CRH to stimulate. Typically 1.5 mg of dexamethasone is given in the evening, plasma cortisol is measured about 16 hours later the next day, and an infusion of 100 micrograms of CRH is then given with cortisol and ACTH measured repeatedly over the following 75 minutes (Kaplan & Sadock 2024). Depressed patients show an exaggerated cortisol (and ACTH) response to the CRH challenge despite dexamethasone pre-treatment, and this test detects HPA dysregulation more sensitively than the DST alone (Kaplan & Sadock 2024). Critically, the refinement does not rescue the diagnostic idea: abnormalities in the combined test appear across bipolar disorder, major depression, schizophrenia and PTSD, so its sensitivity and specificity still

do not make it a reliable diagnostic tool (Kaplan & Sadock 2024). Its main value has been as a state-dependent research marker of HPA-axis abnormality, normalising with clinical recovery.

> **PEARL**
>
> The DST and the dexamethasone/CRH test are *state* markers, not *trait* markers: the abnormalities remit when the patient recovers, and normalisation of the dexamethasone/CRH response (like the fall of elevated CSF CRH after ECT or fluoxetine) tracks treatment response. Persistent non-normalisation during treatment can be a harbinger of relapse (Kaplan & Sadock 2024).

25.8 The stress and stress-diathesis models: early-life adversity

Stress into biology. The stress-diathesis model holds that a depressive episode emerges from the interaction of a predisposing vulnerability (diathesis) with precipitating stress, and the HPA axis is the mechanism that translates one into the other. Depressed patients experience more negative life events than non-depressed patients, particularly chronic stress (Kaplan & Sadock 2024). The crucial developmental claim is that early-life stress sensitises the HPA axis and raises the risk of later depression (Kaplan & Sadock 2024). Adults abused as children show altered HPA responses to stress; depressed women who were victims of childhood abuse show an exaggerated ACTH and cortisol response to a psychosocial stressor, presumably from CRH hypersecretion, and depressed men with a history of childhood abuse show marked HPA hyperactivity on the combined dexamethasone/CRH test (Kaplan & Sadock 2024). Childhood maltreatment is described as leaving a neurohormonal "scar" of CRH hypersecretion that becomes a vulnerability factor for mood and anxiety disorders (Kaplan & Sadock 2024). This is the mechanistic bridge by which early adversity is written into adult risk, and it interlocks with the gene-environment findings taught in the neighbouring mood-neurobiology topic.

RULE **Early-life adversity sensitises the HPA axis.** Childhood maltreatment leaves a CRH-hypersecretion "scar" that exaggerates the later cortisol response to stress and raises the vulnerability to depression.

25.9 The glucocorticoid cascade and hippocampal neurotoxicity

When cortisol turns on the brain. If stress-induced cortisol secretion is not contained, persistently elevated levels become harmful, and the hippocampus is particularly vulnerable (Kaplan & Sadock 2024). High glucocorticoid levels impair cell survival, alter cell metabolism and change cell morphology; genomic and non-genomic actions of cortisol in hippocampal cells promote enzymatic processes that can lead to cell death (Kaplan & Sadock 2024). This is the glucocorticoid-cascade hypothesis: the hippocampus normally mediates negative feedback of cortisol release, so cortisol-induced hippocampal damage impairs that feedback, which permits still higher cortisol, which does further damage, a self-amplifying loop (Kaplan & Sadock 2024). It offers a mechanism for the reduced hippocampal volume repeatedly reported in chronic depression, likely related to cortisol excess (Companion 2010). The loop is not one-way and not purely destructive: reducing cortisol can reverse it, decreasing cortisol after treatment of Cushing disease reverses hippocampal atrophy (Kaplan & Sadock 2024). This links directly to the neurotrophic account, where chronic stress and cortisol suppress BDNF and neurogenesis,

developed in the neighbouring topic; the imaging principles behind the volumetric findings are cross-referenced to the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

TRAP **Do not read hippocampal volume loss as a fixed structural scar of depression.** The glucocorticoid-cascade damage is at least partly reversible: lowering cortisol (e.g. after treating Cushing disease, or with successful antidepressant treatment) can reverse hippocampal atrophy.

STRAND	THE MECHANISM / CLAIM	THE LIMITATION TO ATTACH
HPA overactivity	Hypercortisolaemia, blunted feedback, raised CSF CRH: the most consistent finding in biological psychiatry	**A state marker that normalises on recovery, not a trait or a proven cause**
Adrenal / pituitary change	Increased adrenal size and ACTH sensitivity; blunted ACTH to CRH from pituitary receptor downregulation	**End-organ correlates of central drive, not diagnostic and not specific to depression**
Subtype link	Non-suppression commoner in melancholia; hypercortisolaemia mediates features of psychotic depression	**A correlate of severity and subtype; the diagnosis stays clinical**
The 1 mg DST	Dexamethasone suppresses cortisol; non-suppression indicates impaired feedback; ~50% of depressed inpatients non-suppress	**Poor specificity (also mania, schizophrenia, dementia, weight loss); never became a clinical diagnostic test**
Combined dexamethasone/CRH test	More sensitive probe: exaggerated cortisol response despite dexamethasone	**Abnormal across bipolar, MDD, schizophrenia and PTSD, so still not a reliable diagnostic test**
Stress-diathesis / glucocorticoid cascade	Early-life adversity sensitises the HPA axis; chronic cortisol is neurotoxic to the hippocampus, a self-amplifying loop	Hippocampal damage is at least partly reversible when cortisol falls

The HPA-axis story taught mechanism-with-limitation: each strand paired with the fact that keeps it out of the clinic; the highlighted cells are the limitations the examiner tests, above all the DST's poor specificity.

MNEMONIC

HYPER: Hypercortisolaemia, feedback, Endless (state marker), Poor specificity, Early stress, Reversible hippocampus

Hypercortisolaemia with blunted feedback is the robust HPA finding in depression. **Y**ields the DST: dexamethasone normally suppresses cortisol; non-suppression means impaired feedback. **P**oor specificity: non-suppression also in mania, chronic schizophrenia and dementia, so the DST is not a diagnostic test. **E**arly-life stress sensitises the axis. **R**eversible: chronic cortisol harms the hippocampus, but lowering cortisol can reverse the atrophy.

INDIA

In Indian practice the DST is not used as a diagnostic test, consistent with the global position: it demonstrates HPA dysregulation but its poor specificity keeps it out of routine clinical diagnosis. The strong HPA signal in psychotic and melancholic depression is clinically relevant here because these are precisely the severe presentations for which ECT remains widely available and used in Indian psychiatric practice; the ECT technique itself is cross-referenced to the ECT and neurostimulation notes.

GOOD TO REMEMBER

- **HPA axis in depression:** hyperactivity is the most consistent finding in biological psychiatry: raised cortisol, blunted feedback, blunted ACTH to CRH, raised CSF CRH; a state marker that normalises on recovery (Kaplan & Sadock 2024).
- **Cortisol pattern:** loss of the evening nadir, cortisol high near sleep onset and on waking; raised cortisol predicts future depression risk.
- **Adrenal / pituitary:** increased adrenal size and ACTH sensitivity; pituitary CRH-receptor downregulation gives the blunted ACTH response.
- **Subtype link:** non-suppression commoner in melancholia; hypercortisolaemia mediates features of psychotic depression (mifepristone can help).
- **Dexamethasone suppression test:** 1 mg overnight; dexamethasone normally suppresses cortisol, non-suppression indicates impaired feedback; ~50% of depressed inpatients non-suppress; the one eponym is Carroll (1981).
- **The key limitation:** good sensitivity in melancholic/psychotic depression but poor specificity (also mania, chronic schizophrenia, dementia), so the DST never became a clinical diagnostic test.
- **Combined dexamethasone/CRH test:** more sensitive refinement (1.5 mg dexamethasone, then 100 microgram CRH infusion), but abnormal across many disorders, so still not diagnostic.
- **Stress / glucocorticoid cascade:** early-life adversity sensitises the HPA axis (CRH-hypersecretion "scar"); chronic cortisol is neurotoxic to the hippocampus in a self-amplifying loop, at least partly reversible when cortisol falls.

HOLD THIS

The DST shows HPA dysregulation (dexamethasone normally suppresses cortisol; ~50% of depressed inpatients fail to suppress) but is not a diagnostic test for depression: sensitivity is decent in melancholic and psychotic depression yet specificity is poor, because mania, chronic schizophrenia and dementia also non-suppress.

26 · Neuroplasticity, BDNF and the neurotrophic hypothesis

Why this matters. The **neurotrophic hypothesis** is the integrative model that examiners now expect after the monoamine story is punctured: it reframes depression not as a chemical deficit but as a state of impaired **neuroplasticity**, and it is the one account that offers a clean explanation for the therapeutic lag. The high-yield structure is the same discipline used across this mood-neurobiology band: state the mechanism, cite the two classes of supporting evidence (the structural imaging findings and the serum **bdnf** changes), then attach the limitations that keep it a leading but unproven account. It is also the bridge to the rapid-acting agents, because the glutamatergic/ketamine mechanism is best understood as a fast route into the very plasticity pathway this hypothesis describes.

The frame to carry: stress and glucocorticoids lower brain-derived neurotrophic factor and suppress hippocampal neurogenesis, while antidepressants, electroconvulsive therapy and exercise act downstream to raise BDNF and CREB signalling and restore plasticity, over a timescale that matches clinical recovery (Kaplan & Sadock 2024; Stahl 2021). The intracellular signalling mechanics (the Trk/CREB/mTORC cascades) and the neuroimaging principles are owned by the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the mood application is taught here.

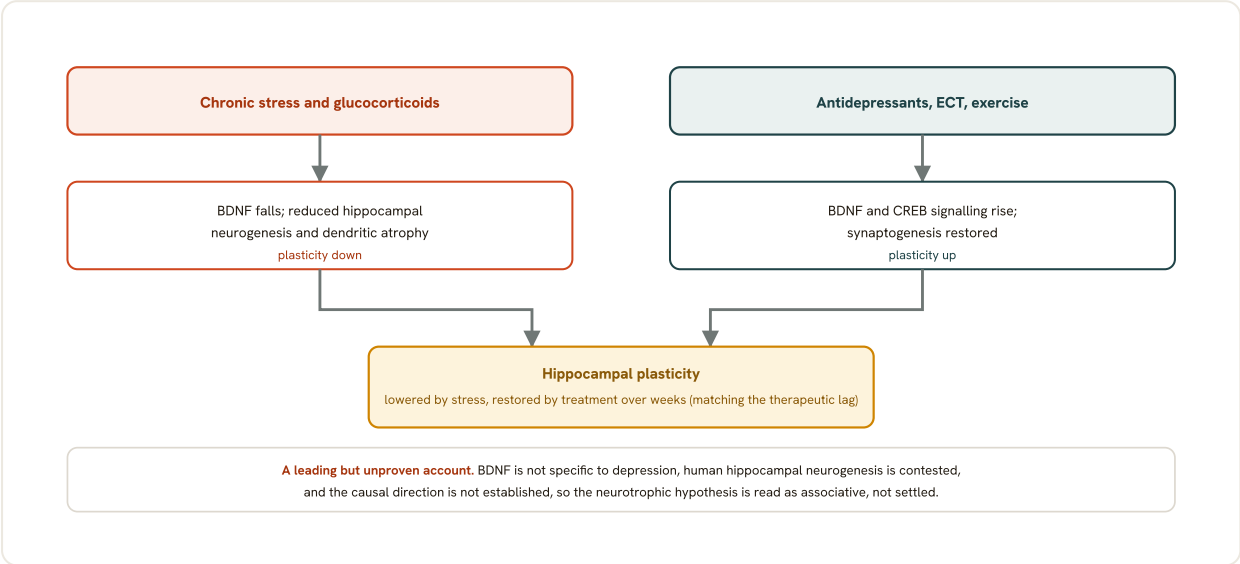


Fig 11.13 The neurotrophic hypothesis. Chronic stress and glucocorticoids lower BDNF and hippocampal neurogenesis, while antidepressants, ECT and exercise raise BDNF and CREB signalling and restore synaptogenesis; the two routes converge on hippocampal plasticity, which is reduced in depression and restored by treatment over the same weeks-long timescale as clinical improvement, which is what links it to the therapeutic lag. It is taught as a leading but associative account, not a proven cause.

26.1 The hypothesis: depression as impaired neuroplasticity

The neurotrophic hypothesis of depression proposes that stress, perhaps aided by cortisol hypersecretion, leads to atrophy and death of neurons and to downregulation of adult neurogenesis, particularly in the hippocampus (Shorter Oxford 2018, after Duman 2009). Reframed for the examiner, depression is read as a state of impaired neuroplasticity: not a bare shortage of a transmitter, but a failure to build and maintain the synaptic and cellular architecture that healthy mood regulation requires. The central molecule is BDNF (brain-derived neurotrophic factor), the best-studied neurotrophin in mood disorders, which supports neuronal maturation, survival, synaptic plasticity and the regulation of monoamine, glutamate and GABA release (Kaplan & Sadock 2024). Under chronic stress, corticotropin-releasing hormone and glucocorticoids suppress **bdnf** synthesis, and the loss of this trophic support is proposed to drive the loss of synaptic maintenance, dendritic arborisation and, in the model's strong form, neurons themselves (Kaplan & Sadock 2024; Stahl 2021). This is the plasticity story that the refined monoamine account hands over to: the monoamine change is the trigger, the neurotrophic and neuroplastic change is the proposed substrate.

RULE **The neurotrophic account links the therapeutic lag to slow plasticity change.** Stress lowers BDNF and neurogenesis; antidepressants raise them downstream over weeks, which is why mood recovers on the plasticity timescale, not the transmitter timescale.

26.2 Stress and glucocorticoids lower BDNF and suppress neurogenesis

The upstream limb is the stress-neurotrophin link. Acute and chronic stress trigger corticotropin-releasing hormone and the release of cortisol and other glucocorticoids, which, directly or indirectly, decrease the synthesis of key neurotrophic factors including BDNF (Kaplan & Sadock 2024). Prolonged glucocorticoid exposure and chronic stress suppress hippocampal neurogenesis, the generation of new neurons in the dentate gyrus, and are associated with structural change in the hippocampus in depressed humans, especially those with a history of early trauma (Kaplan & Sadock 2024). The hippocampus is the pivotal region because it is dense in glucocorticoid receptors and normally provides feedback inhibition of the HPA axis, so its trophic injury both reflects and perpetuates the stress response. The HPA-axis mechanics themselves are cross-referenced to the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the point to hold here is directional: stress and cortisol drive BDNF and neurogenesis down.

26.3 Antidepressants, ECT and exercise raise BDNF and CREB signalling

The downstream limb is the treatment-neurotrophin link, and it is where the model earns its keep. A wide range of antidepressant interventions, the tricyclics, MAOIs, SSRIs, SNRIs, noradrenaline-reuptake inhibitors and ketamine, together with non-pharmacological treatments including electroconvulsive therapy, repetitive transcranial magnetic stimulation, exercise and psychotherapy, increase BDNF (Kaplan & Sadock 2024). Mechanistically, sustained monoamine signalling initiates second-messenger cascades that phosphorylate the transcription factor CREB (cyclic-AMP response element-binding protein), which drives expression of trophic genes, raising BDNF and promoting synaptogenesis, cell survival and neurogenesis (Stahl 2021; Kaplan & Sadock 2024). Crucially these adaptive changes unfold over **weeks**, the same timescale as clinical improvement, so the neurotrophic account supplies exactly what the bare monoamine model could not: a molecular event that correlates in time with recovery. That temporal match is the whole reason the hypothesis is taught, and it is what accounts for the therapeutic lag. The deep pharmacology of the individual agents belongs to the Mood disorders: pharmacotherapy notes; the ECT technique is owned by the ECT and neurostimulation notes.

HOLD THIS

Stress and glucocorticoids lower BDNF and hippocampal neurogenesis; antidepressants, ECT and exercise raise BDNF and CREB signalling downstream over weeks, and that plasticity timescale, not the hours-fast transmitter rise, is what matches clinical recovery and explains the therapeutic lag.

26.4 The supporting evidence: imaging and serum BDNF

Two lines of human evidence built the hypothesis (Kaplan & Sadock 2024; Shorter Oxford 2018). First, structural neuroimaging: depressed patients, particularly with recurrent or chronic

illness and early trauma, show reductions consistent with the model, including hippocampal structural change and reduced pyramidal-cell and glial density on postmortem study. Second, the serum BDNF signal: peripheral BDNF levels are reduced in depressed and manic bipolar patients relative to controls, low levels track clinical severity, and successful antidepressant treatment is associated with a rise in BDNF; one study reported that an increase in serum BDNF to **126% of baseline** after a week of treatment, alongside a 50% fall in HAM-D, predicted eventual response with high specificity (Kaplan & Sadock 2024). Serum BDNF thus behaves as a state marker that moves with illness and with treatment. Read carefully, this is associative evidence: BDNF changes travel with the depressive state and its resolution, which is consistent with the hypothesis but does not by itself establish that the BDNF change causes or resolves the illness.

weeks	126%	hippocampus
PLASTICITY CHANGE, MATCHES RECOVERY	SERUM BDNF AT 1 WK PREDICTING RESPONSE	KEY REGION FOR NEUROGENESIS SUPPRESSION

26.5 The limitations: a leading but unproven account

The hypothesis is powerful but must be stated with cautious causal language, because three limitations keep it unproven (Kaplan & Sadock 2024; Shorter Oxford 2018). First, **BDNF is not specific to depression.** Low BDNF is reported across many psychiatric and neurological conditions, the correlation with depression severity and recurrence has been inconsistent, and peripheral BDNF and proBDNF have proved too mixed and inconclusive to serve as reliable diagnostic biomarkers (Kaplan & Sadock 2024). Second, **human hippocampal neurogenesis is contested.** The extent, and even the existence, of ongoing neurogenesis in the adult human hippocampus remains disputed, so a mechanism resting on suppressed and restored human neurogenesis rests on uncertain ground. Third, **the causal direction is unproven.** Reduced BDNF, smaller hippocampal volume and impaired neurogenesis are associations; whether they cause depression, result from it, or are epiphenomena of the stress state that accompanies it has not been established. The honest examination line is therefore that the neurotrophic hypothesis is a leading integrative account that unifies stress, plasticity and treatment response, but it is not a proven pathophysiology.

TRAP **Do not state reduced neurogenesis as the proven cause of depression.** BDNF is not disorder-specific, human hippocampal neurogenesis is contested, and the causal direction is unproven; the findings are associative, so keep the language of a leading but unsettled model.

26.6 The bridge to rapid-acting agents: glutamate, ketamine and synaptogenesis

The neurotrophic frame directly previews the next topic. If restoring plasticity is the therapeutic event, an agent that produces a rapid burst of synaptogenesis should act fast, and that is exactly the proposed mechanism of the rapid-acting glutamatergic antidepressants (Tasman 2015; Kaplan & Sadock 2024). The NMDA-receptor antagonist ketamine increases glutamate transmission in the prefrontal cortex, thought to occur through blockade of NMDA receptors on tonic-firing GABAergic interneurons, disinhibiting glutamate release; the glutamate burst triggers BDNF release, which activates mTORC1 signalling and drives synthesis of the proteins needed for synaptogenesis, reinstating synaptic connections within hours rather than weeks

(Tasman 2015). The same account explains selectivity at the receptor level: synaptic NMDA activation promotes BDNF synthesis and is neuroprotective, whereas extrasynaptic NMDA activation suppresses BDNF, so extrasynaptic-preferring blockers such as esketamine and ketamine support BDNF while sparing normal transmission (Kaplan & Sadock 2024). This is the plasticity hypothesis running in fast-forward, and it is where the next topic on the rapid-acting agents begins.

ELEMENT OF THE HYPOTHESIS	THE CLAIM (EVIDENCE)	THE LIMITATION TO ATTACH
Upstream (stress)	Stress and glucocorticoids lower BDNF and suppress hippocampal neurogenesis (Kaplan & Sadock 2024)	**Human hippocampal neurogenesis is contested; the structural changes are associations, not established cause**
Downstream (treatment)	Antidepressants, ECT and exercise raise BDNF and CREB signalling over weeks, matching recovery (Kaplan & Sadock 2024; Stahl 2021)	**Correlation of the BDNF rise with recovery does not prove the BDNF change is the therapeutic mechanism**
Serum BDNF marker	Peripheral BDNF falls with the depressive state and rises with successful treatment	**Not specific to depression; correlation with severity and recurrence inconsistent, unreliable as a biomarker**
Rapid-acting bridge	Ketamine drives a glutamate burst, BDNF release and mTORC1-dependent synaptogenesis within hours (Tasman 2015)	The synaptic gains destabilise with stress and relapse, so restored plasticity is necessary but not sufficient for durable recovery

The neurotrophic hypothesis taught mechanism-with-limitation: each limb paired with the fact that keeps it a leading but unproven account; highlighted cells are the limitations the examiner tests.

PEARL

The single strongest argument for the neurotrophic hypothesis is timing: BDNF and CREB-driven plasticity changes accrue over **weeks**, in lockstep with clinical improvement, which is the therapeutic lag the monoamine model could never explain. Timing is the evidence that promotes plasticity from footnote to leading account.

INDIA

Electroconvulsive therapy is one of the interventions shown to raise BDNF, and it remains widely available and heavily used in Indian practice for severe, psychotic and treatment-resistant depression, where it is often the neurostimulation option most accessible to patients (Kaplan & Sadock 2024). The technique and its indications are owned by the ECT and neurostimulation notes; the point here is only that a genuinely plasticity-enhancing treatment is in routine Indian use.

GOOD TO REMEMBER

- **Neurotrophic hypothesis:** depression as impaired neuroplasticity; stress and cortisol lower BDNF and downregulate adult hippocampal neurogenesis (Duman 2009; Shorter Oxford 2018).
- **BDNF:** the best-studied neurotrophin in mood disorders; suppressed by glucocorticoids under chronic stress; the core molecule of the whole model (Kaplan & Sadock 2024).
- **Downstream restoration:** antidepressants, ECT, rTMS and exercise raise BDNF and CREB signalling and restore plasticity over **weeks**, matching clinical recovery and accounting for the therapeutic lag.
- **Supporting evidence:** hippocampal structural reductions on imaging and serum BDNF that falls with the depressive state and rises with treatment (a rise to **126% of baseline** at 1 week predicting response).
- **The limitations:** BDNF is not specific to depression, human hippocampal neurogenesis is contested, and the causal direction is unproven; the evidence is associative, so a leading but unsettled account.
- **Rapid-acting bridge:** ketamine raises glutamate and BDNF and drives mTORC1-dependent synaptogenesis within hours, the plasticity hypothesis in fast-forward.

27 · Glutamatergic and inflammatory hypotheses

Why this matters. After the monoamine and the neurotrophic accounts, two newer mood-neurobiology models earn examiner attention because each reframes depression around a mechanism the monoamine story could not reach. The **glutamatergic hypothesis** reads depression, in part, as a disorder of glutamatergic plasticity, and it is carried by the most dramatic pharmacological fact in modern affective neuroscience: the rapid antidepressant effect of ketamine, an NMDA-receptor antagonist. The **inflammatory hypothesis** reads a subgroup of depression as immune-driven, with raised pro-inflammatory cytokines, a sickness-behaviour phenotype and a kynurenine-pathway link that ties immunity back to glutamate. The high-yield move on both is identical to the rest of this band: state the mechanism with its supporting evidence, then attach the limitation, and never generalise either model to every depressed patient.

The frame to carry: both hypotheses are convergent and partial, not settled aetiologies. Each is best supported in a subgroup, the causal direction is unproven, and the field now treats them as complementary windows on a heterogeneous illness rather than a single lesion (Kaplan & Sadock 2024; New Oxford 2020). The synaptic mechanics of the glutamate and NMDA system and the anatomy of the immune-to-brain routes are owned by the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the mood application is taught here, and the deep drug pharmacology of ketamine and esketamine is owned by the Mood disorders: pharmacotherapy notes.

27.1 The glutamatergic hypothesis: NMDA and glutamate dysregulation in depression

The **glutamatergic hypothesis** proposes that dysregulated **glutamate** signalling, and in particular altered function of the NMDA receptor, contributes to depressive pathophysiology (Kaplan & Sadock 2024). Glutamate is the principal excitatory transmitter, and excess glutamatergic stimulation is neurotoxic; glutamate binding to extrasynaptic NMDA receptors

(with the GluN2B subunit) produces excitotoxicity and suppresses BDNF synthesis, whereas activation of synaptic NMDA receptors (GluN2A subunit) promotes BDNF and is neuroprotective (Kaplan & Sadock 2024). The supporting evidence is the neuroimaging signal: magnetic resonance spectroscopy studies find altered glutamate markers in the hippocampi of chronically depressed patients versus controls, reduced glutamate in the ventromedial prefrontal cortex that correlates with illness duration, and lower anterior cingulate glutamate in both unipolar and bipolar depression, changes evident even at a first lifetime episode (Kaplan & Sadock 2024). This reframes depression, in part, as a disorder of **glutamatergic** plasticity rather than of monoamine tone alone.

PEARL

The synaptic-versus-extrasynaptic split is the mechanistic hinge: synaptic NMDA activity (GluN2A, d-serine coagonist) is neuroprotective and pro-BDNF, while extrasynaptic NMDA activity (GluN2B, glycine coagonist) is excitotoxic and suppresses BDNF (Kaplan & Sadock 2024). Chronic stress and hypercortisolaemia push glutamate transmission toward the harmful, atrophy-producing pole, tying the glutamate story to the hippocampal-volume and neurotrophic findings of the neighbouring topics.

27.2 The ketamine evidence: a rapid antidepressant via AMPA throughput and synaptogenesis

The clinical driver of the hypothesis is the striking rapid antidepressant effect of ketamine, a noncompetitive NMDA-receptor antagonist (Kaplan & Sadock 2024). Trullas and Skolnick first postulated in 1990 that reducing NMDA neurotransmission might be antidepressant; Berman and colleagues showed an antidepressant effect within 72 hours of a single subanaesthetic intravenous infusion in 2000; and Zarate and colleagues confirmed in 2006 a rapid response, with onset within **24 hours** and peak effect within **1 day**, in treatment-resistant unipolar and bipolar depression (Kaplan & Sadock 2024). The proposed mechanism is not simple receptor blockade but a downstream plasticity burst: NMDA antagonism at GABAergic inhibitory interneurons disinhibits presynaptic pyramidal neurons, producing a transient **glutamate** surge; the released glutamate drives an AMPA-receptor throughput that, via BDNF release, mTOR signalling and rapid protein synthesis, triggers **synaptogenesis** and synaptic potentiation (Kaplan & Sadock 2024). The examinable line: ketamine works through an AMPA-throughput and synaptogenesis burst, so its speed points to glutamatergic plasticity, not monoamine correction. Its intranasal S-enantiomer esketamine (Spravato) is FDA-approved for treatment-resistant depression; the dosing, adverse-effect and REMS detail is owned by the Mood disorders: pharmacotherapy notes.

RULE **Ketamine's rapid effect points to a glutamatergic mechanism beyond the monoamines.** An NMDA antagonist relieves depression within 24 hours by an AMPA-throughput and synaptogenesis burst, a timescale and mechanism the monoamine hypothesis cannot explain.

WORKED EXAMPLE

A patient with treatment-resistant depression, unimproved through serial monoamine antidepressants over months, receives a single subanaesthetic ketamine infusion and reports a clear lift in mood and a fall in suicidal ideation within a day, an effect that peaks at one day and wanes over several days without repeat dosing. The lesson the examiner wants: the response is far too fast for a monoamine mechanism and is read as evidence that acute glutamatergic plasticity (AMPA throughput, BDNF, synaptogenesis) can produce antidepressant effects, reframing depression as, in part, a disorder of glutamatergic plasticity. The pharmacology of repeat dosing and maintenance belongs to the Mood disorders: pharmacotherapy notes.

27.3 The inflammatory hypothesis: raised pro-inflammatory cytokines in a subgroup

The **inflammatory hypothesis** proposes that, in a subgroup of patients, depression is associated with a low-grade pro-inflammatory state (New Oxford 2020; Kaplan & Sadock 2024). The core finding is raised peripheral **cytokine** levels: elevated interleukin-6 (IL-6) has been reported repeatedly, alongside raised tumour necrosis factor alpha (TNF-alpha) and the downstream acute-phase marker C-reactive protein (CRP), with IL-6 rises linked to increased CRP (New Oxford 2020). Mechanistically, pro-inflammatory cytokines induce glucocorticoid resistance and promote HPA-axis hyperactivity, activate microglia to a pro-inflammatory phenotype, and amplify neuroinflammation through reactive oxygen and nitrogen species, producing sustained brain inflammation that may drive depressive-like states (New Oxford 2020). Crucially, the association holds in a subset: not all depressed patients show cytokine changes, and the elevation clusters in an inflamed subgroup rather than characterising the disorder as a whole (New Oxford 2020). This is the immune complement to the monoamine and glutamate stories, not a replacement for them.

IL-6	TNF-alpha	CRP
RAISED MOST CONSISTENTLY	RAISED PRO-INFLAMMATORY CYTOKINE	ACUTE-PHASE MARKER, SUBGROUP

27.4 Sickness behaviour and cytokine-induced depression: the interferon model

The strongest causal-direction evidence is cytokine-induced sickness behaviour and cytokine-induced depression (Kaplan & Sadock 2024; New Oxford 2020). Systemic immune activation produces **sickness behaviour**, a stereotyped state of low mood, anergia, anhedonia, anorexia, hypersomnia and social withdrawal that overlaps closely with the depressive syndrome; in humans, a low dose of endotoxin raises plasma IL-6 and TNF-alpha and lowers mood in healthy volunteers (New Oxford 2020). The clinical proof-of-principle is interferon therapy: interferon-alpha, given for hepatitis C or malignant melanoma, precipitates a depressive syndrome in a substantial proportion of treated patients, the clearest demonstration that raising a cytokine can produce depression rather than merely accompany it (Kaplan & Sadock 2024). Interferon-alpha administration also increases MRS glutamate signals and reduces presynaptic dopamine function, and its behavioural effects are attenuated by the serotonin-reuptake inhibitor paroxetine, linking the inflammatory model directly to the monoamine and glutamate systems (Kaplan & Sadock 2024).

PEARL

The interferon-alpha model is the examinable exemplar of cytokine-induced depression: a cytokine given as a licensed treatment reliably induces a depressive syndrome in a proportion of patients, which is why it is cited as the closest thing to an experimental proof that inflammation can cause, and not merely mark, depression (Kaplan & Sadock 2024).

27.5 The kynurenine pathway: the link from inflammation back to glutamate

The kynurenine pathway is the mechanistic bridge that joins the two hypotheses (New Oxford 2020; Kaplan & Sadock 2024). Pro-inflammatory cytokines, chiefly interferon-gamma and TNF-alpha, induce the enzyme indoleamine 2,3-dioxygenase (IDO), which shunts tryptophan away from serotonin synthesis and down the kynurenine pathway (New Oxford 2020). This has two consequences the examiner rewards. First, it depletes tryptophan and so limits serotonin synthesis, tying inflammation to the monoamine limb. Second, it shifts the balance of kynurenine metabolites toward the neurotoxic arm: the pro-inflammatory drive reduces the neuroprotective NMDA-antagonist metabolite kynurenic acid relative to the putatively neurotoxic metabolites 3-hydroxykynurenine and quinolinic acid, an NMDA-receptor agonist (New Oxford 2020). Because quinolinic acid is a glutamatergic NMDA agonist, inflammation feeds directly into the glutamate excitotoxicity story, and the kynurenic-acid-to-quinolinic-acid ratio correlates with hippocampal volume in mood disorders (New Oxford 2020). The kynurenine link is thus why the inflammatory and glutamatergic hypotheses are taught as one connected system.

27.6 The anti-inflammatory augmentation signal in inflamed subgroups

The therapeutic corollary is the anti-inflammatory augmentation signal, and it is instructive precisely because it is subgroup-restricted (New Oxford 2020). A proof-of-concept randomised controlled trial of infliximab, a TNF-alpha monoclonal antibody, improved symptoms specifically in treatment-resistant depression with high baseline inflammation, and the IL-6-receptor antagonist tocilizumab has been proposed on the same logic (New Oxford 2020). In bipolar depression, a meta-analysis found that anti-inflammatory drugs exert antidepressant effects and can potentiate monoaminergic antidepressants, with N-acetylcysteine showing an antidepressant and antioxidant effect (New Oxford 2020). The decisive qualifier is that positive results with anti-inflammatory agents appear restricted to the subset of patients with raised inflammatory biomarkers at baseline; they do not benefit unselected depressed patients (New Oxford 2020). The augmentation signal therefore supports the inflammatory hypothesis and simultaneously defines its boundary. The treatment-level detail of these augmentation strategies is owned by the Mood disorders: pharmacotherapy notes.

TRAP **Do not generalise the inflammatory model to every depressed patient.** Raised cytokines and anti-inflammatory response are found only in an inflamed subgroup; not all depressed patients show cytokine changes, and unselected patients do not benefit from anti-inflammatory drugs.

27.7 The limitations of both hypotheses: heterogeneity, subgroup and unproven causation

Both models share the same three limitations, and naming them is the mark of a candidate who understands the band (New Oxford 2020; Kaplan & Sadock 2024). First, heterogeneity:

depression is not a single disease, and neither glutamatergic nor immune abnormalities are uniform across patients. Second, subgroup restriction: the cytokine elevation and the anti-inflammatory response are confined to an inflamed minority, and the glutamate abnormalities are most marked in chronic and recurrent illness rather than universal. Third, causation is unproven: even the strongest evidence, the interferon model and the biomarker-stratified trials, establishes an association and a plausible mechanism, but for most patients it remains unclear whether the glutamate change or the inflammation is cause, consequence or epiphenomenon of the depressed state (New Oxford 2020; Kaplan & Sadock 2024). As with the monoamine hypothesis, each mechanism is best held as a partial window on a heterogeneous illness, taught with its limitation attached and never stated as the settled lesion.

HYPOTHESIS	THE CLAIM AND EVIDENCE	THE LIMITATION TO ATTACH
Glutamatergic	NMDA and glutamate dysregulation; MRS glutamate changes in depression; ketamine, an NMDA antagonist, gives a rapid antidepressant effect via AMPA throughput and synaptogenesis	**Glutamate changes cluster in chronic and recurrent illness; ketamine response is not universal; causation unproven**
Inflammatory	Raised IL-6, TNF-alpha and CRP in a subgroup; cytokine-induced sickness behaviour and interferon-induced depression; anti-inflammatory augmentation in inflamed patients	**Only a subgroup shows cytokine changes; unselected patients do not benefit from anti-inflammatory drugs; association not proven causal**
The shared link	Cytokines induce IDO, shunting tryptophan down the kynurenine pathway to the NMDA-agonist quinolinic acid, feeding inflammation into glutamate excitotoxicity	Connects the two models mechanistically but does not resolve whether either drives the primary illness

The two newer mood-neurobiology hypotheses taught mechanism-with-limitation, joined by the kynurenine pathway; highlighted cells are the subgroup-and-causation limitations the examiner tests.

MNEMONIC

GLUE: Glutamate plasticity, Ketamine rapid, Cytokines in a subgroup, Kynurenine link

GLutamate: depression as, in part, a disorder of glutamatergic plasticity. **K**etamine (in GlUE, the rapid arm): NMDA antagonist, rapid antidepressant via AMPA throughput and synaptogenesis. **U**nit of inflammation: raised IL-6, TNF-alpha and CRP in a subgroup only, with cytokine-induced sickness behaviour and interferon-induced depression. **E**nzyme link: cytokines induce IDO, driving the kynurenine pathway to the NMDA-agonist quinolinic acid, joining inflammation to glutamate.

INDIA

Ketamine is on the World Health Organization list of essential medicines and is widely available in Indian anaesthetic practice, which makes intravenous ketamine an accessible, low-cost option for treatment-resistant and acutely suicidal depression in Indian settings where intranasal esketamine is not routinely available; its use as an antidepressant remains off-label and specialist-supervised (Kaplan & Sadock 2024). This chapter is otherwise generic on drug detail, which belongs to the Mood disorders: pharmacotherapy notes.

HOLD THIS

Ketamine, an NMDA antagonist, produces a rapid antidepressant effect within 24 hours via an AMPA-throughput and synaptogenesis burst, reframing depression as, in part, a disorder of glutamatergic plasticity; the inflammatory hypothesis raises IL-6, TNF-alpha and CRP but only in a subgroup, and both models explain a subgroup, not all depression.

GOOD TO REMEMBER

- **Glutamatergic hypothesis:** NMDA and glutamate dysregulation in depression; supported by MRS glutamate changes; the one fact to hold is ketamine's rapid response.
- **Ketamine and esketamine:** an NMDA-receptor antagonist giving a rapid antidepressant effect (onset within **24 hours**) via an AMPA-throughput and synaptogenesis burst (BDNF, mTOR); drug detail owned by the Mood disorders: pharmacotherapy notes.
- **Inflammatory hypothesis:** raised pro-inflammatory cytokines (IL-6 most consistent, TNF-alpha, CRP) in a subgroup; the discriminating point is that it is subgroup-restricted, not universal.
- **Cytokine-induced depression:** sickness behaviour overlaps the depressive syndrome, and interferon-alpha therapy (hepatitis C, melanoma) induces depression, the clearest causal signal.
- **Kynurenine link:** cytokines induce IDO, shunting tryptophan to quinolinic acid, an NMDA agonist, joining inflammation to glutamate excitotoxicity.
- **Anti-inflammatory augmentation:** infliximab (anti-TNF) helps treatment-resistant depression with high baseline inflammation only; the signal defines its own subgroup boundary.
- **Shared limitations:** heterogeneity, only a subgroup, causation unproven; both explain a subgroup, not all depression.

28 · Genetics and gene-environment interaction in mood

Why this matters. Mood disorders are the family in which the **genetics of mood** is most examinable, because the two headline disorders sit at opposite ends of the heritability scale: bipolar disorder is one of the most heritable conditions in all of psychiatry, while major depression is only moderately heritable. The board move is to hold the two figures, to know that both are polygenic (many common variants of tiny effect, no single major gene), and to know that the strongest genetic signal for bipolar disorder is shared not with unipolar depression but with schizophrenia. On top of this genetic architecture the examiner wants one worked example of **gene-environment** interaction, the serotonin-transporter-by-stress story, taught with its controversy attached rather than as settled fact.

The frame to carry: mood disorders are complex, non-Mendelian, polygenic traits arising from the joint action of many small-effect genes in a context of environmental exposure, with the whole picture best read through a diathesis-stress lens (Shorter Oxford 2018; Kaplan & Sadock

2024). The raw descriptive definitions of the mood symptoms and the rating scales are cross-referenced to the Psychometry, Assessment and Descriptive Psychopathology notes; the HPA-axis mechanics that mediate the stress limb of gene-environment interaction are owned by the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and applied to mood in the neighbouring HPA topic.

28.1 Heritability: the concept and how it is measured

Heritability is the proportion of the variation of a trait in a population that can be attributed to variation in genetic factors (Kaplan & Sadock 2024). It is a population statistic, not an individual one: it cannot be applied to a single patient, and it varies with the population and the environmental conditions under which it is estimated (Shorter Oxford 2018). The classic tool is the twin study, which compares the concordance rate (the proportion of co-twins also affected) in monozygotic (MZ) versus dizygotic (DZ) pairs: because MZ twins share essentially all their genes and DZ twins about half, a higher MZ than DZ concordance implies a genetic contribution, and it is the *difference* in concordance, not the absolute MZ rate, that indexes heritability (Shorter Oxford 2018). Family studies (raised risk in first-degree relatives, expressed as morbid risk or expectancy rate) establish familial aggregation as a first step, and adoption studies separate the genetic from the shared-environmental component. A modest MZ concordance can still denote high heritability provided the DZ rate is much lower.

RULE **Heritability is the difference in concordance, not the MZ rate alone.** A bipolar MZ concordance near 60% with a DZ rate near 20% yields a heritability around 85%, because it is the MZ-minus-DZ gap that measures the genetic contribution.

28.2 The strong heritability of bipolar disorder

Bipolar disorder is among the most heritable of all psychiatric disorders, on a par with schizophrenia and autism (Shorter Oxford 2018; Kaplan & Sadock 2024). The concordance rate for mood disorder in the MZ co-twin of a bipolar proband is around **60%**, against only about **20%** in DZ co-twins, giving a heritability estimated at around **85%** (Bienvenu et al. 2011; Shorter Oxford 2018). The brief you must carry states the twin range for bipolar disorder as **60 to 85 percent**, reflecting the span of twin-derived estimates across studies; the widely quoted single figure is around 85% (Bienvenu et al. 2011). The same 60% MZ concordance also proves that genetics is not destiny: roughly 40% of MZ co-twins of a bipolar proband are unaffected, which means environmental (and stochastic) factors are also required (Craddock & Sklar 2013). First-degree relatives of bipolar probands carry a raised risk of both bipolar and unipolar mood disorder, and of schizoaffective disorder.

TRAP **Do not read the 60% MZ concordance as "60% genetic".** The 60% is the MZ concordance; the heritability is around 85%, and the 40% of discordant MZ pairs is precisely the evidence that environment matters.

GOOD TO REMEMBER

- **Bipolar heritability:** among the highest in psychiatry; twin estimates around **60 to 85 percent**, the headline figure around 85% (Bienvenu et al. 2011); MZ concordance ~60%, DZ ~20%.
- **The one discriminator:** bipolar disorder is far more heritable than major depression, and its molecular signal overlaps more with schizophrenia than with unipolar depression.
- **The number to hold:** ~85% (bipolar) versus 37% (major depression), both from the same twin synthesis (Bienvenu et al. 2011).

28.3 The moderate heritability of major depression

Major depression is only moderately heritable, and this contrast with bipolar disorder is a favourite examination point (Shorter Oxford 2018). Depression aggregates in families, with the risk in a first-degree relative of a proband raised about **threefold** (Sullivan et al. 2000; Shorter Oxford 2018). Twin studies confirm a genetic component, with MZ concordance around **45%** and DZ around **20%**, and the heritability of major depression has been estimated at **37%**, considerably less than that of bipolar disorder or schizophrenia (Bienvenu et al. 2011; Shorter Oxford 2018). The brief figure to carry is a moderate heritability of major depression of around **35 to 40 percent**, consistent with this 37% estimate. Two further points sharpen the picture. First, the environmental effect in depression is mediated mainly by influences specific to the individual (non-shared environment) rather than by shared family experience (Sullivan et al. 2000). Second, relatives of unipolar depressed probands do *not* show increased rates of bipolar disorder or schizoaffective disorder, which is a clean nosological asymmetry: bipolar loads for unipolar, but unipolar does not load for bipolar (Shorter Oxford 2018).

~85%	37%	threefold
BIPOLAR HERITABILITY	MAJOR DEPRESSION HERITABILITY	MDD RISK IN FIRST-DEGREE RELATIVES

GOOD TO REMEMBER

- **Major depression heritability:** moderate, around **35 to 40 percent** (estimate 37%, Bienvenu et al. 2011); MZ concordance ~45%, DZ ~20%; first-degree relative risk raised ~threefold.
- **The discriminating asymmetry:** bipolar probands raise relatives' risk of unipolar depression, but unipolar probands do not raise relatives' risk of bipolar disorder or schizoaffective disorder.
- **Environment in MDD:** acts mainly through non-shared (individual-specific) rather than shared family environment (Sullivan et al. 2000).

28.4 Familial aggregation and shared genetic loading across mood and psychotic disorders

The old Kraepelinian wall between the affective and the psychotic diatheses is genetically porous. First-degree relatives of bipolar probands carry raised risks not only of bipolar and unipolar disorder but of schizoaffective disorder, and molecular data now show that many of the risk alleles identified for bipolar disorder are also risk alleles for schizophrenia (Harrison 2016; Shorter Oxford 2018). It is striking that the molecular-genetic overlap in risk alleles is *greater* between bipolar disorder and schizophrenia than between bipolar disorder and unipolar depression (Harrison 2016). This shared loading is the genetic counterpart of the clinical spectrum and of schizoaffective disorder as an intermediate category; the mood-with-psychotic-

features and schizoaffective boundary is developed in the Other psychotic disorders, delusional syndromes and catatonia notes. The formal concept behind this cross-disorder sharing is **pleiotropy**: genes that affect multiple traits or increase risk for multiple disorders, so that many of the same genes raise the risk for schizophrenia, bipolar disorder and autism (Kaplan & Sadock 2024).

PEARL

The single most counter-intuitive genetic fact in mood disorders: bipolar disorder shares more genetic risk with schizophrenia than with unipolar depression (Harrison 2016). This is why cross-disorder GWAS repeatedly find loci that straddle the schizophrenia-bipolar border, and why the affective-psychotic dichotomy is better read as a genetic continuum than a boundary.

28.5 The molecular picture: polygenicity, GWAS loci of small effect, and polygenic risk scores

At the molecular level, mood disorders are **polygenic**: the inherited risk is conferred by hundreds, or even thousands, of genes each of small individual effect, rather than by a single major gene (Kaplan & Sadock 2024; Shorter Oxford 2018). Formally, polygenicity is a trait influenced by many genes of small individual effect (Kaplan & Sadock 2024). Early molecular strategies failed to deliver: linkage studies and candidate-gene association studies of mood disorders were largely unrevealing, positive findings proving difficult to replicate, consistent with small effect sizes and genetic heterogeneity (Shorter Oxford 2018). The breakthrough came from the genome-wide association study (GWAS), which tests SNP markers across the whole genome for association with disease in very large samples; adequately powered GWAS in tens of thousands of bipolar patients have found replicable risk loci, most famously CACNA1C, which encodes a subunit of the L-type voltage-gated calcium channel, with around ten replicated loci identified and calcium-channel signalling emerging as a candidate pathway (Harrison 2016; Shorter Oxford 2018). To aggregate this diffuse signal, the polygenic risk score (PRS) sums an individual's burden of risk alleles weighted by GWAS effect sizes, and can be used to estimate genetic liability and to test for shared risk between disorders (Kaplan & Sadock 2024). Two caveats are examinable: PRS still explains only a modest fraction of the twin heritability (the "missing heritability" gap), and current PRS suffer from a Eurocentric ancestry bias in the GWAS samples that limits their equity across populations (Kaplan & Sadock 2024).

RULE **Mood disorders are polygenic, not Mendelian.** Risk is spread across many common variants of small effect captured en masse by a polygenic risk score; there is no single "bipolar gene" or "depression gene".

TERM	DEFINITION	MOOD-DISORDER EXAMPLE
Heritability	Proportion of population trait variance attributable to genetic variation	**~85% bipolar, 37% major depression (Bienvenu et al. 2011)**
Polygenicity	A trait influenced by many genes of small individual effect	Hundreds to thousands of small-effect variants (Kaplan & Sadock 2024)
Pleiotropy	Genes that affect multiple traits or raise risk for multiple disorders	**Shared risk alleles across schizophrenia and bipolar disorder**
GWAS	Genome-wide test of SNP-marker association with disease	CACNA1C (L-type calcium channel) in bipolar disorder (Harrison 2016)
Polygenic risk score (PRS)	Weighted sum of an individual's risk alleles across the genome	Modest variance explained; Eurocentric-ancestry bias (Kaplan & Sadock 2024)

The molecular vocabulary of mood-disorder genetics, each term paired with its mood example; highlighted cells are the discriminators the examiner tests, the heritability contrast and the schizophrenia-bipolar pleiotropy.

28.6 Gene-environment interaction: the 5-HTTLPR-by-stress paradigm and its controversy

Gene-environment interaction (a genotype altering an individual's sensitivity to an environmental exposure) is examined through one paradigm case, and it must be taught with its controversy attached (Companion 2010; Kaplan & Sadock 2024). The 5-HTTLPR (the serotonin-transporter-linked polymorphic region, written 5-httlpr in some sources), a length polymorphism in the promoter (regulatory) region of the serotonin-transporter gene (SLC6A4) with a short (S) and a long (L) allele, alters transporter expression, the S allele being associated with lower expression and, it was proposed, greater environmental reactivity (Companion 2010). The landmark finding, the Caspi hypothesis, was that carriers of the short allele who were exposed to **stressful life events** or to childhood maltreatment showed a higher rate of depression than long-allele homozygotes with the same exposure, whereas in the absence of stress the genotypes did not differ (Caspi et al. 2003). This became the textbook illustration of a diathesis: the gene did not cause depression directly but moderated the depressogenic impact of adversity. The essential caveat is that later large meta-analyses questioned this specific 5-HTTLPR-by-stress interaction, several failing to replicate it (Risch et al. 2009; Munafo), so the finding is now presented as the classic but contested example rather than settled science. It is best held as the paradigm of gene-environment interaction whose specific effect remains disputed, not as an established mechanism (Companion 2010).

TRAP **Do not cite the 5-HTTLPR-by-stress interaction as settled.** Caspi et al. (2003) is the paradigm example, but later meta-analyses (Risch et al. 2009; Munafo) failed to replicate the specific interaction; state it always with its replication caveat.

WORKED EXAMPLE

Two adults suffer comparable severe life stressors in a year. On the Caspi model, the short-allele (S) carrier is at higher risk of developing a depressive episode than the long-allele (L/L) homozygote, because the S allele is proposed to raise stress-reactivity, while under low adversity the two genotypes look alike (Caspi et al. 2003). The examinable second half: when this was tested across many cohorts in meta-analysis, the specific genotype-by-stress interaction did not consistently replicate (Risch et al. 2009), so the example teaches the *principle* of gene-environment interaction and diathesis-stress, not a validated clinical predictor. No genotype should be used to counsel an individual patient about their depression risk.

28.7 Diathesis-stress and epigenetic framing

The integrating model is **diathesis-stress**: an inherited (or early-acquired) vulnerability, the diathesis, that is expressed as illness only when environmental stress exceeds the individual's capacity to cope (Companion 2010; New Oxford 2020). Individuals differ in the size of their diathesis, so a small stressor precipitates illness in the highly vulnerable while the resilient withstand large stressors; gene-environment interaction is simply the molecular instance of this model, the genotype setting the height of the vulnerability (Companion 2010). A complementary mechanism is **epigenetic**: environmental exposures, particularly early-life stress, can alter gene *expression* without changing the DNA sequence, through mechanisms such as DNA methylation and histone modification, and these changes can be stable and in some models transmitted across generations (Stahl 2021; Tasman 2015). Epigenetics thus supplies a molecular bridge between environment and the genome that helps explain how adversity leaves a durable biological trace on mood-disorder risk. Both frames answer the same examination cue: mood disorders are neither purely genetic nor purely environmental but emerge from the interplay, and the candidate who names diathesis-stress and epigenetic mediation while flagging the 5-HTTLPR replication caveat has the complete answer.

HOLD THIS

Bipolar disorder is highly heritable (twin estimates ~60 to 85%, headline ~85%) and major depression only moderately so (~35 to 40%, estimate 37%); both are polygenic, bipolar overlaps more with schizophrenia than with unipolar depression, and the 5-HTTLPR-by-stress interaction is the classic but contested example of gene-environment interaction.

INDIA

The genetic architecture of mood disorders is not population-specific in its broad form, but PRS derived from Eurocentric GWAS samples transfer poorly to South Asian and other non-European ancestries, so genetic risk prediction cannot yet be applied equitably to Indian patients (Kaplan & Sadock 2024). In routine Indian practice the practical message is unchanged: a detailed family history remains the single most useful genetic tool, and a bipolar family history in a patient presenting with depression is a red flag that should prompt screening for a past hypomanic episode before any antidepressant is started.

MNEMONIC

BIG-P: Bipolar Is Greatly heritable, Polygenic; Depression Moderate

Bipolar **I**s **G**reatly heritable (~85%), and **P**olygenic (many small-effect variants, overlapping schizophrenia); depression is only **M**oderate (~37%). The tail to append: 5-HTTLPR-by-stress is the classic gene-environment example, contested on replication.

GOOD TO REMEMBER

- **Genetics of mood, headline:** bipolar highly heritable (~60 to 85%, ~85%), major depression moderately heritable (~35 to 40%, 37%); both polygenic (Bienvenu et al. 2011; Kaplan & Sadock 2024).
- **Molecular signal:** GWAS loci of small effect, PRS aggregating them, CACNA1C the flagship bipolar locus; bipolar risk overlaps schizophrenia more than unipolar depression (Harrison 2016).
- **Gene-environment:** 5-HTTLPR short allele by stressful life events raising depression risk (Caspi et al. 2003) is the classic but contested example, later meta-analyses failing to replicate the specific interaction (Risch et al. 2009).
- **Framing:** diathesis-stress plus epigenetic mediation (methylation and histone change altering expression without changing sequence); polygenicity with gene-environment interplay is the rule.

29 · Neuroimaging and the limbic-cortical circuit model

Why this matters. The neurochemical hypotheses tell you which molecules are disturbed; **neuroimaging** tells you where in the brain the disturbance lives, and it is the bridge from a scattered list of findings to a single organising picture, the **limbic-cortical circuit model** of depression. The examinable arc is three-part and taught the same way as its neurobiology neighbours, each finding handed straight to its limitation: the structural changes (shrunken hippocampus and prefrontal cortex, white-matter hyperintensities in late-life and bipolar depression) and the functional changes (a hypoactive cognitive cortex over a hyperactive limbic core); the circuit model that ties these into a reciprocal dorsal-ventral imbalance hinged on the subgenual cingulate (the Mayberg model), which doubles as a treatment target; and the hard limitation that all of this is group-level and overlapping, never diagnostic in the single patient.

The frame to carry: imaging in mood disorder is a research and mechanistic tool, not a diagnostic test. Every finding here is a mean difference between a patient group and controls, with heavily overlapping distributions, so a scan cannot diagnose depression in the person in front of you. The imaging physics and the general anatomy of these regions are owned by the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the mood application is taught here.

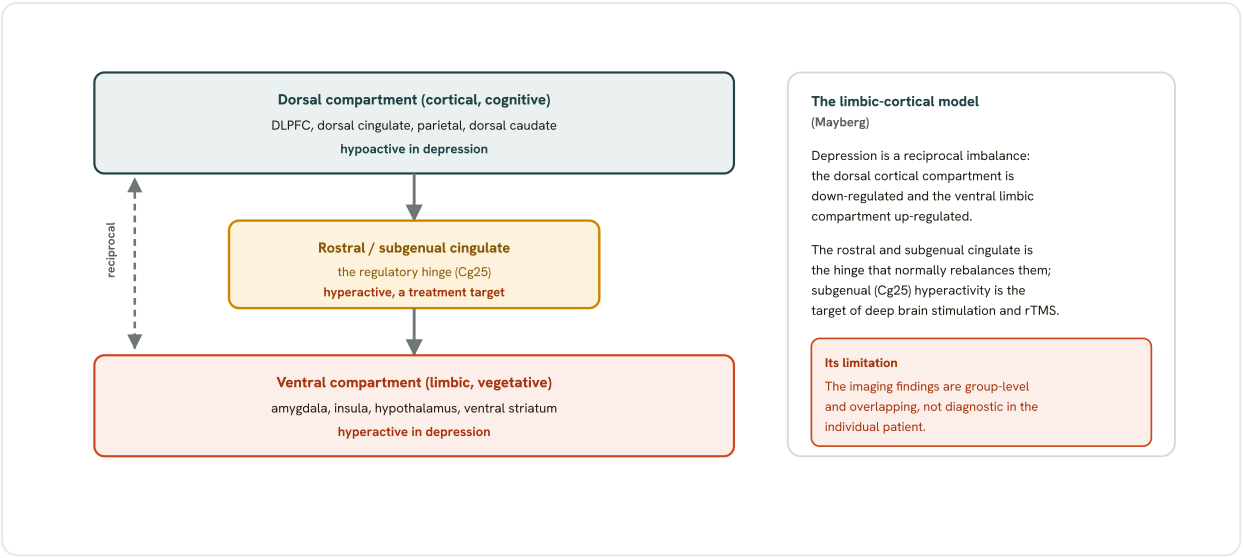


Fig 11.14 A schematic of the limbic-cortical circuit model of depression. The dorsal cortical compartment (cognitive) is down-regulated and the ventral limbic compartment (vegetative) up-regulated, and the two are reciprocally related. The rostral and subgenual cingulate is the hinge that normally rebalances them, and subgenual cingulate hyperactivity is a treatment target. The imaging findings are group-level and overlapping, not diagnostic in the individual.

29.1 Structural findings: hippocampal and prefrontal volume loss

The shrinking cortico-limbic core. Higher-resolution structural MRI documents reduced volume in a consistent set of mood-relevant regions: the hippocampus, the medial orbital cortex and the anterior cingulate (Kaplan & Sadock 2024). Morphological changes appear in both neurons and glia across the hippocampus, amygdala and prefrontal cortex (New Oxford 2020). The hippocampal signal is the most robust and carries a dose relationship: the volume reduction is directly proportional to the number and duration of depressive episodes, especially in early-onset MDD, and in several studies tracks illness chronicity such as lifetime days of untreated depression (Kaplan & Sadock 2024; New Oxford 2020). Mechanistically the loss is attributed partly to reduced glial support, to cortisol excess acting on the glucocorticoid-receptor-rich hippocampus, and to suppression of BDNF-mediated connectivity and neurogenesis, which is why this topic interlocks with the HPA and neurotrophic accounts (Kaplan & Sadock 2024; New Oxford 2020). Crucially the volume reduction is not purely a scar of chronic illness: it has been documented in younger patients in a first depressive episode and is partly heritable in primates (Kaplan & Sadock 2024).

RULE **Hippocampal volume loss in depression scales with illness burden.** The reduction is proportional to the number and duration of episodes, especially in early-onset MDD, and is linked to cortisol excess and suppressed BDNF and neurogenesis.

29.2 White-matter hyperintensities in late-life and bipolar depression

The vascular signature. A commonly observed abnormality in depressive disorders is an increased frequency of white-matter hyperintensities in subcortical regions, the periventricular white matter, the basal ganglia and the thalamus (Kaplan & Sadock 2024). These are more common in bipolar I disorder and among older adults, and they appear to reflect atherosclerotic change, illustrating the deleterious interaction of aging and recurrent affective episodes (Kaplan

& Sadock 2024). This is the imaging anchor of the vascular depression hypothesis, the proposal that cerebrovascular disease predisposes to, precipitates or perpetuates some late-life depressive syndromes, supported by the high prevalence of hyperintensities in late-onset depression and the tie between hyperintensity burden and executive dysfunction and poor antidepressant response (Kaplan & Sadock 2024). Non-specifically, ventricular enlargement, cortical atrophy and sulcal widening have also been reported in more severe recurrent affective illness (Kaplan & Sadock 2024).

GOOD TO REMEMBER

- **Hippocampal volume loss:** the most robust structural finding; proportional to episode number and duration, especially early-onset MDD; tied to cortisol and reduced BDNF/neurogenesis (Kaplan & Sadock 2024).
- **Prefrontal and cingulate volume loss:** reduced medial orbital cortex and anterior cingulate volume; morphological change in neurons and glia across hippocampus, amygdala and PFC (New Oxford 2020).
- **White-matter hyperintensities:** increased subcortical/periventricular hyperintensities, more common in bipolar I and late-life depression, reflecting atherosclerotic change; the imaging basis of the vascular depression hypothesis (Kaplan & Sadock 2024).
- **Non-specific atrophy:** ventricular enlargement, cortical atrophy and sulcal widening in severe recurrent illness (Kaplan & Sadock 2024).

29.3 Functional findings: cortical hypofunction over limbic hyperactivity

The activation pattern. PET and fMRI convert the structural picture into a functional one, and it splits cleanly. The most widely replicated PET finding in depression is decreased anterior brain metabolism, generally more pronounced on the left, with reduced cerebral blood flow and glucose metabolism in the dorsolateral prefrontal cortex that is severity-dependent and correlates with impaired executive problem-solving, reduced abstraction and difficulty inhibiting negative affect (Kaplan & Sadock 2024). This **hypofrontality** reverses in concert with the shift from depression into hypomania (Kaplan & Sadock 2024). Against this cortical hypoactivity sits limbic overactivity: increased glucose metabolism in limbic regions, particularly in severe recurrent depression with a family history, correlating with intrusive rumination, and increased metabolic activity in the amygdala that behaves as an independent dysfunction from the DLPFC hypometabolism and is reversible with effective pharmacotherapy (Kaplan & Sadock 2024). The amygdala is characteristically hyperreactive to negative stimuli, and resting-state connectivity is abnormally increased in the default-mode network (Kaplan & Sadock 2024). This dissociation, a hypoactive cognitive cortex sitting over a hyperactive limbic core, is exactly the substrate the circuit model formalises.

left > right	DLPFC down	amygdala up
ANTERIOR HYPOMETABOLISM (PET) IN DEPRESSION	SEVERITY-DEPENDENT, EXECUTIVE DEFICITS	HYPERREACTIVE TO NEGATIVE STIMULI

29.4 The limbic-cortical circuit model: the two compartments

The Mayberg synthesis. The limbic-cortical circuit model organises these findings into two reciprocally related, functionally opposed compartments (Mayberg 1997; Kaplan & Sadock

2024; New Oxford 2020). The *dorsal compartment* is cortical and cognitive: the dorsolateral and dorsal anterior cingulate cortex and the dorsomedial prefrontal cortex, the machinery of attention, executive control and the top-down regulation of affect, and it is **hypoactive** in depression. The *ventral compartment* is limbic-paralimbic and vegetative: the subgenual cingulate, amygdala, hippocampus, insula and hypothalamus, the machinery of the somatic and autonomic features of mood, and it is **hyperactive** in depression. The core proposition is a **dorsal-ventral imbalance**: the depressed state is a failure of the cortical dorsal compartment to regulate an overactive limbic ventral compartment, mapping neatly onto the imaging dissociation of hypofrontality with amygdala hyperactivity. Recovery, on this account, is a re-normalisation of the balance, with dorsal metabolism rising and ventral limbic metabolism falling.

RULE **The limbic-cortical model frames depression as a dorsal-ventral imbalance with the subgenual cingulate as the hinge.** A hypoactive dorsal (cortical, cognitive) compartment fails to regulate a hyperactive ventral (limbic, vegetative) compartment.

29.5 The subgenual anterior cingulate as the regulatory hinge

Where the two compartments meet. The rostral and subgenual anterior cingulate cortex (the subgenual cingulate, Brodmann area 25) is the pivot of the model, the node that mediates between the dorsal cognitive and ventral limbic compartments and is proposed to be the site whose modulation lets one compartment shift the other (Mayberg 1997; Kaplan & Sadock 2024). Its practical importance is that it is a treatment target. On the observation that the subgenual cingulate cortex (Brodmann area 25) is metabolically *overactive* in treatment-resistant depression, deep brain stimulation was applied to Brodmann area 25 and produced a striking and sustained remission in some previously treatment-resistant patients in an open study (Mayberg 2005; New Oxford 2020). The example makes the model concrete: subgenual cingulate hyperactivity is both the imaging hinge of the dorsal-ventral imbalance and a stimulation target for correcting it. The stimulation technique itself belongs to the ECT and neurostimulation notes; here the point is the circuit logic.

PEARL

The subgenual cingulate is examinable in two directions at once. As a *marker*, its hyperactivity indexes the ventral-limbic overactivity of the depressed state. As a *target*, its overactivity in treatment-resistant depression is what motivated deep brain stimulation of Brodmann area 25 (Mayberg 2005). One region, two exam angles: the hinge of the model and a therapeutic node. Note the honest caveat, no randomised controlled trial has confirmed the deep-brain-stimulation antidepressant effect (New Oxford 2020).

29.6 Amygdala hyperreactivity and prefrontal hypofunction: the working core

The two-node shorthand. Stripped to its examinable minimum, the functional model is a two-node imbalance: **amygdala hyperreactivity** and **prefrontal hypofunction**. The amygdala over-responds to negative and threat-related stimuli and drives the negative processing bias of depression, the skew of attention and memory towards negative material that involves the amygdala, hippocampus, anterior cingulate and PFC (New Oxford 2020; Kaplan & Sadock 2024).

The dorsolateral and dorsomedial prefrontal cortex, normally exerting top-down control over the amygdala, is hypometabolic, so the brake is weakened and the limbic response goes unregulated (Kaplan & Sadock 2024). This is the microcosm of the whole dorsal-ventral story: a hyperactive ventral node (amygdala) released from a hypoactive dorsal node (prefrontal cortex). It is also the point of contact with the neurochemistry, since reduced prefrontal top-down control and heightened limbic reactivity are how the monoamine and glutamate accounts express themselves at the circuit level.

29.7 The limitation: group-level, overlapping, not diagnostic

Why none of this is a test. The decisive limitation, and the single most examined point, is that these findings are **group-level**, overlapping and not diagnostic at the individual level. They are mean differences between patient groups and controls in case-control designs, with distributions that overlap so heavily that no structural or functional measure separates a depressed person from a healthy one reliably enough to diagnose (New Oxford 2020). Imaging studies in psychiatry have often been too small and report effect sizes potentially inflated by post-hoc statistics and publication bias, so the field prefers pooled analyses of many comparable studies to any single scan (New Oxford 2020). Attempts to build imaging classifiers that predict diagnosis or treatment response in the individual patient have used modest samples, could not be tested on a fully held-out sample, and reached within-sample accuracies of only about 60% to 70%, short of clinical use (New Oxford 2020). The conclusion is firm: neuroimaging in mood disorder is a research and mechanistic tool, not a diagnostic test, and there is no scan that diagnoses depression.

TRAP **Do not read a scan as diagnostic of depression.** The structural and functional findings are group-level mean differences with overlapping distributions; no imaging measure diagnoses depression in the individual patient.

29.8 The findings and their limitations, at a glance

Mechanism handed to its limitation. The table lays the imaging story out in the standard neurobiology format for this block: each finding paired with the qualifier that keeps it honest, and the highlighted cells are the limitations the examiner tests.

DOMAIN	THE FINDING	THE LIMITATION / QUALIFIER
Structural: hippocampus	Reduced volume, proportional to episode number and duration, especially early-onset MDD	**Also present in first-episode and partly heritable; a group mean, overlapping, not diagnostic**
Structural: prefrontal / cingulate	Reduced medial orbital cortex and anterior cingulate volume; neuronal and glial change in PFC and amygdala	**Overlapping distributions; non-specific atrophy also in severe recurrent illness**
Structural: white matter	Increased subcortical/periventricular hyperintensities, more common in bipolar I and late-life depression	**Atherosclerotic and age-related; not specific to depression, basis of the vascular hypothesis only**

DOMAIN	THE FINDING	THE LIMITATION / QUALIFIER
Functional: cortex	Decreased anterior metabolism (left > right); DLPFC hypofunction, severity-dependent	**State-dependent, reverses into hypomania; not a diagnostic signature**
Functional: limbic	Amygdala hypermetabolism/hyperreactivity to negative stimuli; increased default-mode connectivity	**Independent of DLPFC change and reversible with treatment; a correlate, not a test**
Circuit: subgenual cingulate	Subgenual cingulate (BA25) overactive in treatment-resistant depression; the dorsal-ventral hinge and a DBS target (Mayberg 2005)	Open-study benefit only; no RCT has confirmed the DBS antidepressant effect

The neuroimaging story taught mechanism-with-limitation: each finding paired with the qualifier that keeps it out of the clinic; the highlighted cells are the limitations the examiner tests, above all that no scan is diagnostic at the individual level.

MNEMONIC

DVH: Dorsal down, Ventral up, Hinge is the subgenual cingulate

Dorsal compartment (dorsolateral and dorsal cingulate, dorsomedial PFC): cortical, cognitive, top-down control, **hypoactive** in depression. **V**entral compartment (subgenual cingulate, amygdala, hippocampus, insula, hypothalamus): limbic, vegetative, **hyperactive**. **H**inge: the subgenual anterior cingulate (Brodmann area 25) is the regulatory pivot and a deep-brain-stimulation target. And over the whole picture: imaging is not diagnostic.

INDIA

In Indian practice neuroimaging in mood disorder is used to exclude organic and structural causes of a mood presentation, for example the white-matter and vascular changes of a late-life depression, not to make or confirm the diagnosis of depression, which stays clinical and is consistent with the global position that no scan is diagnostic. Structural imaging is more accessible than functional imaging (PET and research fMRI remain largely research tools), so the everyday clinical use is the structural exclusion scan, not the circuit-level functional picture taught here.

GOOD TO REMEMBER

- **Limbic-cortical circuit model:** the Mayberg model of depression as a reciprocal dorsal-ventral imbalance; the dorsal (cortical, cognitive) compartment is hypoactive, the ventral (limbic, vegetative) compartment hyperactive (Mayberg 1997).
- **Subgenual anterior cingulate:** the rostral/subgenual cingulate (Brodmann area 25) is the regulatory hinge; its hyperactivity in treatment-resistant depression is a deep-brain-stimulation target (Mayberg 2005); the one eponym is Mayberg.
- **Two-node core:** amygdala hyperreactivity to negative stimuli plus prefrontal (DLPFC) hypofunction, a released limbic node under a weakened cortical brake.
- **Structural findings:** reduced hippocampal (episode-proportional), medial orbital and anterior cingulate volume; white-matter hyperintensities in bipolar I and late-life depression (Kaplan & Sadock 2024).
- **Functional findings:** decreased anterior/DLPFC metabolism (left > right, severity-dependent), amygdala hypermetabolism, increased default-mode connectivity (Kaplan & Sadock 2024).
- **The key limitation:** all findings are group-level, overlapping and not diagnostic at the individual level; imaging is a research and mechanistic tool, not a diagnostic test for depression (New Oxford 2020).

HOLD THIS

The limbic-cortical (Mayberg) model reads depression as a dorsal-ventral imbalance: a hypoactive dorsal cortical-cognitive compartment fails to regulate a hyperactive ventral limbic-vegetative compartment, with the subgenual cingulate (BA25) as the hinge and a DBS target, but every imaging finding is group-level and overlapping, so no scan diagnoses depression in the individual patient.

30 · Psychological theories of depression

Why this matters. Alongside the monoamine, HPA and neurotrophic accounts, the examiner expects a clean map of the **psychological theories of depression**: the cognitive, the learned-helplessness and the behavioural models, with a nod to the psychodynamic and interpersonal frames. These are not merely of historical interest, because each one names the mechanism it targets and so grounds a specific psychotherapy: beck's cognitive theory grounds cognitive therapy, learned helplessness and its attributional reformulation ground the reattribution work inside it, and the behavioural theory of lost reinforcement grounds behavioural activation. The single most rewarded move is to hold each model's core construct and the treatment it justifies, and to treat the models as complementary to the biological ones rather than in competition with them.

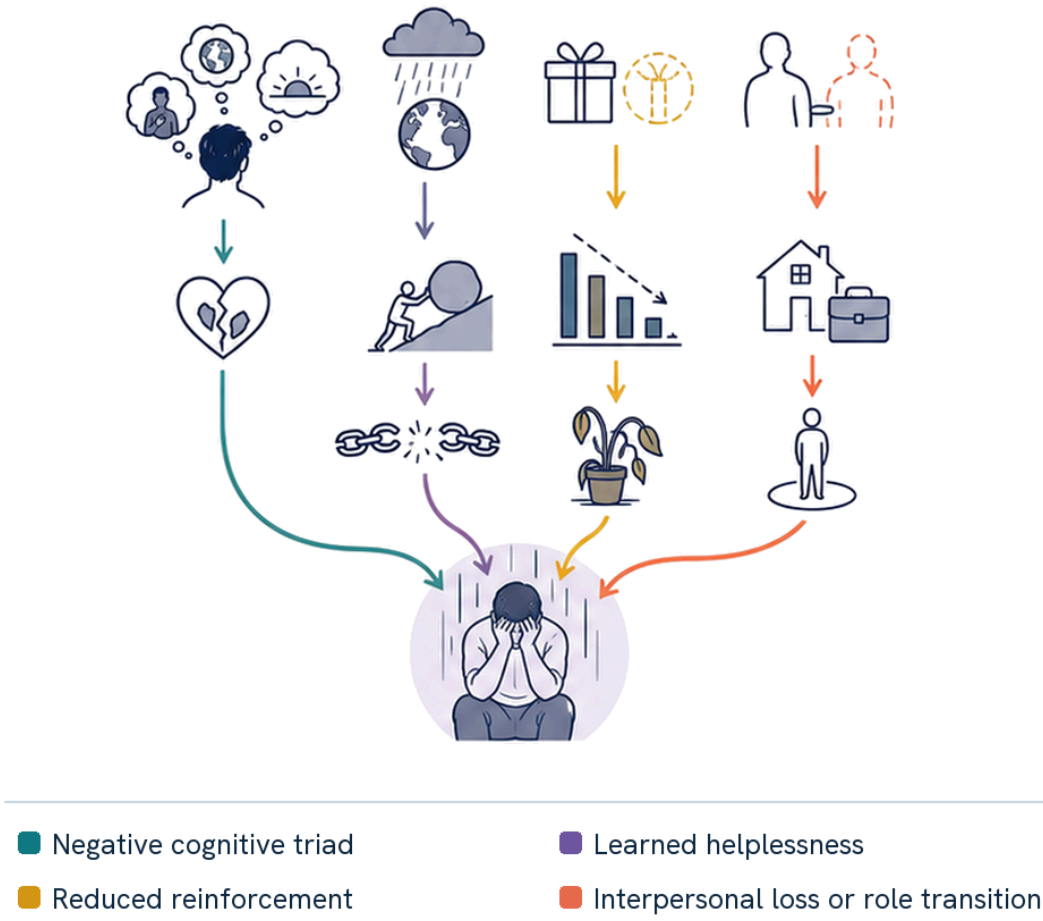


Fig 11.15 Four complementary psychological models of depression: negative beliefs about self, world and future; learned helplessness; reduced environmental reinforcement; and interpersonal loss, dispute or role transition.

This topic teaches the theories, the constructs they turn on, and the discriminating feature of each. The raw descriptive definitions of the mood symptoms and the rating scales are owned by the Psychometry, Assessment and Descriptive Psychopathology notes; the drug and neurostimulation treatments sit in the Mood disorders: pharmacotherapy notes and the ECT and neurostimulation notes; here the concern is the psychological mechanism and the psychotherapy it anchors.

30.1 Beck's cognitive theory: the cognitive triad

The central psychological model of depression is beck's cognitive theory, developed by Aaron T. Beck at the University of Pennsylvania from the late 1950s (Kaplan & Sadock 2024). Beck trained as a psychoanalyst and set out to test the psychoanalytic idea that depression was retroflected hostility; his studies did not support it, and he instead proposed that depression is associated with highly negative, distorted and dysfunctional thinking, the product of **biased information processing** rather than of unconscious drives (Kaplan & Sadock 2024). In his 1967 monograph he named the hallmark of clinical depression the cognitive triad: negatively biased

cognitions about **the self** ("I am worthless, inadequate"), **the world** and one's ongoing experience of it, including other people ("things are unfair, nothing works out"), and **the future** ("it is hopeless, nothing will change") (Kaplan & Sadock 2024; Tasman 2015). The depressed patient thinks of the self as powerless, interprets most events unfavourably in relation to the self, and believes the future to be hopeless, and this triad drives both the mood and the behaviour, with rumination on it exacerbating the symptoms and hopelessness about the future feeding suicidal ideation (Kaplan & Sadock 2024).

RULE **The cognitive triad is self, world and future, all viewed negatively.** Beck's whole model is that depression is a disorder of biased information processing, and this triad is the surface it produces.

30.2 Negative schemas and the systematic cognitive distortions

Beneath the surface triad, Beck's cognitive theory posits two deeper layers. The first is the negative schema, a hypothesised, relatively enduring mental structure that organises information and encodes the person's most central negative beliefs about the self, others and the world (Kaplan & Sadock 2024). These schemas develop in childhood out of the interaction of temperament and experience, then lie **latent** until activated by a matching stressor, at which point previously dormant dysfunctional beliefs become manifest and the person begins to see the self, the world and others through a negative lens (Kaplan & Sadock 2024). The second layer is the set of cognitive distortions, the systematic errors of logic through which the activated schema keeps confirming itself: **arbitrary inference** (a conclusion drawn without evidence), **selective abstraction** (focusing on one negative detail out of context), **overgeneralization** (a sweeping rule drawn from one event), **magnification and minimization** (over-weighting the negative, discounting the positive), **personalization** (relating external events to oneself without basis), and **dichotomous or all-or-nothing thinking** (Beck 1979; Tasman 2015). Negative automatic thoughts and these cognitive errors are demonstrably more common in depressed patients than in controls, which gives the model its empirical footing (Tasman 2015).

MNEMONIC

"A S>C: Arbitrary, Selective, Over-general, Magnify/Minimize, Personalize, Polarize."

The classic Beck cognitive distortions. Arbitrary inference (conclusion without evidence), Selective abstraction (one negative detail), Overgeneralization (one event becomes a rule), Magnification/Minimization (blow up the bad, shrink the good), Personalization (it must be about me), and dichotomous or Polarized all-or-nothing thinking. When a stem lists thinking errors and asks whose model, the answer is Beck.

30.3 How the cognitive theory grounds cognitive therapy

The reason the model earns its place is that it is directly operationalised into treatment. Because the theory locates the pathology in reversible cognitive content, cognitive therapy works by helping the patient **identify, test and modify** the biased thoughts and the schemas that generate

them: the automatic thoughts are examined against evidence, the distortions are labelled and challenged, and the therapy aims ultimately at the underlying negative schemas and the reversal of the cognitive triad (Kaplan & Sadock 2024). The first randomised controlled trial of cognitive therapy for depression (Rush et al. 1977) showed patients responding at least as well as those on pharmacotherapy and with fewer relapses, and later work confirmed efficacy in severe depression (Kaplan & Sadock 2024). The virtue of the model, and the point to state, is that it focuses on **reversible clinical dimensions**, helplessness, hopelessness and suicidal ideation, while providing a testable and practical psychotherapy.

RULE **The cognitive triad and the negative schemas are the target of cognitive therapy.** The therapy identifies, tests and modifies the biased thoughts and the schemas that generate them, aiming to reverse the triad.

The model's own limitation is worth holding: because it was built from retrospective study of already-depressed patients, it cannot prove that negative cognitions **cause** depression rather than being a symptom of it, and negative cognitions alone are unlikely to account for the sleep, appetite, autonomic and psychomotor disturbance of melancholic depression, where cognitive therapy is also less likely to succeed on its own (Kaplan & Sadock 2024). This is exactly why the psychological models are read as complementary to, not substitutes for, the biological ones.

GOOD TO REMEMBER

- **beck's cognitive theory:** depression as biased information processing; the discriminating construct is the **cognitive triad** of negative views of the self, the world and the future, underpinned by latent negative schemas and systematic cognitive distortions; the eponym to hold is **Aaron Beck** (triad described 1967), and it grounds **cognitive therapy**.
- **Negative schemas:** enduring childhood-formed mental structures holding core negative beliefs; the discriminating feature is that they lie **latent** until activated by a matching stressor.
- **Cognitive distortions:** systematic logical errors (arbitrary inference, selective abstraction, overgeneralization, magnification/minimization, personalization, dichotomous thinking) through which the schema confirms itself.

30.4 Learned helplessness and its reformulation into the hopelessness model

The second model is learned helplessness, which Kaplan and Sadock describe as, in some ways, an experimental analog of the cognitive model (Kaplan & Sadock 2024). It began with Martin Seligman's animal work in which dogs prevented from escaping inescapable shock later failed to escape even when escape became available; from the accumulation of such uncontrollable episodes Seligman postulated a learned trait, defining learned helplessness as the belief that it is futile to initiate personal action to reverse an aversive situation (Kaplan & Sadock 2024). Applied to depression, the person who has learned that their responses do not control outcomes stops trying, which maps onto the passivity, low hostility and self-blame of some depressions (Kaplan & Sadock 2024).

The original model could not explain **why** only some people who meet uncontrollable events become depressed, so it was reformulated. The human reformulation introduced attributional style, the characteristic way a person explains the causality, controllability and impact of events

(Abramson, Seligman & Teasdale 1978). People vulnerable to depression tend to explain bad events with attributions that are **internal** (personally controllable, "it is my fault"), **stable** (enduring, "it will always be so") and **global** (far-reaching, "it will affect everything") (Tasman 2015). This **depressive attributional style** was carried forward by Abramson, Metalsky and Alloy (1989) into the hopelessness model, which recast a theory-based **hopelessness depression** in which the internal, stable and global attribution for negative events, together with an expectation that desired outcomes will not occur, generates the hopelessness that is the proximal cause of the depressive symptoms (Abramson et al. 1989).

TRAP **The depressive attributional style is internal, stable and global for BAD events.** Do not swap the dimensions or attach them to good events; it is negative events explained as "my fault, permanent and pervasive" that mark vulnerability.

GOOD TO REMEMBER

- **learned helplessness (Seligman):** the belief that action is futile to change aversive circumstances, learned from uncontrollable events; the discriminating feature is the animal (inescapable-shock) origin and the resulting passivity; the eponym to hold is **Seligman**.
- **Depressive attributional style:** explaining bad events as **internal, stable and global**; this is the reformulated cognitive-vulnerability construct that marks who becomes depressed.
- **hopelessness depression (Abramson, Metalsky & Alloy 1989):** a theory-based subtype in which the depressive attributional style plus negative-outcome expectancy produces **hopelessness** as the proximal cause of symptoms.

30.5 The behavioural theory: Lewinsohn and lost reinforcement

The third model is the behavioural theory, developed by the psychologist Peter Lewinsohn and colleagues, which locates depression in a deficit of **response-contingent positive reinforcement**: depressive behaviour results from a low rate of reward that is contingent on the person's own actions (Kaplan & Sadock 2024). The rate falls for identifiable reasons, an environment that offers few rewarding opportunities, rewards delivered non-contingently (the gratis provision of undeserved rewards, which can itself lower self-esteem), or inadequate **social skills** that reduce the person's chances of eliciting reward from the environment (Kaplan & Sadock 2024). The reduced reinforcement lowers activity and mood, which further reduces engagement, closing a self-perpetuating loop. This is precisely the mechanism that grounds behavioural activation, the treatment that works by systematically re-scheduling access to rewarding, response-contingent activity to break the low-reinforcement cycle; behavioural activation is a recognised evidence-based psychotherapy for depression in its own right (Companion 2010; Kaplan & Sadock 2024). The model's own caveat is that a low rate of reinforced behaviour may in part **reflect** the psychomotor retardation of the depressive illness rather than cause it, so it too is a partial account (Kaplan & Sadock 2024).

RULE **Behavioural = lost reinforcement.** Lewinsohn's reduced response-contingent positive reinforcement is the deficit, and behavioural activation is the treatment that restores it.

GOOD TO REMEMBER

- **behavioural theory (Lewinsohn):** depression from a low rate of **response-contingent positive reinforcement**; the discriminating feature is the reward-deficit mechanism (few rewards, non-contingent rewards, poor social skills); the eponym to hold is **Lewinsohn**, and it grounds **behavioural activation**.

30.6 The psychodynamic and interpersonal frames

Two older frames complete the map. The **psychodynamic** account begins with Freud's 1917 paper Mourning and Melancholia, in which he drew attention to the resemblance between mourning and depression and argued that, just as mourning follows the death of a loved person, melancholia follows the loss of a loved **object**, which may be an actual person or an internal representation or abstraction (Freud 1917; Shorter Oxford 2018). The distinctive feature is the self-directed hostility: the depressed patient's self-reproach was read as a disguised reproach against the lost, ambivalently loved object, whose associated **hostility is turned back against the self** after the object is lost and internalised, so that depression arises where love and hostility (ambivalence) coexist (Shorter Oxford 2018). This is the classic examination phrase, depression as **loss and introjected anger**. The **interpersonal** frame, by contrast, does not commit to intrapsychic mechanism; it holds that depressive episodes arise and are maintained in the context of disturbed current relationships, grief, role disputes, role transitions and interpersonal deficits, and it grounds interpersonal psychotherapy as an evidence-based treatment (Companion 2010). Both are complementary lenses, not rivals to the cognitive and behavioural accounts.

TRAP **Do not treat the psychological models as mutually exclusive, or as rivals to the biological ones.** The cognitive, learned-helplessness, behavioural, psychodynamic and interpersonal frames are complementary, and they sit alongside the monoamine, HPA and neurotrophic accounts, not against them.

GOOD TO REMEMBER

- **Psychodynamic (Freud, Mourning and Melancholia 1917):** depression as **loss and introjected anger**; the discriminating idea is loss of an ambivalently loved object with hostility redirected against the self; the reference to hold is **Mourning and Melancholia**.
- **Interpersonal frame:** depression arising and maintained in disturbed current relationships (grief, role disputes, role transitions, interpersonal deficits); grounds interpersonal psychotherapy.

HOLD THIS

Three models, three targets, three therapies: **beck**'s **cognitive theory** (the cognitive triad of self, world and future, on negative schemas and cognitive distortions) grounds cognitive therapy; **learned helplessness** (Seligman), reformulated into the internal-stable-global depressive attributional style and the hopelessness model, grounds reattribution work; and the **behavioural theory** (Lewinsohn's lost response-contingent positive reinforcement) grounds behavioural activation, with the psychodynamic (loss and introjected anger) and interpersonal frames as complementary lenses to the biological accounts.

INDIA

Cognitive therapy and behavioural activation are the psychological treatments most widely delivered for depression in Indian practice because they are structured, manualised and briefer, which suits the high patient load of public psychiatry; the Indian Psychiatric Society clinical practice guideline for depression lists cognitive behaviour therapy, behavioural activation and interpersonal therapy among the recommended psychotherapies, and their theory bases are exactly the cognitive, behavioural and interpersonal models set out here.

Discriminate, apply and consolidate

31 · Apply: four worked vignettes

Why this matters. The mood block rewards recognition, not recitation. The examiner rarely asks "list the criteria for a hypomanic episode"; more often a short **vignette** is put in front of the candidate and the discrimination has to be made in a sentence: is this depression unipolar or bipolar, is this "depression" actually a mixed state, is this good spell a genuine hypomania, is this a melancholic or an atypical picture. This topic drills exactly that reflex. Each case is a compressed clinical scenario, then the reasoning that reads it, then the resolution, so that the criteria taught elsewhere in this chapter are exercised as they will actually be tested.

The four vignettes reuse only figures and criteria already established and verified in this chapter's own topics: the depressive-episode criteria (at least two weeks, five of nine, one cardinal), the hypomanic-episode criteria (at least four days DSM-5-TR, at least several days ICD-11, three or more DIGFAST symptoms, under the ceilings), the mixed-features rule (at least three non-overlapping opposite-pole symptoms), and the melancholic-versus-atypical split (loss of mood reactivity versus its preservation). Nosology is ICD-11 primary with DSM-5-TR cross-mapped. The deep pharmacology and the specific first-line agents are owned by the Mood disorders: pharmacotherapy notes and only pointed to here; the clinical suicide-risk assessment behind the mixed-state case belongs to the Somatic-symptom, sexual, impulse-control disorders and suicide notes.

31.1 Vignette 1: the unipolar-versus-bipolar depression screen

An atypical, recurrent depression that hides a hypomania. The single most consequential act in assessing any depressed patient is deciding which of two illnesses is in front of you, because the wrong answer means an antidepressant given alone to someone who needed a mood stabiliser (Kaplan & Sadock 2024). The reflex the examiner tests is that *every* depression is screened for a past hypomanic episode before the label major depressive disorder is written, and that the screen leads first through **behavioural activation** (distinct sustained spells of unusual energy, reduced sleep need, racing vivid thinking, over-talkativeness noticed by others) and only then anchors the mood change to those spells (Kaplan & Sadock 2024). An atypical shape to the depression, early onset, recurrence, hypersomnia, hyperphagia and leaden heaviness, is itself a soft-bipolar signal that should raise the index of suspicion (Akiskal 2007).

RULE **Screen every depression for a past hypomanic episode before diagnosing unipolar disorder.** A single lifetime hypomania moves the patient into the bipolar column for life and away from antidepressant monotherapy.

TRAP **Do not start an antidepressant alone on an unscreened recurrent depression.** The atypical, early, recurrent picture is exactly the one most likely to be latent bipolar II; a missed hypomania makes antidepressant monotherapy the wrong first move.

WORKED EXAMPLE

Case: a 24-year-old woman presents with her third episode of low mood since age 18. Each episode runs with hypersomnia (she sleeps eleven hours), a leaden, weighed-down heaviness in her limbs, and carbohydrate craving with weight gain, and her mood still lifts when close friends visit. She denies ever being "manic" and asks for an antidepressant. *Reasoning.* The reactive mood plus reverse-vegetative signs read as atypical features, which carry a recognised affinity with the bipolar spectrum, so the atypical, early, recurrent shape mandates an explicit hypomania screen (DSM-5-TR; Akiskal 2007). Asked first about behavioural activation, she recalls two distinct spells, each five to six days, of needing only four hours of sleep, redecorating her flat overnight, talking so fast that friends teased her, and feeling unusually confident, changes her sister clearly noticed, with no marked impairment, no admission and no psychosis. Count it: elevated mood plus increased activity, over four days, with decreased need for sleep, pressured speech, grandiosity and goal-directed activity, four DIGFAST symptoms, observable and under all three ceilings. *Resolution.* That is a genuine hypomanic episode; with recurrent major depression the diagnosis is bipolar type II disorder, not unipolar depression, and the reflex to start an antidepressant alone is set aside for the guideline-anchored, phase-based plan owned by the bipolar-management topic and the Mood disorders: pharmacotherapy notes.

31.2 Vignette 2: the mixed-features presentation

An agitated, insomniac "depression" with racing thoughts. The most dangerous depression to mismanage is the one carrying manic admixtures, because the reflex to reach for an antidepressant is exactly wrong (Kaplan & Sadock 2024). The DSM-5-TR **with mixed features** specifier applies when full criteria are met for a depressive episode and **at least three** non-overlapping opposite-pole (manic) symptoms are present on most days: elevated or expansive mood, grandiosity, pressured speech or talkativeness, flight of ideas or racing thoughts, increased goal-directed activity or energy, risky pleasurable involvement, and decreased need for sleep (DSM-5-TR). The counting trap sits here: irritability, distractibility, psychomotor agitation and insomnia are **shared** across both poles and are deliberately excluded from the count, so an "agitated, insomniac" label alone does not make the specifier, the discriminating symptoms are the non-overlapping ones such as racing thoughts, pressured speech and grandiosity (DSM-5-TR). Mixed features flag bipolarity, predict a worse course and a poorer lithium response, and carry a raised suicide risk from the coupling of depressive hopelessness to manic drive; the formal risk assessment is owned by the Somatic-symptom, sexual, impulse-control disorders and suicide notes.

RULE **Count only non-overlapping opposite-pole symptoms toward mixed features.** At least three of racing thoughts, pressured speech, grandiosity, elevated mood, increased activity, risky behaviour or decreased sleep need on most days; irritability, agitation, distractibility and insomnia do not count.

TRAP **Do not treat an agitated, mixed depression with an antidepressant alone.** Antidepressant monotherapy into a mixed depression can worsen the mixed and manic pole and raises the already-high suicide risk; screen every activated depression for mixed features first.

WORKED EXAMPLE

Case: a 31-year-old man is brought in with two weeks of profound low mood, hopelessness and passive death wishes, but he is agitated rather than slowed, sleeps only three hours a night, and his thoughts are "racing, too fast to hold", with pressured, over-fast speech and a fleeting sense that he could "fix everything overnight". *Reasoning.* The full depressive episode is present (low mood, hopelessness, suicidality, over two weeks). The examiner-tested move is to count only the non-overlapping manic symptoms: racing thoughts, pressured speech and the transient grandiose expansiveness are three qualifying opposite-pole symptoms, whereas his insomnia and agitation are shared symptoms and are set aside from the count (DSM-5-TR). This is a major depressive episode with mixed features, not a simple agitated depression. *Resolution.* Two consequences follow: the mixed features flag underlying bipolarity and mandate an antidepressant caution, so antidepressant monotherapy is avoided in favour of the mood-stabilising or atypical-antipsychotic-led plan owned by the bipolar-management topic; and the coupling of manic drive to depressive hopelessness raises the suicide risk sharply, so a structured safety assessment is done at once, cross-referred to the Somatic-symptom, sexual, impulse-control disorders and suicide notes.

31.3 Vignette 3: recognising a bipolar II hypomania

A productive, over-active spell without marked impairment. The bipolar II diagnosis rests on documenting a single genuine hypomanic episode that the patient rarely volunteers, because the high is ego-syntonic and often welcomed (Kaplan & Sadock 2024). The threshold is precise: the manic symptom set at a lower altitude, lasting at least **four consecutive days** under DSM-5-TR (ICD-11 asks only for at least several days), with three or more DIGFAST symptoms (four if the mood is only irritable), an unequivocal, uncharacteristic change in functioning that is **observable by others**, and, decisively, staying under the three ceilings: **without marked impairment**, without psychotic features and without any need for hospitalisation (DSM-5-TR; ICD-11 CDDR). The counter-intuitive point the examiner rewards is that *productivity without impairment* does not exclude the diagnosis, it defines it: hypomania by definition does not cause marked impairment, so a genuinely productive four-day high with observable change is a hypomanic episode, and paired with major depression it makes bipolar type II disorder.

RULE **Hypomania is at least four days, observable, and under all three ceilings.** Being productive without marked impairment is what makes it hypomania rather than mania; with a major depressive episode, that yields bipolar type II.

TRAP **Do not upgrade the spell to "mania" or dismiss it as "just feeling well".** If it broke a ceiling it is mania (bipolar I); if it was a distinct four-day observable change without impairment, it is a hypomania and must be counted, not waved away as normal good mood.

WORKED EXAMPLE

Case: a 29-year-old teacher, seen for recurrent depression, describes a distinct four-day spell last year when she slept only four hours yet felt rested, prepared a term's worth of lesson plans in two nights, was unusually talkative and confident, and started three new projects. Colleagues remarked she was "on fire". She functioned well, was never admitted, had no delusions or hallucinations, and looks back on it fondly. *Reasoning.* Elevated mood with increased activity, four consecutive days, most of the day: the duration floor is met (at least four days DSM-5-TR). Within it, decreased need for sleep, more talkative than usual, inflated confidence and a marked increase in goal-directed activity are four DIGFAST symptoms, and the change was observable by others. Crucially, the productivity ran **without marked impairment**, without admission and without psychosis, so all three ceilings are intact, which keeps the episode hypomanic rather than manic. *Resolution.* This is a genuine hypomanic episode; with her recurrent major depressive episodes and no lifetime manic episode, the diagnosis is bipolar type II disorder (F31.81 DSM-5-TR; 6A61 ICD-11). The productive, unimpaired high is not a reason to discount the diagnosis, it is the diagnosis.

31.4 Vignette 4: the melancholic-versus-atypical differential

Two depressions told apart by mood reactivity and the vegetative signs. The organising axis across the depressive subtypes is **mood reactivity**: melancholic depression loses it, atypical depression keeps it (Kaplan & Sadock 2024). Melancholic depression (DSM-5-TR: with melancholic features) requires loss of pleasure or loss of reactivity (mood does not brighten even to good events) plus **three or more** of a distinct quality of depressed mood, AM-worse diurnal variation, early-morning awakening at least **two hours** early, marked psychomotor change, anorexia or weight loss, and excessive guilt (DSM-5-TR). Atypical depression (DSM-5-TR: with atypical features) is the mirror: preserved mood reactivity plus **two or more** of hyperphagia or weight gain, hypersomnia, leaden paralysis and long-standing interpersonal rejection sensitivity (DSM-5-TR). The management implication that the examiner wants is directional, not pharmacological in detail: the melancholic, more biological picture is the one classically responsive to somatic treatment and, at its severe or psychotic end, to ECT (the technique owned by the ECT and neurostimulation notes), while the atypical picture carries the historical MAOI-responsiveness and a bipolar-spectrum affinity that should prompt a hypomania screen; the specific first-line agents belong to the Mood disorders: pharmacotherapy notes.

RULE **Mood reactivity is the pivot: melancholic loses it, atypical keeps it.** Non-reactive mood with early-morning awakening and AM-worse variation reads melancholic; a mood that still brightens with reverse-vegetative signs reads atypical and prompts a bipolar screen.

TRAP **Do not read reversed vegetative signs as "not real depression".** Hypersomnia and hyperphagia are the core of a defined subtype (atypical depression) and a soft-bipolar red flag, not evidence against a mood disorder.

WORKED EXAMPLE

Case: two depressed patients, told apart on one axis. A 52-year-old woman has three weeks of severe low mood that does not lift even when her grandchildren visit, wakes at 4 AM (about two hours early), feels worst in the mornings, is visibly slowed, has lost 5 kg and voices intense guilt about being a burden. A 28-year-old man is also depressed, but his mood still brightens when friends call, he sleeps eleven hours, eats more than usual, describes his legs as leaden and has a lifelong hypersensitivity to rejection. *Reasoning.* The first patient shows non-reactive mood plus a distinct-quality mood, early-morning awakening, AM-worse diurnal variation, psychomotor retardation, weight loss and guilt, well over the three-of-six melancholic threshold: melancholic depression. The second shows preserved mood reactivity plus two reverse-vegetative features (hypersomnia, hyperphagia) with leaden paralysis and long-standing rejection sensitivity, meeting the two-of-four atypical threshold: atypical depression. *Resolution.* The management implication diverges on the axis: the melancholic, more biological picture is the one to consider for somatic treatment and, if severe or psychotic, for ECT; the atypical picture, with its reverse-vegetative signs, is a soft-bipolar signal that mandates a screen for a past hypomanic episode before committing to any antidepressant, with the drug-level detail deferred to the Mood disorders: pharmacotherapy notes.

31.5 The four moves, side by side

Read across the four vignettes and one common architecture appears: a presenting depression, a single decisive discriminator, and a management consequence that turns on it. The grid below is the revision object, each row a worked example collapsed to its trigger, its discriminator and what it changes.

VIGNETTE	PRESENTING PICTURE	THE ONE DISCRIMINATOR	WHAT IT CHANGES
1. Unipolar vs bipolar	Atypical, early, recurrent depression, patient wants an antidepressant	**A documented past hypomanic episode on behavioural-activation screening**	Reclassifies to bipolar II; away from antidepressant monotherapy
2. Mixed features	Agitated, insomniac "depression" with racing thoughts	**At least three non-overlapping manic symptoms (racing thoughts, pressured speech, grandiosity); insomnia and agitation excluded**	Mixed-features specifier; antidepressant caution; raised suicide risk assessed
3. Bipolar II hypomania	Productive, over-active four-day spell without impairment	**Four-plus days, observable change, under all three ceilings (no marked impairment, no psychosis, no admission)**	Genuine hypomania; with recurrent MDE, bipolar type II
4. Melancholic vs atypical	Two depressions, one non-reactive, one reactive	**Mood reactivity (lost in melancholic, preserved in atypical) plus the vegetative direction**	Somatic treatment/ECT vs bipolar screen; different management axis

The four worked vignettes reduced to trigger, discriminator and management consequence; the highlighted cells are the single discriminators the examiner tests.

PEARL

Every one of the four cases turns on the same underlying vigilance: the reflex to screen a depression for hidden bipolarity. Vignette 1 finds it in a past hypomania, vignette 2 in mixed features, vignette 3 in a recognised hypomanic spell, and vignette 4 in the atypical reverse-vegetative signal. The mood block is, at heart, a single repeated question asked four ways: is there bipolarity behind this depression (Kaplan & Sadock 2024)?

HOLD THIS

Four vignettes, one spine: read the discriminator in a sentence. Past hypomania on screening makes a recurrent atypical depression bipolar II (not antidepressant-alone); three non-overlapping manic symptoms in an agitated depression make it mixed features (antidepressant caution, high suicide risk); a productive four-day observable spell under all three ceilings is a hypomania (bipolar II); and mood reactivity separates melancholic from atypical depression and sets the management axis.

GOOD TO REMEMBER

- **Move 1, screen every depression for a past hypomanic episode:** ask behavioural activation first; a single documented hypomania reclassifies a recurrent atypical depression as bipolar II and steers away from antidepressant monotherapy; hold "ever high, then bipolar."
- **Move 2, count only non-overlapping symptoms for mixed features:** at least three opposite-pole symptoms (racing thoughts, pressured speech, grandiosity, elevated mood, increased activity, risky behaviour, decreased sleep need); irritability, agitation, distractibility and insomnia do not count; hold "mixed features raise suicide risk and forbid an antidepressant alone."
- **Move 3, keep the hypomania under the three ceilings:** at least four days (DSM-5-TR) or several days (ICD-11), observable, without marked impairment, psychosis or admission; productivity without impairment defines it; hold "four days, no ceiling broken, plus an MDE = bipolar II."
- **Move 4, split melancholic from atypical on mood reactivity:** melancholic loses reactivity (distinct-quality mood, early-morning awakening at least two hours early, AM-worse variation, psychomotor change, anorexia, guilt; three of six); atypical keeps it (hyperphagia, hypersomnia, leaden paralysis, rejection sensitivity; two of four); hold "reactivity is the pivot, and the vegetative signs run down in melancholic, up in atypical."

32 · Consolidate: mnemonic, retrieval and synthesis

The chapter is long, but it hangs on one spine that the examiner rewards over and over: name the mood **episode** first, split on **polarity**, then let the lifetime pattern name the disorder, and treat by **phase**. **Chain, do not list.** This topic closes the loop by turning the whole chapter into one memorable chain, a set of answer-free recall prompts, and a single map you can redraw on scrap paper before you walk into the hall.

Everything here is a compression of what the earlier topics taught in full. The raw descriptive definitions of the mood symptoms and the rating scales sit in the Psychometry, Assessment and Descriptive Psychopathology notes; the deep drug pharmacology and treatment-resistant algorithms sit in the Mood disorders: pharmacotherapy notes; the HPA-axis mechanics and monoamine pathway anatomy sit in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes. Consolidation does not re-teach them; it wires them together.

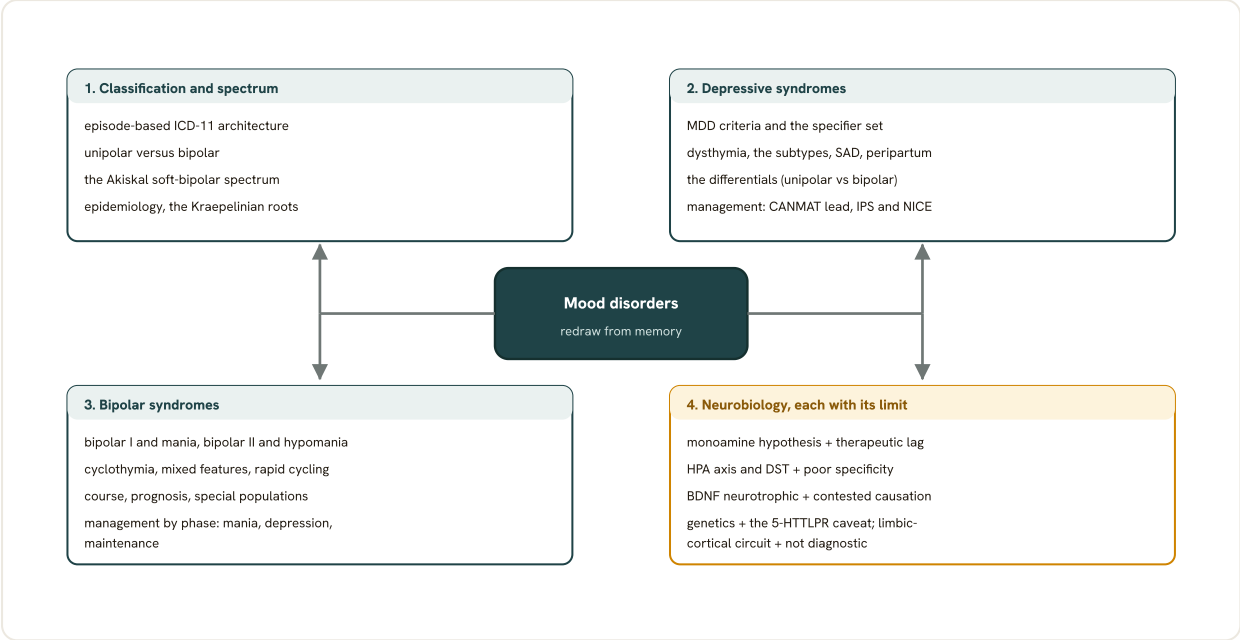


Fig 11.16 The whole-chapter synthesis map, to redraw from memory. Four branches hang off the mood-disorder core: the classification and the Akiskal spectrum; the depressive syndromes and their management; the bipolar syndromes and their phase-based management; and the neurobiology, where every hypothesis is held together with its limitation. Cover the branches and rebuild them.

32.1 The master mnemonic: one chain for the whole chapter

This is the pay-off of the Step-2 seed. The seed gave you the skeleton ("EPISODE first, then POLARITY; CLASSIFY, DEPRESS, then BIPOLAR; MANAGE by phase; MECHANISM with its limit"); here every letter is unpacked into the actual content, band by band, so that reciting the chain walks you through the entire chapter in order. Say it aloud until the branches fall out of the acronym without effort.

MNEMONIC

"EPISODE, then POLARITY → CLASSIFY · DEPRESS · BIPOLAR · MANAGE by phase · MECHANISM with its LIMIT"

Recite the chain as five linked bands, unpacking every letter.

EPISODE, then POLARITY (the two-beat core). **E**pisode: name the mood episode and check its threshold first, depressive (at least **two weeks**, five of nine, one cardinal symptom), manic (at least **one week** or any duration if hospitalised, the mood-and-energy gate, three DIGFAST or four if irritable-only), hypomanic (at least **four days**, same set, no marked impairment, no psychosis, no admission), or mixed (three non-overlapping opposite-pole symptoms). **P**olarity: split on the one question, has there ever been a hypomanic or manic episode; unipolar means depressions only, one lifetime hypomania or mania fixes bipolar for life.

CLASSIFY (band 1, the classification and the spectrum). **C**lassify the family episode-based, not by snapshot: ICD-11 primary, DSM-5-TR cross-mapped, ICD-10 flagged where exams still use it; the Kraepelinian dichotomy underneath. **L**adder the Akiskal soft-bipolar Akiskal spectrum before you enter type I: one-half (schizobipolar), I (mania), one-and-a-half (protracted hypomania), II (spontaneous hypomania with depression), two-and-a-half (cyclothymic depressions), III (antidepressant-mobilised hypomania), three-and-a-half (substance-linked bipolarity), IV (depression on a hyperthymic temperament); a heuristic for vigilance, not a coded nosology.

DEPRESS (band 2, the depressive syndromes and their management). **D**epressive episode and major depressive disorder, single versus recurrent. **E**ndophenotype specifiers: melancholic (loses mood reactivity), atypical (keeps reactivity, hyperphagia, hypersomnia, leaden paralysis, rejection sensitivity), psychotic (mood-congruent delusions), catatonic, peripartum, seasonal, anxious distress, mixed features. **P**ersistent depressive disorder (dysthymia, at least two years) and double depression. **R**eproductive and rhythm forms: premenstrual dysphoric disorder (prospective daily rating over two cycles), peripartum depression, seasonal affective disorder. **M**anage guideline-first (CANMAT lead): first-line a second-generation antidepressant or evidence-based psychotherapy, continuation 6 to 9 months after remission.

BIPOLAR (band 3, the bipolar syndromes and their management). **B**ipolar I (one manic episode ever). **I**I (a hypomanic plus a major depressive episode, never a manic one). **C**yclothymia (at least two years sub-threshold). **M**ixed features and **R**apid cycling (four or more episodes in twelve months). **P**hase-based management (CANMAT lead): acute mania stop the antidepressant and give lithium, valproate or an atypical; bipolar depression give quetiapine, lurasidone or lamotrigine (never an antidepressant alone); maintenance lithium leads.

MECHANISM with its LIMIT (band 4, the neurobiology, each hypothesis with its caveat). **M**onoamine, limited by the therapeutic lag (transmitters rise in hours, mood recovers over weeks). **E**ndocrine HPA and the dexamethasone suppression test, limited by poor specificity (mania, schizophrenia, dementia also non-suppress). **N**eurotrophic BDNF and neurogenesis, limited to a plasticity timescale that matches recovery, not a proven lesion. **G**ene-environment (the 5-HTTLPR-by-stress finding), limited by the replication controversy. Glutamate and inflammation each explain a subgroup only; the circuit (Mayberg dorsal-ventral, subgenual BA25) is group-level and diagnoses no individual.

RULE **Recite the chain, then hang the content on it.** The acronym is only a coat-hook: EPISODE and POLARITY are the two-beat core, then the four branches (classify, depress, bipolar, mechanism-with-limit) unpack in the fixed order the chapter taught.

TRAP **Do not stop at reciting letters.** A mnemonic you cannot unpack is worthless in the viva; if you can say "MENG" but cannot pair each hypothesis with its limitation, you have memorised a sound, not the neurobiology.

32.2 Retrieval practice, cover the answers

Reading is recognition; the exam is recall. The single most powerful study move at this stage is **active recall** under self-testing: **retrieval practice** forces the memory trace to reconstruct itself, which strengthens it far more than re-reading. Work the prompts below with the answers hidden, produce the full answer from memory, then check against the earlier topics. Do not peek; the effort of the failed retrieval is where the learning happens.

RETRIEVAL PRACTICE, COVER THE ANSWERS

Twelve to fifteen answer-free prompts across the five bands. Cover the answers, say each answer aloud in full, then verify against the topic it came from. The answers are deliberately not printed.

1. State the full depressive-episode criteria: duration, the number of symptoms, and the cardinal-symptom rule.
2. Give the manic-episode gate and the DIGFAST threshold, including the change when the mood is irritable only.
3. Define hypomania and list the three features whose presence would instead make the episode manic.
4. Name the single question that separates unipolar from bipolar, and why it must be asked of every depression.
5. Lay out the Akiskal soft-bipolar spectrum from one-half to IV, giving the one-line descriptor for each numbered type.
6. Contrast melancholic and atypical depression on the mood-reactivity discriminator and list two further features of each.
7. Define persistent depressive disorder by its duration rule and state what "double depression" means.
8. Give the diagnostic requirements for premenstrual dysphoric disorder, including the confirmation method and the symptom count.
9. Distinguish bipolar I from bipolar II by the one episode each absolutely requires and each absolutely excludes.
10. Define mixed features and rapid cycling, with the exact number in each definition.
11. For depression management, name the CANMAT first-line options and the continuation duration after remission, then state the Indian Psychiatric Society and NICE positions.
12. For bipolar management, give the phase-by-phase first-line choice for acute mania, bipolar depression and maintenance, and name the one agent never used alone in bipolar depression.
13. State the monoamine hypothesis and its single defining limitation.
14. State what the dexamethasone suppression test shows, the approximate non-suppression figure in depressed inpatients, and why it is not a diagnostic test.
15. Name the neurotrophic (BDNF) and the gene-environment (5-HTTLPR) hypotheses, each with the caveat that stops it being read as settled.

RULE **Test, do not re-read.** One cycle of answer-free retrieval practice beats three re-readings of the same page; schedule the prompts, do not just skim them.

32.3 The synthesis map to redraw from memory

The last consolidation move is spatial. Close the notes and draw the whole-chapter **synthesis map** from a blank centre labelled "Mood disorders", with four branches you **redraw from memory**: branch one, classification and the spectrum (the episode-then-polarity spine, the Kraepelinian dichotomy, ICD-11 versus DSM-5-TR, and the Akiskal ladder from one-half to IV); branch two, the depressive syndromes (major depressive disorder single and recurrent, the

specifiers, dysthymia and double depression, and the reproductive and seasonal forms); branch three, the bipolar syndromes (type I, type II, cyclothymia, mixed features and rapid cycling), each hung on its phase-based management; and branch four, the neurobiology, where you must write each hypothesis (monoamine, HPA and the dexamethasone suppression test, neurotrophic BDNF, gene-environment, glutamate and inflammation, the Mayberg circuit) paired with its own limitation, because a mechanism without its caveat is an exam error. If you can redraw all four branches with the management folded into the two clinical branches and every mechanism carrying its limit, the chapter is consolidated. This is Fig 11.12.

HOLD THIS

The whole chapter is one chain: name the EPISODE, split on POLARITY, then CLASSIFY, work the DEPRESSive then the BIPOLAR syndromes with their phase-based management, and finish on the neurobiology with every MECHANISM held to its LIMIT.

GOOD TO REMEMBER

- **The master chain:** "EPISODE, then POLARITY; CLASSIFY, DEPRESS, BIPOLAR; MANAGE by phase; MECHANISM with its LIMIT" is the whole chapter in one line; episode-then-polarity is the two-beat core.
- **Active recall:** retrieval practice with the answers covered strengthens memory far more than re-reading; the failed-retrieval effort is the learning.
- **The synthesis map:** four branches to redraw from memory, classification and spectrum, depressive syndromes, bipolar syndromes, neurobiology, with management folded into the clinical branches and each mechanism paired with its limitation (Fig 11.16).
- **The one discriminator:** a past hypomanic or manic episode is the single feature that reorders the entire grid from unipolar to bipolar; screen it in every depression.
- **The one management rule:** phase decides the drug, and an antidepressant is never given alone in a bipolar or mixed depression (CANMAT lead, with the Indian Psychiatric Society IPS guidelines and NICE concordant on stepped care).

Previously asked

The mood block is examined heavily and across the whole range: long diagnose-and-manage essays on major depression and on the bipolar disorders, a recurring interest in the bipolar spectrum and its soft forms, and a steady stream of short notes on the individual syndromes. The single most reliable long question is a full case of depression or of bipolar disorder taken from clinical features through differential diagnosis to management, so the criteria, the discriminators and the guideline-anchored plan in these notes are built to answer it. The genuine questions on record are grouped by band below. The individual drug pharmacology that several management questions also reward is developed in the Mood disorders: pharmacotherapy notes.

? HOW THIS TERRITORY IS ACTUALLY TESTED

Q **Classification and the bipolar spectrum.** The spectrum is a favourite: "bipolar spectrum disorder" has been asked as a 10-mark note, and the concept has twice carried a full 25-mark essay, once as "recent research in bipolar spectrum disorders with emphasis on soft bipolar disorders" and once as "the conceptual overview of bipolar spectrum disorder" paired with the management of treatment-refractory

bipolar II. Prepare the episode-based classification, the unipolar-versus-bipolar distinction and the detailed Akiskal soft-bipolar spectrum to be defined and drawn, and to open a bipolar essay. essay and short note, recurring

Q **Depressive syndromes.** "Define depressive disorder, describe the epidemiology of mood disorders, manage a case and add a note on suicide prevention" and "discuss the etiopathogenesis, clinical features and management of major depression" are the flagship 25-mark essays, so the depressive-episode criteria, the epidemiology and the subtypes must be exam-ready. "Dysthymia" has been asked as a 10-mark note, and the premenstrual and postpartum presentations recur as short notes. Prepare the criteria and specifiers, the subtypes keyed on their discriminators, and the guideline-anchored management. essay and short note, recurring

Q **Bipolar syndromes.** "Describe the clinical features and management of the various types of bipolar disorder" and "the clinical features, differential diagnosis and management of bipolar depression" are recurring 25-mark essays, and "the differential diagnosis and management of a patient with substance use and symptoms of mania" tests the manic differential. "Cyclothymia" and "rapid cycling bipolar disorder" are 10-mark notes. Prepare bipolar I and the manic episode, bipolar II and the hypomania threshold, mixed features, and the interleaved differential. essay and short note, recurring

Q **Management, guidelines-first.** Every long mood question ends in management, and "treatment of refractory mania", "the management of treatment-resistant depression" and "the management of resistant depression" have come as standalone questions. Prepare the CANMAT-led, phase-based plan for depression and for acute mania, bipolar depression and maintenance, and be able to state the Indian Psychiatric Society and NICE positions; the individual agents and the treatment-resistant algorithms are developed in the Mood disorders: pharmacotherapy notes. essay and short note, recurring

Q **Neurobiology and aetiology.** The etiopathogenesis of major depression is asked inside the long essay, and the monoamine and stress systems recur through the basic-science papers. Prepare the monoamine hypothesis with its limitations, the HPA axis and the dexamethasone suppression test, and the neurotrophic and circuit models, each with its evidence and its caveat, to supply the aetiology half of a depression or bipolar essay. essay component, recurring

Prepare this material to be defined, discriminated and managed, not just recited: the episode-based classification and the Akiskal spectrum, the criteria-anchored good-to-remember boxes, the interleaved differential and the guideline-anchored management topics in these notes are built to the way the block is examined. The individual drug pharmacology, the newer antidepressants and the treatment-resistant algorithms live in the Mood disorders: pharmacotherapy notes; the mood-with-psychotic-features boundary and catatonia live in the Other psychotic disorders, delusional syndromes and catatonia notes; the wider perinatal frame lives in the Perinatal/women's mental health and emergency psychiatry notes; and clinical suicide risk assessment lives in the Somatic-symptom, sexual, impulse-control disorders and suicide notes.

Quick review

The whole subject in one table	
CLASSIFICATION	ICD-11 is episode-based: name the mood episode (depressive, manic, mixed, hypomanic), split on polarity (any lifetime manic or hypomanic episode makes it bipolar for life), then the lifetime pattern names the disorder. Qualify the current episode with severity and psychotic-symptom and specifier layers. ICD-11 primary, DSM-5-TR cross-mapped, ICD-10 (F-codes) still used in Indian settings.
ICD-11 CHANGES	Episode-based architecture; the mixed presentation is a qualifier on an episode (DSM-5-TR "with mixed features", at least three opposite-pole symptoms), never a free-standing disorder; ICD-11 retains a mixed episode, DSM-5 deleted it. Severity (mild/moderate/severe) and the without/with psychotic symptoms qualifier are now separate, so psychosis no longer forces a severe rating as it did in ICD-10.
UNIPOLAR VS BIPOLAR; AKISKAL	Unipolar has depressive episodes only; one lifetime manic or hypomanic episode makes it bipolar. Bipolar depression: earlier onset, more recurrent with shorter episodes, retarded and hypersomnic, antidepressant switch risk. Akiskal's soft spectrum (bipolar one-half through IV) shows bipolarity shading into apparent unipolar depression; screen every depression for a past hypomanic episode. Only bipolar I, II and cyclothymia are formal categories.
EPIDEMIOLOGY	Major depression: high lifetime prevalence, roughly two-to-one female preponderance, onset in the twenties to thirties. Bipolar I around one percent, roughly equal sex ratio, earlier onset (late teens to twenties). Both are leading causes of disability with elevated suicide and cardiometabolic mortality. Quote Indian NMHS figures, not Western ones.
MAJOR DEPRESSIVE DISORDER	At least two weeks, five or more of nine symptoms including a cardinal one (depressed mood or anhedonia), plus impairment. Nine symptoms across cardinal, cognitive (guilt, concentration, death/suicidality) and neurovegetative (sleep, appetite/weight, psychomotor, energy) clusters. Specifiers: melancholic, atypical, psychotic, catatonic, peripartum, seasonal, anxious distress, mixed features. Suicide is the key risk.
DYSTHYMIA AND SUBTYPES	Persistent depressive disorder: chronic low mood at least two years (one in youth); double depression is a major episode on top. Subtypes keyed by mood reactivity: melancholic loses it (early waking, anorexia, morning worsening), atypical keeps it (hypersomnia, hyperphagia, leaden paralysis, rejection sensitivity), psychotic adds mood-congruent delusions, catatonic adds catatonic signs.
SAD, PERIPARTUM, PMDD	Seasonal affective disorder: recurrent episodes with a regular seasonal onset and remission, often atypical, light therapy first-line. Peripartum depression: onset in pregnancy or within four weeks

The whole subject in one table	
	of delivery; screen with the Edinburgh scale; sertraline preferred in breastfeeding (CANMAT), ECT for severe or psychotic. PMDD: luteal-phase symptoms confirmed by prospective rating, SSRI first-line.
DEPRESSION MANAGEMENT	Guideline-first on locus (outpatient default; admit for suicide risk, psychosis, severe self-neglect or ECT), focus (acute aim remission; continuation 6 to 9 months at the acute dose; maintenance 2 years or more if recurrent) and modus. CANMAT first-line: a second-generation antidepressant or CBT/IPT/behavioural activation, combination superior; do not combine two antidepressants at initiation. rTMS/iTBS first-line, ECT for severe/psychotic/resistant. IPS names SSRIs first-line (Gautam 2017); psychotic depression needs antidepressant plus antipsychotic, or ECT.
BIPOLAR I AND THE MANIC EPISODE	One manic episode ever defines bipolar I. Manic episode: elevated, expansive or irritable mood plus increased activity or energy, at least one week (or any duration if hospitalised), with three or more DIGFAST symptoms (four if only irritable), marked impairment, sometimes psychosis. Over the lifetime more time is spent depressed than manic.
BIPOLAR II AND HYPOMANIA	A hypomanic episode plus a major depressive episode, no manic episode ever. Hypomania: at least four days (several days ICD-11), an observable change, but without marked impairment, without psychosis and without hospitalisation. Any of those three makes it a mania. Never diagnose bipolar II without a documented hypomanic episode.
CYCLOTHYMIA, MIXED, RAPID CYCLING	Cyclothymia: at least two years of sub-threshold highs and lows. Mixed features: at least three opposite-pole symptoms in one episode, a qualifier, high suicide risk, antidepressant caution (dysphoric mania, agitated depression). Rapid cycling: four or more episodes of any polarity in twelve months, commoner in women and bipolar II, driven by antidepressants and hypothyroidism; withdraw the antidepressant.
BIPOLAR COURSE AND POPULATIONS	Recurrent and lifelong with inter-episode recovery but residual sub-syndromal and cognitive impairment; mixed and rapid-cycling course predict worse outcome; high suicide and cardiometabolic mortality. Special populations: require clear episodicity before diagnosing paediatric bipolar (versus DMDD), exclude an organic or vascular cause in new late-life mania, and manage the high postpartum relapse risk (avoid valproate in women of childbearing potential).
BIPOLAR MANAGEMENT	By phase (CANMAT/ISBD 2018). Acute mania: stop any antidepressant; first-line lithium, quetiapine, divalproex, asenapine, aripiprazole, paliperidone, risperidone or cariprazine, or an atypical plus lithium/divalproex if severe; lithium acute level 0.8 to 1.2. Bipolar depression: quetiapine, lurasidone, lithium or lamotrigine, never an antidepressant alone. Maintenance: lithium leads (level 0.6 to 1.0),

The whole subject in one table	
	plus psychoeducation, LAI if non-adherent. IPS (Shah 2017) and NICE broadly agree.
THE MOOD DIFFERENTIAL	Polarity (a past hypomania or mania) is the master discriminator: screen every depression. MDD versus persistent depressive disorder versus adjustment by duration and threshold and stressor. Melancholic versus atypical by mood reactivity. Bipolar I versus II versus cyclothymia by mania versus hypomania versus sub-threshold. Mixed features versus an agitated depression by the count of opposite-pole symptoms.
NEUROBIOLOGY: MONOAMINE AND HPA	Monoamine hypothesis: a functional deficiency of serotonin, noradrenaline and dopamine; the therapeutic lag and the failure of depletion to depress healthy controls are the key limitations, so it is the trigger for slower plasticity changes. HPA axis overactive with blunted feedback; the dexamethasone suppression test shows non-suppression (fair sensitivity in melancholic/psychotic depression, poor specificity), so it is not a clinical diagnostic test.
NEUROBIOLOGY: PLASTICITY, GENES, CIRCUITS	Neurotrophic hypothesis: stress lowers BDNF and hippocampal neurogenesis, antidepressants and ECT restore them over weeks (matching the lag), but the evidence is associative. Glutamate/NMDA (rapid ketamine effect) and inflammation (raised cytokines) explain a subgroup. Bipolar is highly heritable (roughly 60 to 85 percent), depression moderately (35 to 40 percent), polygenic; the 5-HTTLPR by stress interaction is the classic but contested example. Limbic-cortical model: dorsal-cortical hypoactive, ventral-limbic hyperactive, subgenual cingulate the hinge, not diagnostic. Psychological: Beck's cognitive triad, learned helplessness and hopelessness, Lewinsohn's lost reinforcement.

References

The content is grounded in the standard clinical, psychopharmacology and guideline sources (the source hierarchy below), which anchor the settled facts on the criteria, the syndromes and the neurobiology; the nosology follows ICD-11 (CDDR) primary with DSM-5-TR cross-mapped, and the management is guideline-first (CANMAT leading, with the Indian Psychiatric Society and the British Association for Psychopharmacology). Every diagnostic criterion, duration threshold, epidemiological number, mechanism-with-its-limitation and guideline recommendation has been checked against these sources. Each journal PMID here was verified against PubMed this build, matched on title, first author and year; any identifier that did not resolve to the cited paper was corrected or dropped rather than guessed. The classic conceptual sources that seed the models (Kraepelin, Leonhard, Beck 1967, Freud's Mourning and Melancholia 1917, Abramson, Seligman and Teasdale 1978, Lewinsohn, and Mayberg's limbic-cortical model) are cited in the prose by author and year.

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PART V

V

Mood Disorders: Pharmacotherapy, Antidepressants, Mood Stabilisers, Lithium

Treating mood disorder: the antidepressants, the mood stabilisers, and lithium, with the rules for using each.

01 Antidepressant pharmacotherapy

02 Mood stabilisers and lithium

03 Treatment resistance, augmentation and special populations

04 Apply and consolidate

PAPER II

Mood disorders: pharmacotherapy

Four sections · one complete notes document

This material closes the mood block, gathering into one document the drug treatment of the depressive and bipolar disorders. The first band is **antidepressant pharmacotherapy**: the classification of the antidepressants and the action of each class at the synapse, the SSRIs, SNRIs, tricyclics, monoamine oxidase inhibitors, mirtazapine, bupropion and the newer multimodal agents with their pharmacology, adverse effects and interactions, serotonin syndrome and the discontinuation syndrome, the rapid-acting glutamatergic agents ketamine and esketamine, and how to choose an antidepressant and manage the phases of an acute depressive episode. The second band is **mood stabilisers and lithium**: lithium in depth, its mechanism, initiation, dosing, monitoring, toxicity and every organ-system effect and interaction and its use in pregnancy, then valproate, carbamazepine, lamotrigine and the antipsychotics used as mood stabilisers, and the guideline-anchored choice of stabiliser across acute mania and maintenance. The third band is **treatment resistance, augmentation and the special populations**: treatment-resistant depression and its staging, the augmentation ladder, depression in the elderly, the suicide-risk and pharmacological angle, ECT and neuromodulation and the psychotherapies in the algorithm, and the dedicated management of bipolar depression, bipolar mixed episodes and bipolar maintenance. The examinable skill is the safe, guideline-anchored choice and monitoring of every mood drug: which agent for which patient and phase, at what dose and serum level, with which adverse effect and interaction watched, and when to escalate.

HOW TO USE THESE NOTES

Read the four bands as one continuous account of how mood disorder is treated with medicines. The **antidepressant** band teaches each class at the synapse and then every agent with its dose range, its signature adverse effect and its key interaction, ending with how to choose and how to run the phases of treatment. The **mood stabiliser** band gives lithium the depth it carries in the examination, its therapeutic window, its monitoring schedule, its toxicity and its organ effects, then valproate, carbamazepine, lamotrigine and the atypicals, and the guideline choice of stabiliser by phase. The **treatment resistance** band teaches the augmentation ladder and the special populations and closes with three dedicated bipolar-management topics: bipolar depression, bipolar mixed episodes and maintenance. Every management recommendation is guideline-anchored, led by the CANMAT guidelines with the Indian Psychiatric Society, BAP and NICE positions stated, on the where-to-treat, target-by-phase, modes-of-treatment spine; every named agent ends with a **Good to remember** box giving the mechanism, the signature adverse effect or interaction, and the one dose or first-line indication. Figures declare one axis and code it in colour: **petrol** marks structure and the neutral case, **coral** marks the trap or the danger, and **marigold** highlights the number to hold. Several boundaries are worth stating up front: the mood-disorder classification, the depressive and bipolar clinical syndromes and the guideline-anchored management plan are taught in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes and are cross-referenced here rather than repeated; the monoamine pathway anatomy, the receptor systems and CYP metabolism live in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the technique of electroconvulsive therapy and of rTMS, VNS and DBS lives in the ECT and neurostimulation notes, and only their place in the algorithm is taught here; the full clinical suicide risk assessment lives in the Somatic-symptom, sexual, impulse-control disorders and suicide notes; the wider emergency and perinatal frames live in the Perinatal/women's mental health and emergency psychiatry notes; and the psychotherapy technique lives in the Psychotherapies, clinical assessment, MSE and nosology notes. This is doctor-facing revision, so the full technical vocabulary is used, brand names lead with the Indian brand, and every dose, serum level, monitoring interval, teratogenicity fact and first-line recommendation is verified against a source or omitted and flagged.

Antidepressant pharmacotherapy

1 . Classifying the antidepressants and the treatment algorithm

This is the opening map of the whole pharmacotherapy block. Two schemas orient everything that follows: a **class map** of the antidepressants and mood stabilisers ordered by what each drug does at the synapse, and a phase-based **treatment algorithm** that tells you which agent, in which phase, on which line. Get both in your head first and every later topic (the SSRIs, lithium and its monitoring, valproate, the mood-stabiliser and antidepressant-selection topics, the emergencies, treatment resistance) becomes a slot to fill, not a list to memorise cold.

The board rewards a resident who reasons in two moves: **first** name the drug by its primary synaptic action, **then** place the patient in a phase and polarity and treat accordingly. Lead with

the CANMAT guidelines (CANMAT 2016 for depression, CANMAT 2018 for bipolar disorder), then state the Indian Psychiatric Society (IPS) position and where the BAP and NICE agree. The mood classification, the depressive and bipolar syndromes, the criteria and the guideline-anchored management PLAN are owned by, and cross-referred to, the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes; this block owns the pharmacology, the doses, the monitoring and the algorithm.

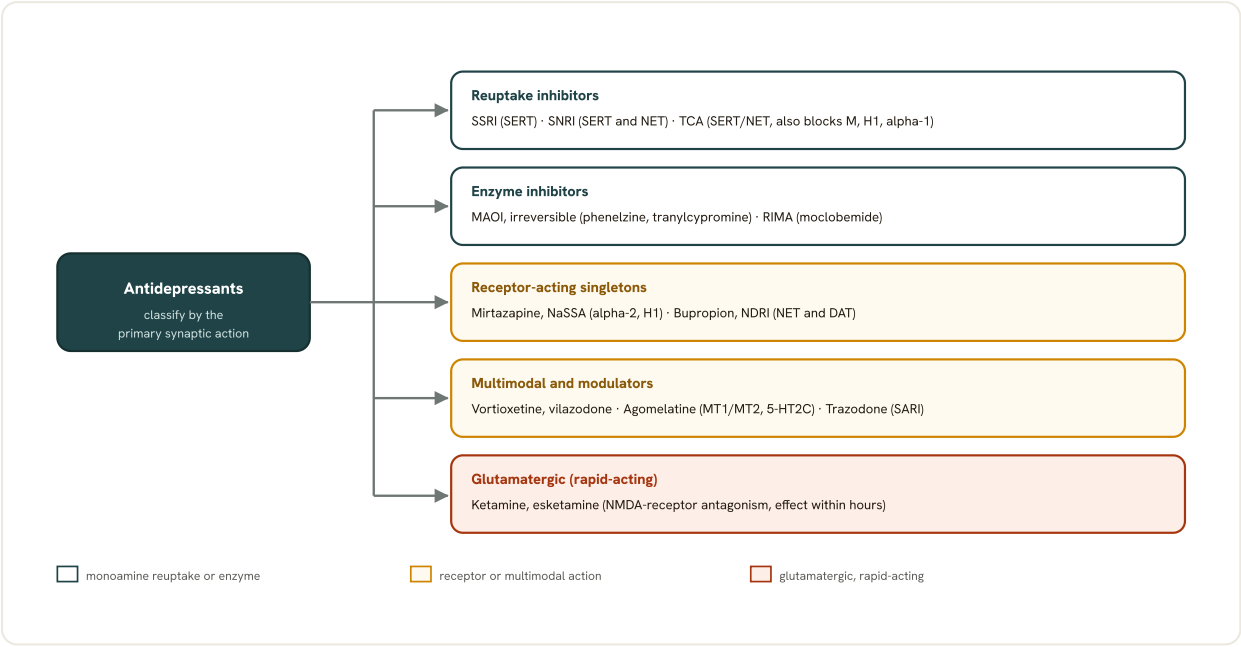


Fig 12.1 The antidepressants classified by their primary synaptic action, which predicts both tolerability and the dangerous interactions. The reuptake inhibitors (SSRI, SNRI, TCA) and the enzyme inhibitors (MAOI, RIMA) act on the monoamine supply; the receptor-acting singletons (mirtazapine, bupropion) and the multimodal and modulator agents (vortioxetine, agomelatine, trazodone) act at specific receptors; and the glutamatergic agents (ketamine, esketamine) act at the NMDA receptor with an effect within hours.

1.1 The organising principle: classify by mechanism, then treat by phase

Two schemas, in order. The **classification of antidepressants** is by **primary synaptic action**: which transporter or receptor the drug primarily hits, and therefore which monoamine it raises and which adverse effects and interactions follow. That single fact predicts most of the tolerability profile and most of the dangerous interactions. The **treatment algorithm** is the second schema: once the drug is classified, the patient is treated by **phase** (acute to remission, then continuation, then maintenance) and by **polarity** (unipolar depression versus bipolar disorder, which are treated with different classes). The monoamine pathway anatomy, the receptor systems and the CYP metabolism that sit underneath the mechanisms are cross-referred to the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

RULE **Classify an antidepressant by its synaptic action, then treat by phase.** Mechanism predicts the adverse-effect and interaction set; phase and polarity dictate the agent.

TRAP **Treating every depression the same regardless of phase or polarity.** A bipolar depression treated as a unipolar depression, or a patient stopped at response instead of remission, is the classic examinable error.

1.2 The class map: antidepressants by primary action

The **class map** groups every antidepressant by what it primarily does at the synapse (Stahl 2021; Maudsley 2021). The reuptake-inhibitor families come first, then the receptor-acting families, then the enzyme inhibitors, then the multimodal and glutamatergic agents. The SSRIs (selective serotonin reuptake inhibitors: escitalopram, sertraline, fluoxetine, paroxetine, citalopram, fluvoxamine) block the serotonin transporter (SERT). The SNRIs (serotonin-noradrenaline reuptake inhibitors: venlafaxine, desvenlafaxine, duloxetine) block both SERT and the noradrenaline transporter (NET). The tricyclic antidepressants (amitriptyline, imipramine, clomipramine, nortriptyline) block SERT and NET but additionally antagonise muscarinic, histamine H1 and alpha-1 receptors, which is why they carry the anticholinergic, sedative, orthostatic and cardiotoxic burden and are dangerous in overdose. The monoamine oxidase inhibitors (MAOIs: phenelzine, tranylcypromine as irreversible; moclobemide as the reversible RIMA) inhibit the enzyme that degrades monoamines, raising serotonin, noradrenaline and dopamine, and carry the tyramine (cheese) and serotonergic interaction hazards. The receptor-acting singletons are the NaSSA mirtazapine (a noradrenergic and specific serotonergic antidepressant: alpha-2 autoreceptor and heteroreceptor antagonist plus H1 blockade) and the NDRI bupropion (a noradrenaline-dopamine reuptake inhibitor with no direct serotonergic action). The multimodal and serotonin-modulator agents are vortioxetine (SERT inhibition plus 5-HT1A agonism and 5-HT3/5-HT7 antagonism), agomelatine (melatonin MT1/MT2 receptor agonist plus 5-HT2C antagonist) and trazodone (a serotonin antagonist and reuptake inhibitor, SARI). The glutamatergic agents are ketamine and its S-enantiomer esketamine, NMDA-receptor antagonists that act rapidly and outside the monoamine framework.

CLASS	PROTOTYPE AGENTS	PRIMARY SYNAPTIC ACTION	SIGNATURE TO HOLD
SSRI	escitalopram, sertraline, fluoxetine, paroxetine, citalopram, fluvoxamine	**Selective SERT (serotonin transporter) blockade**	First-line for tolerability and overdose safety
SNRI	venlafaxine, desvenlafaxine, duloxetine	**SERT plus NET (noradrenaline transporter) blockade**	Dose-dependent blood-pressure rise (venlafaxine)
Tricyclic (TCA)	amitriptyline, imipramine, clomipramine, nortriptyline	**SERT/NET blockade plus muscarinic, H1, alpha-1 antagonism**	Anticholinergic load, cardiotoxic, lethal in overdose
MAOI (irreversible)	phenelzine, tranylcypromine	**Irreversible inhibition of monoamine oxidase**	Tyramine (cheese) reaction, serotonergic interactions

CLASS	PROTOTYPE AGENTS	PRIMARY SYNAPTIC ACTION	SIGNATURE TO HOLD
RIMA	moclobemide	**Reversible inhibition of MAO-A**	Far lower tyramine risk than irreversible MAOIs
NaSSA	mirtazapine	**Alpha-2 autoreceptor/heteroreceptor antagonism plus H1 blockade**	Sedation, appetite and weight gain; useful with insomnia
NDRI	bupropion	**Noradrenaline and dopamine reuptake inhibition**	Activating, no sexual dysfunction; lowers seizure threshold
Multimodal (serotonin modulator)	vortioxetine	**SERT inhibition plus 5-HT1A agonism, 5-HT3/5-HT7 antagonism**	Nausea commonest; pro-cognitive claims
Melatonergic	agomelatine	**MT1/MT2 agonist plus 5-HT2C antagonist**	Sleep-promoting; monitor liver function
SARI	trazodone	**5-HT2 antagonism plus weak SERT inhibition**	Sedating; priapism risk; used for insomnia
Glutamatergic	ketamine, esketamine	**NMDA-receptor antagonism**	Rapid action; dissociation and blood-pressure rise

Fig 12.1 in prose: the antidepressant class map keyed to primary synaptic action. The highlighted mechanism cell is the fact that predicts each class's tolerability and its dangerous interactions.

GOOD TO REMEMBER

- **SSRIs:** block SERT selectively; first-line for MDD; hold escitalopram **10 to 20 mg/day** as the type case (CANMAT 2016).
- **SNRIs:** block SERT and NET; venlafaxine raises blood pressure dose-dependently; hold venlafaxine **75 to 225 mg/day** (CANMAT 2016).
- **TCAs:** block SERT/NET but add muscarinic, H1 and alpha-1 antagonism, so anticholinergic, sedating and cardiotoxic; lethal in overdose; second-line (CANMAT 2016).
- **MAOIs:** inhibit monoamine oxidase; signature hazard is the tyramine (cheese) reaction and serotonergic interactions; reserved third-line (CANMAT 2016).
- **Mirtazapine (NaSSA):** alpha-2 antagonist plus H1 blockade; signature is sedation and weight gain; first-line, useful with insomnia; hold **15 to 45 mg/day** (CANMAT 2016).
- **Bupropion (NDRI):** noradrenaline-dopamine reuptake inhibitor; activating, spares sexual function, lowers seizure threshold; first-line; hold **150 to 300 mg/day** (CANMAT 2016).
- **Vortioxetine (multimodal):** SERT inhibition plus receptor modulation; nausea commonest; first-line; hold **10 to 20 mg/day** (CANMAT 2016).
- **Agomelatine (melatonergic):** MT1/MT2 agonist plus 5-HT2C antagonist; sleep-promoting; monitor LFTs; first-line; hold **25 to 50 mg/day** (CANMAT 2016).
- **Trazodone (SARI):** 5-HT2 antagonist with weak reuptake inhibition; sedating, priapism risk; second-line, common as a hypnotic (CANMAT 2016).
- **Ketamine/esketamine (glutamatergic):** NMDA antagonists; rapid antidepressant and anti-suicidal effect; monitor blood pressure and dissociation; adjunct in treatment resistance (CANMAT 2016).

PEARL

The whole tolerability story of the tricyclics is off-target receptor blockade, not the reuptake inhibition. Muscarinic antagonism gives the dry mouth, constipation and urinary hesitancy; H1 gives the sedation and weight gain; alpha-1 gives the postural drop; and sodium-channel blockade gives the overdose cardiotoxicity. The SSRIs are "clean" precisely because they do none of this.

1.3 The mood stabilisers alongside the class map

The class map does not stop at the antidepressants. The bipolar arm of this block is built on the **mood stabilisers**: lithium (the archetype, with anti-manic, prophylactic and specific anti-suicide effect), the anticonvulsants valproate (sodium valproate and divalproex), carbamazepine (and its keto-analogue oxcarbazepine) and lamotrigine (the depression-predominant stabiliser), and the atypical antipsychotics used as mood stabilisers (quetiapine, olanzapine, aripiprazole, risperidone, asenapine, cariprazine, lurasidone). Each is a slot expanded later: lithium initiation, monitoring and toxicity, the valproate topic and its teratogenicity, the lamotrigine titration and the stabiliser-selection topic all belong downstream. The deep antipsychotic pharmacology, including the receptor profiles and the extrapyramidal and metabolic adverse effects, is cross-referred to the Schizophrenia: management, antipsychotics and adverse effects notes.

GOOD TO REMEMBER

- **Lithium:** the archetypal mood stabiliser; first-line for acute mania and maintenance with specific anti-suicide evidence; hold maintenance level **0.6 to 1.0 mmol/L** (CANMAT 2018).
- **Valproate/divalproex:** broad-spectrum anticonvulsant stabiliser; first-line for acute mania; signature hazard is teratogenicity (neural tube defects), so avoid in women of childbearing potential; hold serum **50 to 100 microg/mL** (CANMAT 2018).
- **Carbamazepine:** anticonvulsant stabiliser; signature is enzyme induction, hyponatraemia and the HLA-B*1502 Stevens-Johnson risk in at-risk Asian ancestry; second-line (CANMAT 2018).
- **Lamotrigine:** the depression-predominant stabiliser; first-line for bipolar depression and maintenance; signature hazard is the rash, so titrate slowly; target a minimum of **200 mg/day** starting at 25 mg (CANMAT 2018).
- **Atypical antipsychotics as stabilisers:** quetiapine, olanzapine, aripiprazole, risperidone, asenapine, cariprazine, lurasidone; first-line across mania, bipolar depression and maintenance; signature is metabolic burden (CANMAT 2018).

1.4 The treatment algorithm: the LOCUS-FOCUS-MODUS spine

Every management plan in this block runs on one spine. **LOCUS** is *where*: outpatient (or the day care centre) is the default, and admission is reserved for high suicide risk, psychotic features, severe self-neglect, or the need for inpatient-level treatment such as ECT. **FOCUS** is *the target by phase*: what you are trying to achieve right now. **MODUS** is *the modes of treatment*: which pharmacological and psychological modes each guideline recommends first. This is not a mnemonic for its own sake; it is the order in which a board answer is constructed. Decide the locus, name the phase, then list the guideline-first modes for that phase. The full clinical suicide risk assessment and safety planning that set the admission threshold are cross-referred to the Somatic-symptom, sexual, impulse-control disorders and suicide notes.

RULE **LOCUS then FOCUS then MODUS orders every plan.** Where to treat, which phase you are targeting, then which mode is first-line for that phase.

1.5 FOCUS for depression: acute, continuation, maintenance

The unipolar depression skeleton is three phases (CANMAT 2016; BAP 2015; Gautam et al. 2017). The **acute** phase runs from the outset to **remission** (not merely response): start one first-line second-generation antidepressant, review every **1 to 2 weeks**, and judge the trajectory by **2 to 4 weeks**, optimising the dose or switching if there is no improvement. The **continuation** phase then holds the same agent at the **acute treatment dose** for **6 to 9 months** after remission, to lock in the remission and prevent relapse. The **maintenance** phase extends treatment to **2 years or longer** for recurrent or high-risk illness to prevent recurrence, with CBT or MBCT as the psychological relapse-prevention modes. The individual phase-by-phase management plan, the augmentation and the psychotherapy detail are owned by the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes; here it is the orienting skeleton only.

1 to 2 wk	2 to 4 wk	6 to 9 mo	2 years+
ACUTE REVIEW INTERVAL	JUDGE ACUTE RESPONSE TRAJECTORY	CONTINUATION AFTER REMISSION	MAINTENANCE IF RECURRENT

1.6 FOCUS for bipolar disorder: mania, depression, maintenance

The bipolar skeleton is a different triad because the classes are different (CANMAT 2018; Grover and Avasthi 2017). **Acute mania** is treated with lithium, quetiapine, divalproex, aripiprazole, asenapine, paliperidone, risperidone or cariprazine as first-line monotherapy, or an atypical antipsychotic plus lithium or divalproex in severe presentations; any antidepressant is discontinued. **Bipolar depression** is treated with quetiapine, lurasidone (with or without lithium/divalproex), lithium, lamotrigine or the olanzapine-fluoxetine combination as first-line, and is *not* treated with an antidepressant alone. **Bipolar maintenance** continues the agent that worked acutely, with lithium, quetiapine, divalproex, lamotrigine, asenapine or aripiprazole as first-line monotherapy and a maintenance lithium level of **0.6 to 1.0 mEq/L**. Each limb is expanded later in the block; here it is the skeleton that sits beside the depression skeleton.

TRAP **Giving an antidepressant alone in a bipolar depression.** It risks a manic switch and rapid cycling; the first-line agents are quetiapine, lurasidone, lithium, lamotrigine or the olanzapine-fluoxetine combination (CANMAT 2018).

1.7 The Indian Psychiatric Society, BAP and NICE positions

The Indian Psychiatric Society Clinical Practice Guidelines are the Indian reference and the guideline most likely named in Indian postgraduate examinations. For depression, the **IPS guidelines** (Gautam et al. 2017) name the SSRIs as first-line on tolerability and overdose safety, with TCAs, mirtazapine, bupropion and venlafaxine as further options, and continue treatment after remission with a maintenance phase for recurrent illness. For bipolar disorder, the IPS guidelines (Grover and Avasthi 2017) direct that antidepressants are not used as monotherapy in bipolar depression, prefer bupropion and avoid paroxetine if an antidepressant is added, and name lithium and valproate as the best-evidenced maintenance agents. The BAP and NICE converge on the same spine: SSRIs and other newer agents are first-line for depression because they are better tolerated and safer in overdose (BAP 2015), and NICE names lithium as the first-line long-term treatment for bipolar disorder (NICE 2014). Where the IPS position on a specific point could not be confirmed against the parsed library it is flagged rather than invented.

INDIA

Every drug in this block is available in India; this chapter names no brand, and the Indian brand for each agent, Indian brand first, is given in the individual drug topics that follow (for example escitalopram, sertraline, lithium carbonate, sodium valproate, lamotrigine, quetiapine). The Indian Psychiatric Society Clinical Practice Guidelines are the guideline to cite first in Indian postgraduate examinations: Gautam et al. for depression and Grover and Avasthi for bipolar disorder. Lithium remains a mainstream first-line mood stabiliser in Indian practice, and ECT is widely available and heavily used for severe, psychotic, suicidal or treatment-resistant mood illness across Indian teaching hospitals.

1.8 The master mnemonic: chaining the chapter

One master **mnemonic** chains the four movements of this block so nothing is dropped: the antidepressant classes, then lithium and the mood stabilisers, then the emergencies, then

treatment resistance. Hold it as **"A SNoM LiVeS, then CALM the STORM, then climb the LADDER"**, unpacked below. It is a scaffold, not the content: each capitalised beat is a downstream topic.

MNEMONIC

A-SNoM-Li-VeS then CALM the STORM then the LADDER

The four movements of the pharmacotherapy block. **Antidepressant classes** (A): SSRI, SNRI, NaSSA/NDRI, MAOI, Multimodal (A SNoM). **Mood stabilisers**: Lithium, Valproate, lamotrigine and the Stabiliser antipsychotics (LiVeS). **Emergencies**: serotonin syndrome and lithium toxicity (CALM the STORM). **Treatment resistance**: the switch-augment-combine-neuromodulate ladder (the LADDER). Classify first (A SNoM LiVeS), then know what goes wrong (CALM the STORM), then know the next step when first-line fails (the LADDER).

MOVEMENT	WHAT IT HOLDS	WHERE IT IS EXPANDED
Antidepressant classes	SSRI, SNRI, TCA, MAOI, NaSSA, NDRI, multimodal, SARI, glutamatergic	**The SSRI, SNRI, TCA/MAOI and newer-agent topics in this block**
Lithium and mood stabilisers	Lithium, valproate, carbamazepine, lamotrigine, atypicals	**Lithium initiation/monitoring/toxicity, valproate, lamotrigine, stabiliser-selection topics**
Emergencies	Serotonin syndrome, lithium toxicity	**The emergencies topics in this block; wider acute management cross-referred to the Perinatal/women's mental health and emergency psychiatry notes**
Treatment resistance	Switch, augment, combine, neuromodulate	**The treatment-resistant-depression ladder topic**

The master mnemonic mapped to the four downstream movements of the block; each highlighted cell names where that movement is taught in full.

GOOD TO REMEMBER

- **Classify by mechanism:** name the antidepressant by its primary synaptic action (SERT, NET, receptor, enzyme, NMDA) before you prescribe.
- **The phases are acute, continuation, maintenance:** aim remission, then hold at the acute dose, then extend for recurrence.
- **LOCUS-FOCUS-MODUS orders every plan:** decide where, name the phase, list the guideline-first modes for that phase.
- **Polarity matters:** unipolar depression and bipolar disorder use different classes; do not give an antidepressant alone in bipolar depression.
- **Guideline order:** lead with CANMAT, then state the Indian Psychiatric Society, BAP and NICE positions.

WORKED EXAMPLE

A 30-year-old man presents with a moderate depressive episode, no psychosis, no active suicidal plan and no history of mania. Working the two schemas: the class map says a first-line second-generation antidepressant (an SSRI such as escitalopram), classified as a SERT blocker; the algorithm says LOCUS outpatient, FOCUS the acute phase aiming at remission, MODUS one first-line agent with measurement-based review at 2 weeks and a trajectory judgement by 2 to 4 weeks. On reaching remission by month 3, the continuation phase holds the same agent at the same dose for 6 to 9 months. Had the same man reported a past manic episode, polarity would flip the plan entirely: the class map moves to the mood stabilisers and the bipolar-depression first-line agents, and an antidepressant alone would be a trap.

HOLD THIS

Classify the antidepressant by its primary synaptic action, then treat by phase (acute to remission, continuation 6 to 9 months at the acute dose, maintenance 2 years or longer if recurrent) and by polarity (unipolar and bipolar use different classes), on the LOCUS-FOCUS-MODUS spine, leading with CANMAT.

2 . Selective serotonin reuptake inhibitors

The **selective serotonin reuptake inhibitor** class is the first-line antidepressant group and the single most-prescribed drug family in psychiatry, so the board expects the mechanism, the individual agents with their doses, and the whole adverse-effect set at your fingertips. The organising truth the examiner rewards: the members of the **ssri** class are broadly equal in antidepressant efficacy and differ mainly in **half-life**, **cytochrome interactions** and **adverse-effect emphasis**, not in how well they lift mood (Maudsley 2021; Stahl 2021). This topic teaches the pharmacology; the guideline-anchored choice of which antidepressant, and the discontinuation and serotonin-syndrome detail, are cross-referred where relevant.

Learn each agent by its one distinguishing feature (the long half-life of **fluoxetine**, the QTc ceiling of **escitalopram**, the discontinuation burden of **paroxetine**), then hang the shared class adverse effects on top. The dosing anchors are verified against Stahl's Prescriber's Guide and the Maudsley (Stahl 2021; Maudsley 2021); the monoamine-pathway anatomy and cytochrome metabolism underneath all of this belong to the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

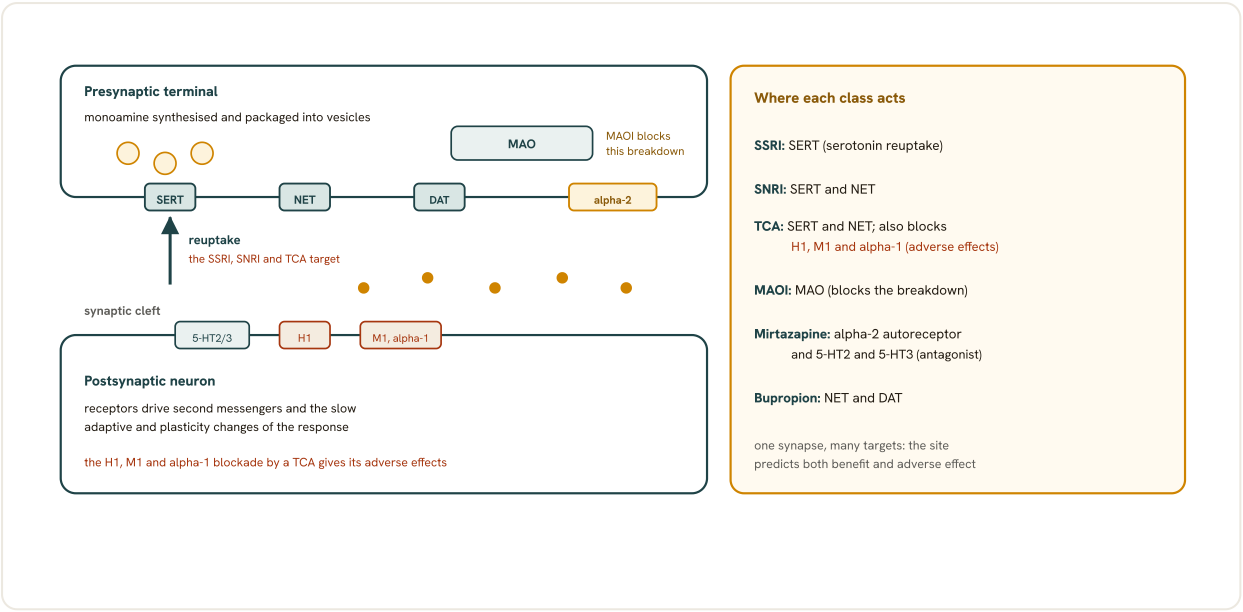


Fig 12.2 The monoamine synapse and where each antidepressant class acts. The reuptake transporters (SERT, NET, DAT) and the enzyme MAO clear the monoamine, and the post-synaptic and autoreceptors shape the signal. The SSRIs block SERT; the SNRIs block SERT and NET; the TCAs block both and, off-target, H1, M1 and alpha-1 (their adverse effects); the MAOIs block MAO; mirtazapine blocks the alpha-2 autoreceptor and 5-HT2/5-HT3; and bupropion blocks NET and DAT. The site of action predicts both the benefit and the adverse-effect profile.

2.1 Mechanism: SERT blockade, then receptor adaptation

The acute action. Every SSRI blocks the presynaptic serotonin transporter (**SERT**, the SLC6A4 protein), the pump that clears serotonin from the synapse back into the neuron. Blocking SERT raises **synaptic serotonin**, which is the immediate pharmacological effect and happens within hours of the first dose (Stahl 2021). Yet the antidepressant benefit does not appear for weeks, and that gap is the key teaching point.

The therapeutic lag. The initial rise in serotonin first stimulates somatodendritic 5-HT1A autoreceptors at the cell body, which shut down neuronal firing and blunt the expected increase in serotonin in the projection fields. Only with continued dosing do these autoreceptors **desensitise and downregulate**, after which firing resumes, serotonin release in the forebrain rises, and downstream postsynaptic receptor adaptation delivers the mood effect. This slow receptor adaptation, not the transporter block itself, is why the clinical response takes about 2 to 4 weeks to build (Stahl 2021; Companion 2010).

RULE **SERT block is immediate; the antidepressant effect is not.** The therapeutic lag reflects 5-HT1A autoreceptor desensitisation, so give an adequate trial before judging efficacy.

2.2 The class as a whole: what "selective" and "equal efficacy" mean

Selective. The SSRIs are highly potent and selective inhibitors of SERT with little direct action on noradrenaline or dopamine transporters and, unlike the tricyclics, little affinity for muscarinic, histaminergic or alpha-adrenergic receptors, which is why they are far safer in overdose and better tolerated (Companion 2010). Sertraline is the partial exception, with a mild dopamine reuptake effect at the top of its range.

Equal efficacy, different profiles. Head-to-head, no SSRI is convincingly more effective than another for major depression; the choice is driven by half-life, cytochrome interactions, and the adverse-effect emphasis of each drug (Maudsley 2021). That single sentence answers most "which SSRI and why" viva questions.

2.3 The individual agents: doses and distinguishing features

Six agents matter. The table gives the verified adult dose range with the unit in the header; the prose gives the one feature that makes each one examinable. All start at or near the minimum effective dose and are given once daily (fluvoxamine often divided).

SSRI (INDIAN BRAND)	DOSE (MG/DAY)	HALF-LIFE	DISTINGUISHING FEATURE	KEY CYP EFFECT
Fluoxetine (Fludac)	**20 to 80**	Parent 2 to 3 days; norfluoxetine ~2 weeks	Longest half-life, activating, self-tapering on stopping	Inhibits CYP2D6 and CYP3A4
Sertraline (Serta, Daxid)	50 to 200	~26 hours	**Broadest first choice; mild dopamine effect; prominent GI upset/diarrhoea**	Weak CYP2D6 inhibitor
Escitalopram (Nexito, S-Citadep)	10 to 20	27 to 32 hours	**Cleanest, fewest interactions; dose-dependent QTc**	Minimal CYP effect
Citalopram	20 to 40	~33 hours	Racemate of escitalopram; QTc cap at 40 (20 in the elderly / 2C19 inhibition)	Weak CYP2D6 inhibitor
Paroxetine (Pexep)	20 to 50	~21 hours (short)	**Anticholinergic, weight gain, worst discontinuation, avoid in pregnancy**	Potent CYP2D6 inhibitor
Fluvoxamine	100 to 300	~13 to 22 hours	OCD workhorse; sedating; no active metabolite	Potent CYP1A2 inhibitor

The six SSRIs with verified adult dose ranges (Stahl 2021), half-lives and the one feature each is tested on; the highlighted cell is the board discriminator for that drug. Doses are for adult depression.

Fluoxetine (Fludac). The prototype. Its very long half-life (parent 2 to 3 days, active metabolite norfluoxetine about 2 weeks) means it effectively self-tapers and rarely causes a discontinuation syndrome, but also means a 5-week washout before an MAOI. It is the most **activating** SSRI and inhibits both CYP2D6 and CYP3A4 (Stahl 2021).

Sertraline (Serta or Daxid). The pragmatic broadest first choice with the widest evidence base and a mild dopamine-reuptake effect at higher doses; its signature adverse effect is

gastrointestinal, especially diarrhoea. It is only a weak CYP inhibitor, which helps in the medically complex or polypharmacy patient (Maudsley 2021).

Escitalopram (Nexito or S-Citadep) and citalopram. Escitalopram is the S-enantiomer of citalopram and the **cleanest** SSRI, with the fewest cytochrome interactions; 10 mg of escitalopram is roughly comparable to 20 mg of citalopram (Stahl 2021). Both carry a **dose-dependent QTc** prolongation: citalopram must not exceed **40 mg/day** (and 20 mg in the elderly or with a CYP2C19 inhibitor), and escitalopram is capped at **20 mg/day**.

Paroxetine (Pexep). The most troublesome of the group: a short half-life with no active metabolite, so it has the **worst discontinuation** syndrome; the most **anticholinergic** SSRI (dry mouth, constipation); the most weight gain; a potent CYP2D6 inhibitor; and the one SSRI specifically to **avoid in pregnancy** (see 2.7).

Fluvoxamine. Positioned mainly for OCD, sedating rather than activating, with no active metabolite. Its defining pharmacological hazard is potent **CYP1A2 inhibition**, which raises levels of theophylline, clozapine, caffeine and duloxetine (Stahl 2021).

GOOD TO REMEMBER

- **Fluoxetine (Fludac):** longest half-life (norfluoxetine ~2 weeks), activating, CYP2D6/3A4 inhibitor; dose **20 to 80 mg/day**.
- **Sertraline (Serta or Daxid):** broadest first choice, mild dopamine effect, GI/diarrhoea; dose **50 to 200 mg/day**.
- **Escitalopram (Nexito or S-Citadep):** cleanest, fewest interactions, dose-dependent QTc; dose **10 to 20 mg/day** (max 20).
- **Citalopram:** escitalopram's racemate; QTc cap at **40 mg/day** (20 in elderly); dose **20 to 40 mg/day**.
- **Paroxetine (Pexep):** short half-life, anticholinergic, weight gain, worst discontinuation, avoid in pregnancy; dose **20 to 50 mg/day**.
- **Fluvoxamine:** OCD agent, strong CYP1A2 inhibitor, sedating; dose **100 to 300 mg/day**.

2.4 The class adverse-effect set: GI, sexual, activation

Gastrointestinal. Nausea, loose stools and dyspepsia are the commonest early adverse effects, driven by gut 5-HT3 stimulation; they are usually dose-related and settle over the first 1 to 2 weeks. Sertraline is the most likely to cause diarrhoea (Maudsley 2021).

Sexual dysfunction. **sexual dysfunction** (use "sexual dysfunction") is very common with all SSRIs (reduced desire, delayed orgasm or anorgasmia, and erectile or ejaculatory difficulty) and is the leading cause of covert non-adherence, so ask about it directly rather than waiting for the patient to volunteer it (Maudsley 2021). Management options include dose reduction, switching to a lower-risk agent (bupropion, mirtazapine or agomelatine), a drug holiday, or adding sildenafil/tadalafil. Do not dismiss it: an unasked, untreated sexual side effect is a classic reason a patient silently stops an effective antidepressant.

Early activation and anxiety. A jittery, agitated worsening of anxiety and insomnia can occur in the first days, most with the activating fluoxetine; in anxiety disorders start at half the usual dose

and titrate up. Emergent agitation, especially in a young person, also raises the question of an unmasked bipolar state (Maudsley 2021).

TRAP **Dismissing or never asking about sexual dysfunction.** It is very common, patient-limiting, and the commonest silent cause of SSRI non-adherence; ask directly and act.

2.5 Hyponatraemia, bleeding and QTc: the systemic risks

Hyponatraemia and SIADH. All SSRIs can cause hyponatraemia through the syndrome of inappropriate antidiuretic hormone secretion, and the risk is greatest in the **elderly**, in women, in low body weight, and with co-prescribed diuretics; it is a first-month risk (Maudsley 2021; Stahl 2021). In an older patient who becomes confused, drowsy, unsteady or has a seizure after starting or increasing an SSRI, check the sodium before anything else.

Bleeding. By depleting platelet serotonin, SSRIs impair platelet aggregation and raise the risk of gastrointestinal and other bleeding, and this risk is amplified when combined with **NSAIDs** or antiplatelet or anticoagulant drugs; co-prescribe gastroprotection where an NSAID or antiplatelet cannot be avoided (Maudsley 2021).

QTc. Citalopram and escitalopram cause a dose-dependent QTc prolongation, which is the reason for the hard dose ceilings above; caution with other QT-prolonging drugs, hypokalaemia and pre-existing cardiac disease.

TRAP **Missing SSRI-induced hyponatraemia in an older patient.** New confusion, falls, unsteadiness or a seizure weeks into an SSRI is hyponatraemia until the sodium proves otherwise.

2 to 4 wk	40	20
THERAPEUTIC LAG TO RESPONSE	CITALOPRAM QTC CEILING (MG/DAY)	ESCITALOPRAM MAXIMUM (MG/DAY)

2.6 The paediatric suicidality signal and serotonin syndrome

Paediatric suicidality. A small but real increase in suicidal ideation and behaviour (not completed suicide) is seen with antidepressants in children, adolescents and young adults up to about age 25, prompting a boxed warning and close monitoring in the early weeks; the same reanalyses show a reduction in suicidality with antidepressants in adults over 65 (Stahl 2021). The message is monitoring in the young, not avoidance: untreated depression is itself a suicide risk. The full clinical suicide risk assessment and safety planning are owned by the Somatic-symptom, sexual, impulse-control disorders and suicide notes.

Serotonin syndrome. Combining an SSRI with another serotonergic drug, above all an MAOI (including moclobemide), tramadol, triptans, linezolid or another serotonergic antidepressant, can precipitate serotonin syndrome, the triad of neuromuscular excitation (clonus, hyperreflexia, tremor), autonomic instability and altered mental state. An adequate washout is mandatory when switching to or from an MAOI, and the long half-life of fluoxetine means a 5-week gap. The acute recognition and emergency management of serotonin syndrome are cross-referred to the Perinatal/women's mental health and emergency psychiatry notes.

RULE **Never co-prescribe an SSRI with an MAOI.** Leave 14 days after an MAOI, and 5 weeks after fluoxetine before starting one, to avoid serotonin syndrome.

2.7 CYP interactions and the discontinuation caveat

Cytochrome interactions in brief. The clinically important inhibitors are the ones to memorise: fluoxetine and paroxetine are potent CYP2D6 inhibitors (fluoxetine also inhibits CYP3A4), and fluvoxamine is a potent CYP1A2 inhibitor. Practical consequences: paroxetine reduces the efficacy of tamoxifen (a CYP2D6-activated pro-drug); fluoxetine raises clozapine and TCA levels; fluvoxamine markedly raises theophylline, clozapine and caffeine levels. Sertraline, escitalopram and citalopram are comparatively clean, which is why escitalopram or sertraline is preferred in the medically complex patient (Maudsley 2021; Stahl 2021).

Discontinuation caveat. Stopping an SSRI abruptly, especially a short-half-life agent, produces a discontinuation syndrome (flu-like symptoms, insomnia, nausea, imbalance, sensory "electric-shock" disturbances and hyperarousal). Paroxetine is the worst offender and fluoxetine essentially exempt because it self-tapers. Always taper; the full discontinuation-and-withdrawal detail is cross-referred to the Perinatal/women's mental health and emergency psychiatry notes.

INDIA

SSRIs are the most-prescribed antidepressants in Indian practice and all six are cheap and freely available as generics and branded generics. Lead with the Indian brand: escitalopram is sold as Nexito or S-Citadep, sertraline as Serta or Daxid, fluoxetine as Fludac, and paroxetine as Pexep; citalopram and fluvoxamine are marketed generically and by brand. Escitalopram and sertraline are the workhorse first-line agents in Indian outpatient departments, and monthly cost is low (a month of a generic SSRI typically costs a small fraction of a single private consultation), which matters for adherence in a largely out-of-pocket health system.

WORKED EXAMPLE

A 72-year-old woman on a thiazide for hypertension is started on an SSRI for a moderate depressive episode. Ten days later she is brought in confused, unsteady and drowsy. Rather than escalating the antidepressant or reaching for an antipsychotic, the first action is a serum sodium, which is 122 mmol/L: SSRI-induced hyponatraemia from SIADH, compounded by the diuretic and her age. The SSRI is stopped, sodium corrected cautiously, and a lower-risk strategy planned. Missing the sodium here is the classic examined error.

PEARL

Match the SSRI to the patient by its non-efficacy features: the anxious or agitated patient may do better away from activating fluoxetine; the medically complex, polypharmacy patient suits clean escitalopram or sertraline; the patient likely to miss doses should avoid short-half-life paroxetine because of its discontinuation burden. The efficacy is broadly the same; the fit is not.

MNEMONIC

FINISH

SSRI discontinuation syndrome, worst with paroxetine: **F**lu-like symptoms, **I**nsomnia, **N**ausea, **I**mbalance, **S**ensory disturbances (the "electric shocks"), **H**yperarousal. Taper slowly; fluoxetine self-tapers.

HOLD THIS

SSRIs are first-line and equally effective, differing in half-life, CYP interactions and adverse-effect emphasis: fluoxetine long and activating, paroxetine short with the worst discontinuation and avoided in pregnancy, escitalopram cleanest with a QTc ceiling, fluvoxamine a CYP1A2 inhibitor for OCD; watch for sexual dysfunction, hyponatraemia in the elderly, NSAID-associated bleeding, and never combine with an MAOI.

3 · Serotonin-noradrenaline reuptake inhibitors

Why this matters. The **serotonin-noradrenaline reuptake inhibitor** (SNRI) class is the most heavily examined second-generation antidepressant group after the SSRIs, and it is where a resident must marry a clean synaptic mechanism to a small set of dose-dependent adverse effects. Every SNRI blocks both the serotonin transporter (SERT) and the noradrenaline transporter (NET), but the noradrenergic action is not free at every dose: with venlafaxine it emerges only as the dose is raised, which is exactly why the blood-pressure rise, the sweating and the urinary effects track dose. The class also carries the single most feared antidepressant discontinuation problem, the venlafaxine withdrawal syndrome.

The examinable skill is threefold: to state the dual SERT and NET mechanism and its dose-dependence, to name and dose each agent (venlafaxine, desvenlafaxine, duloxetine, milnacipran and levomilnacipran) with its signature adverse effect, and to place the class in the algorithm, a common second step after an SSRI, or a first-line choice where depression is comorbid with neuropathic pain. The monoamine-transporter pharmacology and CYP metabolism that underpin this class are developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

3.1 The mechanism: dual SERT and NET blockade with a noradrenergic action that emerges at higher dose

The class name says the mechanism: an SNRI inhibits reuptake at both the serotonin transporter and the noradrenaline transporter, combining two therapeutic actions in one molecule (Stahl 2021; Kaplan & Sadock 2024). What distinguishes the newer SNRIs from the older dual-acting tricyclics is **selectivity**: they have essentially no affinity for muscarinic, histaminergic or alpha-adrenergic receptors, which is why they are far better tolerated than clomipramine or amitriptyline while sharing the dual-reuptake logic (Kaplan & Sadock 2024). The crucial teaching point is that the two actions are not equipotent at every dose. For venlafaxine the affinity for SERT is much greater than for NET, so at the lowest therapeutic dose the drug behaves as a de-facto SSRI, and NET is only reliably engaged as the dose climbs; Stahl frames this as serotonergic actions present at low doses with noradrenergic actions "progressively enhanced as dose

increases" (Stahl 2021). This ascending dose-response is the conceptual spine of the whole topic: the noradrenergic benefits and the noradrenergic adverse effects both arrive together, at higher dose.

RULE **An SNRI is an SSRI at low dose and a dual agent higher up.** The noradrenergic action, and every noradrenergic adverse effect, appears as you push the dose, so dose determines the pharmacology.

3.2 Venlafaxine: the dose-dependent noradrenergic effect and the ascending dose-response

Venlafaxine (Venlor) is a bicyclic phenylethylamine, the prototype SNRI, approved for major depressive disorder, generalised anxiety disorder, social anxiety disorder and panic disorder (Kaplan & Sadock 2024). Its pharmacology is textbook dose-dependence: it acts as a serotonergic agent at the minimum effective dose of **75 mg/day**, whereas the noradrenaline transporter is consistently engaged only at a dose of about **225 mg/day** (Kaplan & Sadock 2024). CANMAT lists venlafaxine as a first-line SNRI for MDD at **75 to 225 mg/day** (CANMAT 2016). The immediate-release form has a short elimination half-life of roughly **4 hours** (its active metabolite O-desmethylvenlafaxine about **10 hours**), and this short half-life is what drives the discontinuation problem covered below (Kaplan & Sadock 2024). The extended-release capsule allows once-daily dosing but does not lengthen the elimination half-life, so it does not abolish the withdrawal risk (Kaplan & Sadock 2024).

WORKED EXAMPLE

A patient on venlafaxine 75 mg/day for depression has partial response with no side effects. Because 75 mg is essentially a serotonergic dose, uptitration towards 150 to 225 mg/day recruits the noradrenergic action and can improve response, but from about 150 mg upward you must begin checking blood pressure, because the noradrenergic effect that helps also raises blood pressure.

3.3 Venlafaxine: the dose-dependent blood-pressure rise and the monitoring rule

The signature venlafaxine adverse effect is a **dose-dependent rise in blood pressure**, a direct consequence of dose-dependent noradrenergic reuptake blockade. With the immediate-release formulation, sustained hypertension was dose-related, rising from about **3 to 7 percent** at doses of 100 to 300 mg/day and to about **13 percent** at doses greater than 300 mg/day (Kaplan & Sadock 2024). Capping the extended-release dose largely attenuated the signal, but the prescribing rule stands: when higher doses are used, monitoring of blood pressure is recommended (Kaplan & Sadock 2024). The Maudsley makes the class point plainly, that the SNRIs venlafaxine and duloxetine are associated with dose-dependent increases in blood pressure (Maudsley 2021). This is the load-bearing SNRI prescribing principle: blood pressure is checked, and checked again, as the dose is raised.

3 to 7	13	75 to 225
SUSTAINED HYPERTENSION AT 100 TO 300 MG/DAY (PERCENT)	SUSTAINED HYPERTENSION ABOVE 300 MG/DAY (PERCENT)	FIRST-LINE VENLAFAXINE RANGE (MG/DAY)

RULE **Venlafaxine's noradrenergic effect and blood-pressure rise are dose-dependent, so monitor blood pressure at higher doses.** Check a baseline and recheck as you titrate past the low serotonergic range.

3.4 Venlafaxine: the short half-life and the marked discontinuation syndrome

Venlafaxine is one of the antidepressants most commonly associated with a discontinuation syndrome, a direct consequence of its short half-life (Kaplan & Sadock 2024). On rapid taper or abrupt cessation, and even after a few missed doses, patients develop dizziness, nausea, insomnia, nervousness, sweating, anorexia, diarrhoea, somnolence and sensory disturbances (the "electric shock" or "brain zap" paraesthesiae) (Kaplan & Sadock 2024). Because the extended-release formulation does not change the elimination half-life, switching to it does not reduce the discontinuation potential (Kaplan & Sadock 2024). The Maudsley notes that antidepressants with noradrenergic effects tend to have more severe withdrawal, and names venlafaxine, desvenlafaxine, duloxetine and paroxetine as the agents most often implicated (Maudsley 2021). Management is prevention: warn the patient not to stop abruptly, and taper slowly, reducing the daily dose by no more than about **75 mg each week** when longer-term treatment must be stopped; a few bridging doses of fluoxetine can smooth the final step (Kaplan & Sadock 2024).

TRAP **Stopping venlafaxine abruptly precipitates a severe discontinuation syndrome.** The short half-life means even missed doses can trigger it; never stop it suddenly, taper by no more than about 75 mg per week.

GOOD TO REMEMBER

- **Venlafaxine (Venlor):** dual SERT and NET reuptake inhibitor, noradrenergic action emerges with dose; signature effect is a dose-dependent blood-pressure rise (monitor at higher doses) plus a marked discontinuation syndrome from its short half-life; hold 75 to 225 mg/day, serotonergic at 75, NET engaged near 225.

3.5 Desvenlafaxine: the active metabolite, less CYP-dependent

Desvenlafaxine is O-desmethylvenlafaxine, the principal active metabolite of venlafaxine, formed from the parent drug by CYP2D6 (Stahl 2021; Kaplan & Sadock 2024). Because it is already the downstream metabolite, its systemic exposure is **less dependent on CYP2D6 conversion** than venlafaxine's, so its plasma levels are more predictable across the genetic polymorphisms of that enzyme (Stahl 2021). It has relatively greater noradrenaline reuptake inhibition than venlafaxine but remains more potent at SERT (Stahl 2021). The minimum therapeutic dose is **50 mg/day**, and controlled trials showed no greater efficacy at higher doses; CANMAT lists it as a first-line SNRI for MDD at **50 to 100 mg/day** (Kaplan & Sadock 2024; CANMAT 2016). Note the Maudsley caveat that desvenlafaxine was not marketed in the UK at the time of writing, so it appears in guidelines as an option rather than a mainstream UK agent (Maudsley 2021).

GOOD TO REMEMBER

- **Desvenlafaxine:** the active O-desmethyl metabolite of venlafaxine, less CYP2D6-dependent so more predictable levels; relatively more noradrenergic than venlafaxine but still SERT-predominant; hold a minimum effective dose of 50 mg/day (first-line range 50 to 100 mg/day).

3.6 Duloxetine: the neuropathic-pain and stress-incontinence indications

Duloxetine (Duzela) inhibits both SERT and NET, and because it has lower affinity for NET than for SERT, doses higher than **60 mg/day** are needed to reliably obtain a central noradrenergic effect (Stahl 2021; Kaplan & Sadock 2024). CANMAT lists duloxetine as a first-line SNRI for MDD at **60 mg/day** (CANMAT 2016). Its distinguishing feature is a set of pain and urological indications that flow from noradrenergic action on descending spinal pathways and on urethral sphincter tone: it is specifically used for **diabetic and other neuropathic pain**, for fibromyalgia, and for **stress urinary incontinence** in women because it increases urethral tone (Tripathi 2019; Kaplan & Sadock 2024). This makes duloxetine the natural first-line antidepressant when depression coexists with a chronic pain syndrome. Its blood-pressure effect is smaller than venlafaxine's and, curiously, does not appear to be dose-dependent, with only about a 1 percent greater risk of sustained hypertension than placebo (Kaplan & Sadock 2024).

INDIA

Duloxetine is widely stocked in India under several brands (Duzela among them); the internationally recognised innovator brand is Cymbalta. When comorbid neuropathic pain drives the choice, duloxetine is often the pragmatic first antidepressant on an Indian formulary because it treats both targets with one drug.

3.7 Duloxetine: the hepatotoxicity caution and key interactions

The specific safety caution for duloxetine is **hepatotoxicity**: the Maudsley references a drug-induced liver injury case series, and the drug should be avoided in patients with significant hepatic impairment or substantial alcohol use, with liver function monitored if there is concern (Maudsley 2021). Metabolically, duloxetine is a CYP1A2 and CYP2D6 substrate: its levels are about 30 percent lower in smokers (CYP1A2 induction) and rise about four-fold with potent CYP1A2 inhibitors such as fluvoxamine and some fluoroquinolone antibiotics, so co-prescription with fluvoxamine is a notable interaction to avoid (Kaplan & Sadock 2024). As with all serotonergic agents, a lethal interaction with monoamine oxidase inhibitors is expected, and the MAOI washout rules must be followed; the acute serotonin-syndrome frame that this interaction can trigger is developed in the Perinatal/women's mental health and emergency psychiatry notes.

TRAP **Co-prescribing duloxetine with fluvoxamine multiplies its level roughly four-fold.** Fluvoxamine is a potent CYP1A2 inhibitor; the combination, and heavy alcohol use, both stack onto duloxetine's hepatotoxicity risk.

GOOD TO REMEMBER

- **Duloxetine (Duzela):** dual SERT and NET inhibitor, doses above 60 mg needed for a central noradrenergic effect; signature niche is neuropathic pain, fibromyalgia and stress urinary incontinence, with a hepatotoxicity caution (avoid in hepatic impairment or heavy alcohol use); hold a first-line dose of 60 mg/day.

3.8 Milnacipran and levomilnacipran in brief

Milnacipran is a dual reuptake inhibitor that, unlike venlafaxine, is preferentially noradrenergic, roughly twice as potent at NET as at SERT; it behaves as a preferential NE uptake inhibitor at its minimum therapeutic dose of **50 mg twice daily** and recruits more serotonergic action as the dose rises to its maximal recommended **200 mg/day** for fibromyalgia (Kaplan & Sadock 2024). In many countries it is licensed for major depressive disorder, but in the United States it is approved only for fibromyalgia (Kaplan & Sadock 2024). Consistent with its noradrenergic bias, its notable adverse effects, at rates higher than an SSRI, are dizziness, sweating and urinary hesitancy (Kaplan & Sadock 2024). Levomilnacipran is the more active enantiomer, developed as a separate once-daily antidepressant for MDD; like the others it must never be given close to an MAOI (Kaplan & Sadock 2024).

GOOD TO REMEMBER

- **Milnacipran:** the preferentially noradrenergic SNRI (about twice as potent at NET as SERT), signature effects sweating and urinary hesitancy; hold a minimum therapeutic dose of 50 mg twice daily (maximum 200 mg/day, licensed mainly for fibromyalgia).
- **Levomilnacipran:** the more active enantiomer of milnacipran, marketed as a once-daily SNRI antidepressant for MDD; never combine with an MAOI.

3.9 The class adverse-effect profile: the noradrenergic signature

Beyond the shared serotonergic effects (nausea, which is more frequent than with SSRIs, sexual dysfunction, headache), the examinable SNRI signature is the **noradrenergic** cluster, all traceable to NET blockade: **sweating**, a rise in **blood pressure**, increased pulse, and **urinary** effects (hesitancy). With venlafaxine these are dose-dependent, tracking the emergence of noradrenergic action at higher dose; milnacipran, being preferentially noradrenergic, shows the sweating and urinary signal even at usual dose (Kaplan & Sadock 2024). Layered on top is the discontinuation liability, most marked for venlafaxine because of its short half-life. Holding these together, the class is well tolerated but demands two things of the prescriber that SSRIs do not: blood-pressure monitoring as the dose rises, and a deliberate, slow taper on stopping.

PEARL

Every noradrenergic SNRI adverse effect, sweating, raised blood pressure, urinary hesitancy, is the same pharmacology (NET blockade) seen from a different organ. If you remember "sweat, pressure, pee" you have reconstructed the class side-effect profile from first principles.

3.10 Adverse-effect comparison across the agents

AGENT (BRAND)	USUAL DOSE (MG/DAY)	NE VS 5-HT BALANCE	SIGNATURE ADVERSE EFFECT / CAUTION
Venlafaxine (Venlor)	75 to 225	SERT > NET; NET recruited with dose	**Dose-dependent blood-pressure rise; marked discontinuation syndrome**
Desvenlafaxine	50 to 100	More NET than venlafaxine, still SERT-predominant	Less CYP2D6-dependent, more predictable levels
Duloxetine (Duzela)	60 (up to 120)	SERT > NET; NET needs >60 mg	**Hepatotoxicity caution; neuropathic pain and stress incontinence indications**
Milnacipran	100 (50 twice daily), max 200	NET > SERT (preferentially noradrenergic)	Sweating, urinary hesitancy; mainly fibromyalgia
Levomilnacipran	40 to 120	Noradrenergic-leaning enantiomer	Once-daily; MAOI contraindication

SNRI agents compared on dose, transporter balance and the single adverse effect or caution to hold for each; blood-pressure monitoring and slow taper apply across the class.

3.11 The place in therapy: a common second step after an SSRI, or first-line with comorbid pain

In the guideline algorithm the SNRIs sit as core options for major depressive disorder. CANMAT names venlafaxine (75 to 225 mg/day), duloxetine (60 mg/day) and desvenlafaxine (50 to 100 mg/day) as **first-line** SNRI agents for MDD, individualising the choice to the patient (CANMAT 2016). The commonest practical use is as a **second step after an SSRI**: when a first-line SSRI fails on efficacy grounds, a switch to an SNRI is a standard next move, and CANMAT directs that for a non-improver at 2 to 4 weeks you increase the dose if tolerated and switch to another agent if tolerability is the problem (CANMAT 2016). The BAP similarly reserves maximised-efficacy agents including venlafaxine at 150 mg or more for more severely ill patients, and NICE positions SNRIs among the alternatives after an initial SSRI (Malhi 2015 for the BAP position on severity; NICE 2014). The other clear first-line indication is **comorbid pain**: duloxetine is the natural first choice when depression coexists with neuropathic pain, fibromyalgia or stress urinary incontinence. For the Indian Psychiatric Society position, kb-search did not return a confirmable IPS depression recommendation on SNRI sequencing in the parsed library, so the specific IPS line could not be confirmed and is flagged rather than invented; the guideline-anchored management plan for depression as a whole is developed in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes.

RULE **An SNRI is a standard second step after a failed SSRI, and first-line when pain is comorbid.** Venlafaxine, duloxetine and desvenlafaxine are all CANMAT first-line SNRIs; duloxetine also treats the pain.

COMMON TRAP

Do not treat a bipolar depression with an SNRI as monotherapy. As with any antidepressant, using it alone in bipolar depression risks a switch into mania or mixed states; the SNRI place in therapy described here is for unipolar depression, and the bipolar-depression algorithm belongs in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes.

HOLD THIS

Every SNRI blocks SERT and NET, but venlafaxine's noradrenergic action, and its blood-pressure rise, are dose-dependent (SSRI-like at 75 mg, NET engaged near 225 mg), so monitor blood pressure as you titrate and never stop it abruptly (short half-life, severe discontinuation syndrome).

MNEMONIC

"VDD-ML": Venlafaxine, Desvenlafaxine, Duloxetine, Milnacipran, Levomilnacipran

The five SNRIs in rough order of exam weight. Venlafaxine carries blood pressure and discontinuation; Desvenlafaxine is its less-CYP-dependent metabolite; Duloxetine owns pain and stress incontinence with a liver caution; Milnacipran and Levomilnacipran are the noradrenergic-leaning, fibromyalgia-associated tail.

4 . Tricyclic antidepressants

The **tricyclic antidepressants** (the **TCAs**) are the oldest effective antidepressant class, and although second-generation agents have displaced them from first line, they remain firmly on the exam because their pharmacology is the teaching template for the whole antidepressant syllabus: a wanted reuptake action bundled with three unwanted receptor blockades that generate the entire adverse-effect picture, and a cardiotoxicity that makes them lethal in overdose. On a guideline reading they are a **second-line** option for major depression (CANMAT 2016) and have specific evidence in treatment-resistant depression and, for clomipramine, in obsessive-compulsive disorder.

Why the class still matters. A resident must be able to say, in one breath, why a TCA works (reuptake blockade), why it is unpleasant (muscarinic, H1 and alpha-1 blockade), and why it kills (quinidine-like sodium-channel blockade in the myocardium). The receptor systems behind these actions are laid out in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the guideline-anchored place of the class within the depression algorithm is in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes.

4.1 Mechanism: reuptake blockade plus three off-target blockades

The wanted action. TCAs block the presynaptic serotonin transporter (SERT) and the noradrenaline transporter (NET), raising synaptic monoamine availability, exactly the shared final pathway of the SSRIs and SNRIs (Stahl 2021). **The unwanted actions.** Unlike the selective

agents, TCAs simultaneously block three off-target receptors, and this promiscuity, not the reuptake action, drives almost every adverse effect: **muscarinic (antimuscarinic)** blockade gives the anticholinergic set, **histamine H1** blockade gives sedation and weight gain, and **alpha-1 adrenergic** blockade gives orthostatic hypotension (Stahl 2021, Kaplan and Sadock 2024). A fourth, separate action, blockade of fast cardiac sodium channels, is what makes overdose dangerous and is covered in 4.6.

Muscarinic (M1) blockade
dry mouth, constipation, blurred vision, urinary hesitancy, tachycardia, cognitive slowing, delirium in the elderly

Histamine H1 blockade
sedation, drowsiness and appetite-driven weight gain

Alpha-1 adrenergic blockade
orthostatic (postural) hypotension, dizziness and reflex tachycardia

Fast sodium-channel blockade
the quinidine-like membrane-stabilising effect on the myocardium, dormant at therapeutic dose but lethal in overdose

4.2 Tertiary versus secondary amines

The structural distinction that predicts tolerability. **Tertiary amine** TCAs (amitriptyline, imipramine, clomipramine, doxepin, trimipramine) are more potent at all the off-target receptors and are therefore more anticholinergic, more sedating and more hypotensive. Their demethylated **secondary amine** metabolites and drugs (nortriptyline from amitriptyline, desipramine from imipramine) are relatively more noradrenergic and, crucially, **less anticholinergic and better tolerated** (Kaplan and Sadock 2024). Nortriptyline in particular has the least orthostatic hypotension of the class and desipramine is the least anticholinergic, which is why the secondary amines are preferred in the elderly.

RULE **Secondary before tertiary in the frail.** If a TCA is unavoidable in an older or medically compromised patient, choose a secondary amine (nortriptyline, desipramine): same reuptake efficacy, lighter anticholinergic and orthostatic load.

AGENT (INDIAN BRAND)	AMINE CLASS	SIGNATURE FEATURE	DOSE (MG/DAY)
Amitriptyline (Tryptomer)	tertiary	**most sedating and cardiotoxic; also pain and migraine prophylaxis**	75 to 200
Imipramine (Depsonil)	tertiary	the original TCA; childhood enuresis	75 to 200
Clomipramine (Anafranil)	tertiary	**most serotonergic; OCD**	up to 250
Nortriptyline	secondary	**best-tolerated; therapeutic window 50 to 150 ng/mL**	75 to 150
Desipramine	secondary	least anticholinergic	100 to 200

Tertiary amines are more sedating, anticholinergic and hypotensive; secondary amines are better tolerated and preferred in the elderly.

4.3 Amitriptyline: the sedating prototype

The workhorse tertiary amine. Amitriptyline (Tryptomer) is strongly serotonergic and noradrenergic but also the most anticholinergic, sedating and cardiotoxic, and it is one of the leading single-drug causes of death by overdose (Kaplan and Sadock 2024). Its sedation and analgesic action make it a standard low-dose agent for **chronic pain** and **migraine prophylaxis**, well below antidepressant doses. Antidepressant dosing runs up through the usual antidepressant range of **75 to 200 mg/day**, and up to 300 mg/day only under specialist supervision (Companion 2010), taken at night to exploit the sedation.

4.4 Imipramine and clomipramine

Imipramine, the original and the enuresis drug. Imipramine (Depsonil) was the first tricyclic; beyond depression it retains a niche use in childhood nocturnal **enuresis**, where the antidepressants (unlike anxiolytics) reduce bed-wetting (Shorter Oxford 2018). **Clomipramine, the serotonergic one.** Clomipramine (Anafranil) is the **most serotonergic** TCA and is the tricyclic with first-line-strength efficacy in obsessive-compulsive disorder (Lopez-Ibor, 1967; Shorter Oxford 2018): conventional TCAs are ineffective in OCD, clomipramine is the exception. Its OCD dosing climbs to a maximum around **250 mg/day** (Maudsley 2021). Because it is the most serotonergic, clomipramine carries the highest serotonin-syndrome risk of the class if combined with an MAOI or another serotonergic drug.

> **COMMON TRAP**
>
> Reaching for a "plain" TCA (amitriptyline, imipramine) for obsessive-compulsive disorder. Only **clomipramine**, the most serotonergic tricyclic, works in OCD; the others are essentially inactive against obsessions and compulsions.

4.5 Nortriptyline: best-tolerated, with a therapeutic window

The monitorable secondary amine. Nortriptyline is the best-tolerated TCA (least orthostatic hypotension, relatively low anticholinergic burden) and is the one TCA with a genuine

therapeutic window: efficacy tracks a plasma level of roughly **50 to 150 ng/mL**, and levels above the window are associated with loss of response and rising toxicity, so plasma-level monitoring is meaningfully used to guide dosing (Kaplan and Sadock 2024, Maudsley 2021). The average dose needed to reach about 100 ng/mL is near **75 mg/day** but varies widely, which is exactly why the level, not just the dose, is checked.

WORKED EXAMPLE

A 70-year-old with recurrent depression needs a TCA after two SSRIs failed. You choose nortriptyline (a secondary amine, least orthostatic), get a baseline ECG, start low, titrate every few days, and draw a plasma level after 5 to 7 days on a steady dose, aiming for the **50 to 150 ng/mL** window rather than pushing the milligram dose blind.

4.6 The adverse-effect set and the cardiotoxicity

The everyday adverse effects follow directly from the three off-target blockades in 4.1: anticholinergic effects (dry mouth, constipation, blurred vision, urinary retention, precipitation of narrow-angle glaucoma, delirium in the elderly), sedation, weight gain, and orthostatic hypotension, which is in fact the single most common reason for stopping a TCA (Kaplan and Sadock 2024). **The cardiotoxicity** is separate and more dangerous. TCAs have a **quinidine-like** (type 1A antiarrhythmic) membrane-stabilising action: by blocking fast cardiac sodium channels they slow intraventricular conduction, which shows on the ECG as **QRS widening** and QT prolongation and, at higher exposure, as ventricular arrhythmia and heart block (Kaplan and Sadock 2024). A pre-existing conduction delay, or a QTc of 450 msec or greater, is a contraindication, and an ECG should precede TCA use in the elderly or the cardiac patient.

50 to 150	450	75 to 200
NORTRIPTYLINE THERAPEUTIC WINDOW (NG/ML)	QTC CONTRAINDICATION THRESHOLD (MSEC)	CLASS ANTIDEPRESSANT RANGE (MG/DAY)

4.7 Key interactions

The two that matter for the exam. The most dangerous is the **TCA plus MAOI** combination: adding a large dose of a tricyclic to a patient already on a monoamine oxidase inhibitor can precipitate a serotonin syndrome or a fatal hypertensive reaction, so an adequate washout is mandatory (Kaplan and Sadock 2024). The second is **pharmacokinetic**: TCAs are cleared by cytochrome P450, and CYP2D6 inhibitors, notably fluoxetine, paroxetine, duloxetine and bupropion, raise TCA plasma levels (fluoxetine roughly triples desipramine levels), pushing an otherwise safe dose toward cardiotoxic territory. Enzyme inducers such as carbamazepine do the reverse and can make a therapeutic level unattainable. The CYP machinery is detailed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

TRAP **Co-prescribing a 2D6 inhibitor with a TCA and not rechecking the level.** Adding fluoxetine or paroxetine to a stable TCA can several-fold raise the tricyclic level and tip a well-tolerated dose into QRS-widening toxicity.

4.8 Overdose: the reason TCAs are feared

A small multiple of the daily dose can be lethal. Because the target population is depressed and at risk of self-harm, overdose lethality is the defining safety problem of the class: a tricyclic overdose of about **10 times the daily dose** can be fatal, and death is most often from cardiac toxicity, with seizures and respiratory depression also occurring (Kaplan and Sadock 2024). The mortality risk with TCAs in overdose is many-fold higher than with SSRIs. The **toxidrome** combines the anticholinergic picture (hot, dry, dilated, delirious, tachycardic, ileus, retention) with central nervous system depression and **seizures**, and the cardiac picture of a **wide QRS**, ventricular arrhythmia and **hypotension**.

The management headline. Secure the airway, get an urgent **ECG**, and give intravenous **sodium bicarbonate** for QRS widening (and for significant arrhythmia or hypotension): serum alkalinisation and a sodium load counteract the quinidine-like sodium-channel block. The rest is supportive, activated charcoal if early, benzodiazepines for seizures, fluids and pressors for hypotension. The full acute-emergency detail, including the wider poisoning and serotonin-syndrome frame, is in the Perinatal/women's mental health and emergency psychiatry notes.

HOLD THIS

A TCA overdose of about ten times the daily dose can be fatal, kills mainly through quinidine-like cardiotoxicity (wide QRS, arrhythmia, hypotension) plus seizures, and the antidote to the widened QRS is intravenous sodium bicarbonate.

4.9 Where the TCAs sit in the guidelines

Second-line, weighed against overdose risk. CANMAT (CANMAT 2016) places TCAs (amitriptyline, clomipramine and others) as a **second-line** monotherapy for major depression, behind the SSRIs and SNRIs, precisely because the newer agents are safer in overdose and better tolerated. The BAP (Cleare, 2015) makes the same point at guideline level, choose antidepressants that are better tolerated and safer in overdose first, and reserves TCAs and MAOIs for when first-line treatment has failed, while noting that TCAs have evidence for **superior efficacy in treatment-resistant depression** where serum levels can guide dosing. The place of the class in the wider stepped algorithm is set out in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes.

INDIA

TCAs remain widely and cheaply available in India: amitriptyline as Tryptomer, imipramine as Depsonil, clomipramine as Anafranil. Low cost keeps them in real-world use, which makes the overdose-lethality counselling in 4.8 and the prescribing rule below all the more important where supply and follow-up may be limited.

RULE **Weigh suicide risk before you prescribe.** TCAs are effective but dangerous in overdose (cardiotoxic), so assess suicide risk first and prefer a safer agent, or dispense small quantities, in anyone at risk.

TRAP **Handing an actively suicidal patient a large quantity of a TCA.** A month's supply of amitriptyline is a lethal stockpile; this is the classic, avoidable prescribing error of the class.

MNEMONIC

TCA overdose: the 3 Cs plus Seize

Convulsions (seizures), **C**oma (CNS depression), **C**ardiotoxicity (wide QRS, arrhythmia, hypotension), on a background of anticholinergic delirium. QRS widening is answered by sodium bicarbonate.

GOOD TO REMEMBER

- **TCA class:** SERT and NET reuptake blockade drives efficacy; muscarinic, H1 and alpha-1 blockade drives the adverse effects; second-line for depression, dangerous in overdose.
- **Tertiary vs secondary amine:** secondary amines (nortriptyline, desipramine) are less anticholinergic and better tolerated; prefer them in the elderly.
- **Amitriptyline (Tryptomer):** sedating, most anticholinergic and cardiotoxic tertiary amine; also used for chronic pain and migraine prophylaxis; antidepressant range 75 to 200 mg/day.
- **Imipramine (Depsonil):** the original TCA; niche use in childhood nocturnal enuresis.
- **Clomipramine (Anafranil):** the most serotonergic TCA; first-line-strength for OCD, up to about 250 mg/day; highest serotonin-syndrome risk with MAOIs.
- **Nortriptyline:** best-tolerated (least orthostatic); therapeutic window 50 to 150 ng/mL, so plasma-level monitoring guides dosing.
- **Cardiotoxicity:** quinidine-like sodium-channel block, QRS widening, arrhythmia; ECG before use, avoid if QTc 450 msec or more.
- **Overdose:** about 10 times the daily dose can be fatal; discriminator is a wide QRS; first management step is ECG plus intravenous sodium bicarbonate.

5 . Monoamine oxidase inhibitors

The **monoamine oxidase inhibitors** (the **MAOIs**) were the first effective antidepressants, and although they have been pushed to a late line by their diet and interaction hazards, they remain firmly on the exam for two reasons: the **tyramine (cheese) reaction** and the **serotonergic interaction** are the most examinable drug-safety stories in the whole antidepressant syllabus, and the class retains a real place in atypical and treatment-resistant depression. A resident must be able to say, in one breath, why they work (they block monoamine breakdown), why the diet matters (dietary tyramine is normally destroyed by gut MAO-A), and why they must never be co-prescribed with a serotonergic drug without a washout.

Why the class still matters. The monoamine oxidase enzyme and the monoamine pathways it acts on are laid out in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the guideline-anchored place of the class within the depression algorithm is in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes. Here the teaching is the pharmacology: the mechanism, the agents, the tyramine reaction, the drug interactions and the mandatory washout intervals.

5.1 Mechanism: irreversible non-selective inhibition of MAO

The target. Monoamine oxidase is the mitochondrial enzyme that oxidatively deaminates the monoamines. It exists as two isoforms: **MAO-A** preferentially metabolises serotonin, noradrenaline and dietary tyramine, and **MAO-B** preferentially metabolises phenylethylamine, while both isoforms handle dopamine and tyramine (Stahl 2021, Companion 2010). **The action.** The classical agents produce **irreversible non-selective inhibition of MAO-A and MAO-B**, so monoamine breakdown is blocked and synaptic serotonin, noradrenaline and dopamine all rise, which is the antidepressant action. Because the inhibition is irreversible, the effect persists until new enzyme is synthesised, which takes about two weeks and is precisely why the washout intervals in 5.6 are so long (Kaplan and Sadock 2024).

RULE **Irreversible means think in weeks, not half-lives.** Enzyme activity returns only as new MAO is made (about two weeks), so the drug's danger outlasts its plasma clearance.

5.2 The agents: irreversible, reversible and transdermal

The irreversible non-selective agents. Phenelzine, tranylcypromine and isocarboxazid are the classical irreversible MAOIs. Phenelzine and isocarboxazid are hydrazines (with a small hepatotoxicity risk); tranylcypromine is a non-hydrazine with an amphetamine-like structure and can be activating (Kaplan and Sadock 2024). **The reversible agent.** Moclobemide is a **reversible inhibitor of MAO-A** (a RIMA), and this is its defining safety advantage: because tyramine can competitively displace it from the enzyme, moclobemide is much safer for the tyramine reaction and does not require adherence to a low-tyramine diet at normal doses (Shorter Oxford 2018). **The transdermal agent.** Transdermal selegiline (a patch) delivers drug systemically for antidepressant effect while, at the lowest patch strength, largely sparing gut MAO-A, so the lowest dose does not require dietary restriction; the higher patch strengths do (Kaplan and Sadock 2024).

AGENT	TYPE	SIGNATURE POINT	DOSE (MG/DAY)
Phenelzine	irreversible non-selective	**hydrazine; most weight gain of the class**	45 to 90
Tranylcypromine	irreversible non-selective	**amphetamine-like, activating**	20 to 60
Isocarboxazid	irreversible non-selective	hydrazine; least used	20 to 60
Moclobemide	**reversible MAO-A (RIMA)**	much safer for tyramine; no strict diet	300 to 600
Selegiline (transdermal)	patch	lowest strength spares gut MAO-A, no diet	see monograph

Phenelzine 45 to 90 and tranylcypromine 20 to 60 mg/day per CANMAT (2016); moclobemide 300 to 600 mg/day per CANMAT (2016).

GOOD TO REMEMBER

- **Phenelzine:** irreversible non-selective MAOI; signature is the tyramine (cheese) reaction and most weight gain of the class; hold the dose **45 to 90 mg/day** and that it is a third-line antidepressant.
- **Tranylcypromine:** irreversible non-selective MAOI, amphetamine-like and activating; signature is the hypertensive tyramine reaction; hold the dose **20 to 60 mg/day**.
- **Isocarboxazid:** irreversible non-selective hydrazine MAOI; signature is the same tyramine and serotonergic hazard; hold that it is third-line and least used.
- **Moclobemide:** reversible inhibitor of MAO-A (a RIMA); signature is that it is much safer for the tyramine reaction and needs no strict diet; hold the dose **300 to 600 mg/day** as a second-line agent (CANMAT 2016).
- **Transdermal selegiline:** patch delivery; signature is that the lowest strength spares gut MAO-A and needs no diet, higher strengths do; hold this as its whole reason for existing.

5.3 The tyramine reaction: the cheese reaction and hypertensive crisis

The mechanism. Dietary **tyramine** is a sympathomimetic amine normally broken down by gut and hepatic MAO-A before it reaches the circulation. On an irreversible MAOI that first-pass breakdown is abolished, so ingested tyramine passes into the circulation and drives a surge of noradrenaline release from sympathetic nerve terminals, producing a **hypertensive crisis** (Kaplan and Sadock 2024). This is the historical **cheese reaction**, first traced by Blackwell at the Maudsley to certain cheeses. **The clinical picture.** A tyramine crisis presents with a severe throbbing occipital headache, palpitations, nausea, vomiting, sweating and a dangerously raised blood pressure, and can progress to arrhythmia, stroke and intracranial haemorrhage (Kaplan and Sadock 2024).

WORKED EXAMPLE

A patient stable on phenelzine eats a mature cheddar and salami platter with a glass of red wine, and within the hour develops a pounding occipital headache, sweating and a blood pressure of 210/130. This is a tyramine-driven hypertensive crisis. The management headline is to treat it as a hypertensive emergency with a rapid-acting agent to lower the pressure, for example intravenous phentolamine, with the wider acute management set out in the Perinatal/women's mental health and emergency psychiatry notes.

The foods to avoid. The high-tyramine foods a patient on an irreversible MAOI must avoid include aged cheeses, aged and cured or fermented meats, improperly stored or spoiled meat, poultry or fish, broad (fava) bean pods, Marmite and other yeast extracts, sauerkraut, soy sauce and soybean condiments, and tap or draught beer (Kaplan and Sadock 2024). Fresh foods and moderate amounts of most everyday items are safe; it is the aged, cured, fermented and spoiled that concentrate tyramine.

MNEMONIC

AGED foods bite the MAOI patient

Aged cheese, Aged and cured meats, Alcohol (tap beer, some wines); Gone-off (spoiled) meat, poultry or fish; broad bEans (fava pods) and yeast extract; Draught beer and soy or fermented (sauerkraut) condiments. The unifying theme is anything Aged, fermented, cured or spoiled, because that is where tyramine accumulates.

5.4 The serotonergic interaction and serotonin syndrome

The most dangerous drug combination. Combining an MAOI with a serotonergic drug can precipitate a potentially fatal serotonin syndrome: the MAOI blocks serotonin breakdown while the second drug raises serotonin further, and the two together can produce runaway serotonergic activity (Stahl 2021, Kaplan and Sadock 2024). The offending drugs are the **SSRIs, SNRIs and clomipramine and other TCAs**, and among analgesics the classic culprits are **tramadol** and **pethidine (meperidine)**, both of which have serotonergic activity and are absolutely contraindicated with an MAOI (Kaplan and Sadock 2024). The clinical triad of serotonin syndrome is neuromuscular excitation (clonus, hyperreflexia, tremor, rigidity), autonomic instability (fever, tachycardia, sweating, diarrhoea) and altered mental state (agitation, confusion), detailed in the Perinatal/women's mental health and emergency psychiatry notes.

The sympathomimetic interaction. Separately, combining an MAOI with a **sympathomimetic** drug, amphetamines, methylphenidate, cocaine, and the sympathomimetic amines in some cold and cough remedies (pseudoephedrine, phenylephrine), produces the same noradrenaline-surge **hypertensive crisis** as the tyramine reaction, by the same final mechanism of unopposed pressor amine (Stahl 2021).

GOOD TO REMEMBER

- **Serotonin syndrome (the discriminator):** the triad is neuromuscular (clonus, hyperreflexia, rigidity), autonomic (fever, tachycardia, sweating) and mental-state (agitation, confusion) change; clonus and hyperreflexia are the features that distinguish it from neuroleptic malignant syndrome. First step: stop all serotonergic drugs and give supportive care.
- **The forbidden co-prescriptions:** never give an MAOI with an SSRI, SNRI, clomipramine, tramadol or pethidine (serotonin syndrome), nor with a sympathomimetic (hypertensive crisis).

5.5 The washout periods when switching

Why washout is non-negotiable. Because irreversible MAO inhibition lasts until new enzyme is made, an adequate **washout** must be observed in both directions when switching between an MAOI and a serotonergic drug, or a serotonin syndrome or hypertensive reaction can result even after the drug itself has cleared (Kaplan and Sadock 2024). **The intervals.** Allow at least **two weeks** after stopping an irreversible MAOI before starting a serotonergic drug (to let new enzyme regenerate), and at least **one week** (about five half-lives) after stopping most SSRIs and SNRIs before starting an MAOI, or two weeks after a tricyclic. The important exception is **fluoxetine**: because of its very long-acting active metabolite norfluoxetine, allow a longer

washout of about **five weeks** after stopping fluoxetine before starting an MAOI (Maudsley 2021, Kaplan and Sadock 2024).

2	1	5
OFF AN MAOI BEFORE A SEROTONERGIC DRUG (WEEKS)	OFF MOST SSRIS/SNRIS BEFORE AN MAOI (WEEKS)	OFF FLUOXETINE BEFORE AN MAOI (WEEKS)

RULE **Never combine an MAOI with a serotonergic drug, and observe the washout both ways.** At least two weeks off an MAOI before a serotonergic drug, and about five weeks off fluoxetine before an MAOI.

TRAP **Starting an SSRI too soon after an MAOI, or missing dietary tyramine counselling.** The commonest lethal errors are ignoring the washout when switching and failing to counsel the patient on the tyramine-rich foods to avoid.

5.6 Where the MAOIs sit in the guidelines

A later-line option. The MAOIs are reserved for **atypical depression** and **treatment-resistant depression** once better-tolerated, safer agents have failed. CANMAT (CANMAT 2016) places the irreversible agents, phenelzine **45 to 90 mg/day** and tranylcypromine **20 to 60 mg/day**, as **third-line** antidepressants, and moclobemide **300 to 600 mg/day**, the reversible MAO-A inhibitor, as a **second-line** option (CANMAT 2016). The BAP (Cleare, 2015) makes the same point at guideline level, reserve older TCAs and MAOIs for when first-line treatment has failed, and initiate an MAOI only with expertise in treating mood disorders. For the Indian Psychiatric Society position, the IPS depression guidance (Gautam et al., 2017) prioritises SSRIs and other second-generation agents first line and does not foreground the MAOIs; the specific IPS line-position for MAOIs could not be confirmed and is therefore not stated here. In pregnancy the MAOIs are to be avoided (CANMAT 2016). The place of the class in the wider stepped algorithm is set out in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes.

INDIA

The irreversible MAOIs (phenelzine, tranylcypromine) are little used in routine Indian practice and are not widely stocked, which is itself protective against the diet and interaction hazards. Where an MAOI is considered, it belongs in specialist hands for atypical or treatment-resistant depression, with explicit tyramine counselling and a documented washout when switching from or to a serotonergic drug.

HOLD THIS

Irreversible non-selective MAOIs (phenelzine, tranylcypromine, isocarboxazid) block tyramine breakdown, so aged, cured and fermented foods cause a hypertensive crisis, and a serotonergic drug causes serotonin syndrome; allow at least two weeks off an MAOI before a serotonergic drug and about five weeks off fluoxetine before an MAOI.

6 . Mirtazapine and bupropion

Two atypical antidepressants that a resident reaches for when an **SSRI is the wrong fit**. Each is a CANMAT Level-1 first-line agent for major depression, yet each is prescribed for its side-effect signature as much as its efficacy: mirtazapine (the **nassa**) is sedating and appetite-boosting, so it suits the depressed patient who cannot sleep and will not eat; bupropion (the **ndri**) is activating and pro-sexual, so it suits the fatigued, apathetic patient and the one whose SSRI killed libido. The mirror-image profiles are the exam point. The one hard caveat is bupropion's dose-dependent lowering of the **seizure threshold**.

Framing. This pair sits next to the SSRI and SNRI monographs; for how they slot into the guideline-anchored selection algorithm see the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes. For the receptor systems and CYP metabolism they act on, see the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes. Verify every dose and the seizure caveat: a wrong one is a prescribing error.

6.1 Mirtazapine: the NaSSA mechanism

Noradrenergic and specific serotonergic antidepressant. Mirtazapine (brand Mirtaz; generic mirtazapine) is a nassa that works without any reuptake blockade (Stahl 2021). It antagonises the **alpha-2 adrenergic autoreceptor** on noradrenergic neurons, removing the noradrenaline brake and so raising noradrenaline release; and it antagonises the **alpha-2 heteroreceptor** sitting on serotonin neurons, which disinhibits and raises serotonin release. On top of this dual monoamine boost it blocks **5-HT2A, 5-HT2C and 5-HT3** serotonin receptors and the **H1 histamine** receptor (Stahl 2021, Maudsley 2021). The receptor set explains the whole clinical picture below.

RULE **Reroute, don't block.** Mirtazapine raises noradrenaline and serotonin by antagonising alpha-2 auto- and heteroreceptors, not by inhibiting a reuptake pump, so it carries none of the SSRI serotonergic-tone side effects.

6.2 Mirtazapine: dose and the paradox of low doses

15 to 45 mg at night. Start **15 mg** in the evening, titrate every 1 to 2 weeks to a usual maximum of **45 mg/day** (Stahl 2021, CANMAT 2016). The counter-intuitive teaching point: **sedation and the antihistamine load are worse at the LOWER dose**. At 7.5 to 15 mg the H1 blockade dominates; as the dose climbs, the rising noradrenergic drive partly offsets the histaminergic sedation, so sedation may not worsen and can even ease (Stahl 2021). Breaking a 15 mg tablet to give 7.5 mg can therefore increase, not reduce, drowsiness.

PEARL

If a patient complains mirtazapine is too sedating at 15 mg, the fix is often to go UP, not down: 30 mg is frequently less sedating than 15 mg because added noradrenergic tone counters the H1 effect (Stahl 2021).

6.3 Mirtazapine: the adverse-effect profile that is the selling point

Sedation and appetite gain, with clean serotonergic tolerability. The signature effects are **sedation** (H1 antagonism) and **increased appetite and weight gain** (H1 plus 5-HT2C antagonism), both of which are the reason to choose it in a depressed patient with insomnia and poor appetite (Stahl 2021, Maudsley 2021). Because it does not raise synaptic serotonin by reuptake blockade and it antagonises 5-HT2 and 5-HT3, it has **minimal sexual dysfunction** (5-HT2 sparing) and **minimal GI upset or nausea** (5-HT3 blockade, the same mechanism as ondansetron). Rare but examinable: dizziness, abnormal dreams, dry mouth, and a rare risk of low white cell count, so flu-like symptoms warrant a blood count (Stahl 2021).

RECEPTOR ACTION	CLINICAL CONSEQUENCE
Alpha-2 auto- and heteroreceptor antagonism	**antidepressant effect (raises noradrenaline and serotonin)**
H1 histamine block	**sedation and weight gain (both worse at low dose)**
5-HT2C block	appetite and weight gain
5-HT2A block	minimal sexual dysfunction; may aid sleep
5-HT3 block	minimal nausea and GI upset (anti-emetic)

Each mirtazapine side effect maps to a specific receptor it blocks (Stahl 2021).

15 to 45 MIRTAZAPINE DOSE (MG/DAY)	**20 to 40** MIRTAZAPINE HALF-LIFE (HOURS)

6.4 Mirtazapine: where it fits, and the interaction to hold

First-line for depression with insomnia and weight loss; a favoured add-on. CANMAT lists mirtazapine 15 to 45 mg/day as a Level-1 first-line antidepressant for major depression, singling out the patient with sleep disturbance (CANMAT 2016). It is a metabolised substrate of CYP2D6, 3A4 and 1A2 with no significant pharmacokinetic interactions of its own (Stahl 2021), which makes it an easy combination partner: added to an SNRI it forms the dual-action combination Stahl nicknames "California rocket fuel", and CANMAT rates mirtazapine or mianserin 30 to 60 mg/day added to an antidepressant as a second-line adjunct (CANMAT 2016). The one dangerous interaction to hold: like all monoaminergic antidepressants it can precipitate serotonin syndrome with an MAOI, so allow a 14-day washout after stopping an MAOI (Stahl 2021). For the acute management of serotonin syndrome see the Perinatal/women's mental health and emergency psychiatry notes.

GOOD TO REMEMBER

- **Mirtazapine (Mirtaz), mechanism:** NaSSA, alpha-2 auto- and heteroreceptor antagonist raising noradrenaline and serotonin, plus 5-HT2/5-HT3 and H1 block, no reuptake inhibition.
- **Mirtazapine, signature effect:** sedation and weight gain (worse at LOWER dose), with minimal sexual dysfunction and minimal nausea.
- **Mirtazapine, one to hold:** 15 to 45 mg/day at night, CANMAT first-line for depression with insomnia and poor appetite; 14-day washout with MAOIs (serotonin syndrome).

6.5 Bupropion: the NDRI mechanism

Norepinephrine-dopamine reuptake inhibitor. Bupropion (brand Bupron; generic bupropion, formerly amfebutamone) is an ndri that blocks the noradrenaline transporter and the dopamine transporter, raising noradrenaline and dopamine neurotransmission (Stahl 2021). Because the prefrontal cortex largely lacks dopamine transporters and clears dopamine via the noradrenaline pump, blocking that pump also lifts prefrontal dopamine. It has essentially **no direct serotonergic action**, which is why its side-effect profile is the mirror image of the SSRIs: it is **activating**, not sedating. It is also a CYP2D6 inhibitor, a fact that matters for interactions (Stahl 2021).

MNEMONIC

DA-NO-BUP

bupropion boosts DA and NA and has NO serotonin action, hence NO weight gain, NO sexual dysfunction, and NO sedation; but it does lower the seizure threshold.

6.6 Bupropion: dose and formulations

Three formulations, one first-line depression range. CANMAT lists bupropion **150 to 300 mg/day** as a Level-1 first-line NDRI for major depression (CANMAT 2016). The formulation determines the dosing schedule and the single-dose ceiling, which exists precisely to cap the seizure risk (Stahl 2021):

FORMULATION	RANGE (MG/DAY)	SCHEDULE	MAX SINGLE DOSE (MG)
Immediate-release (IR)	225 to 450	3 divided doses	**150**
Sustained-release (SR)	200 to 450	2 divided doses	**200**
Extended-release (XL)	150 to 450	once daily	450

Splitting the dose and capping the single dose limits the peak concentration that drives seizures (Stahl 2021).

6.7 Bupropion: the indications, including smoking cessation

Depression, SSRI-adjunct, and nicotine dependence. Beyond monotherapy for major depression, bupropion is the antidepressant of choice as an **adjunct for SSRI-induced sexual dysfunction** and for residual **fatigue, cognitive slowing and apathy** ("SSRI poop-out"), because it adds dopaminergic and noradrenergic drive without serotonergic burden (Stahl 2021). It is separately licensed for **smoking cessation** (as sustained-release bupropion, marketed for that indication as Zyban): begin it 1 to 2 weeks before the quit date, titrating to 150 mg twice daily, and it reduces craving (Stahl 2021).

RULE **Match the deficit to the drug.** Mirtazapine helps depression with insomnia and weight loss; bupropion helps depression with fatigue and sexual dysfunction. Choose by the residual-symptom profile.

6.8 Bupropion: low sexual dysfunction, low weight gain

The tolerability edge. Because it lacks serotonergic action, bupropion causes **little or no sexual dysfunction** and **little or no weight gain** (indeed it is weight-neutral to weight-reducing), and it is less likely to induce hypomania than some antidepressants (Stahl 2021). This is why it is the go-to switch or add-on for the SSRI-treated patient troubled by anorgasmia, low libido or antidepressant-associated weight gain. The trade-off is activation: insomnia, agitation, dry mouth, tremor and, at the extreme, the seizure risk that dominates its contraindications.

6.9 Bupropion: the seizure threshold caveat and contraindications

Dose-dependent lowering of the seizure threshold. The one caveat every examiner wants: bupropion lowers the **seizure threshold** in a **dose-dependent** way (Stahl 2021, Maudsley 2021). It is therefore **contraindicated in a current or past seizure disorder**; in a **current or past eating disorder** (anorexia or bulimia, where electrolyte disturbance and low body weight amplify the risk, the historical signal coming from high-dose immediate-release use in low-weight anorexia); and in a patient **abruptly discontinuing alcohol, sedatives or an anticonvulsant**, since withdrawal itself lowers the threshold (Stahl 2021). Also avoid with an MAOI and within 14 days of stopping one (hypertensive risk), and use caution combining with nicotine replacement (hypertension) (Stahl 2021).

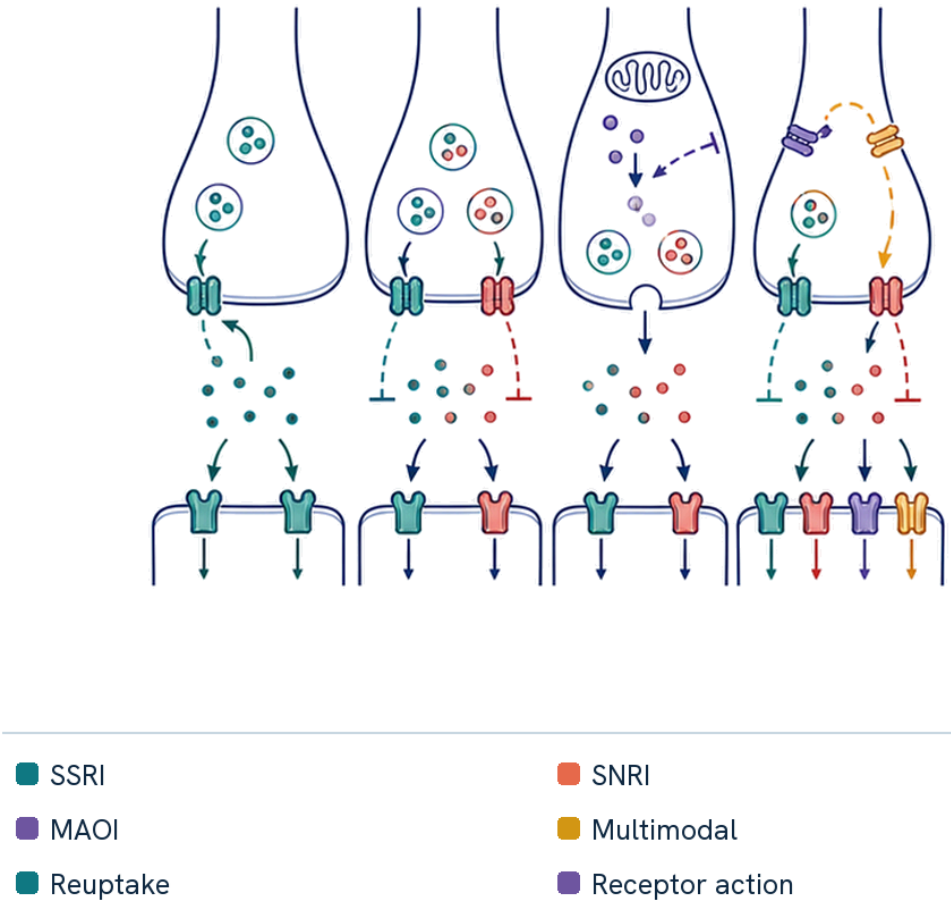


Fig 12.3 Antidepressant mechanism families at the synapse: selective serotonin reuptake inhibition, dual serotonin-noradrenaline reuptake inhibition, monoamine-oxidase inhibition and multimodal transporter-receptor action.

TRAP **The forbidden prescription.** Prescribing bupropion to a patient with a seizure disorder or an eating disorder, or during alcohol/sedative withdrawal, is the classic error: each independently lowers the seizure threshold that bupropion also lowers.

COMMON TRAP

"Low sexual dysfunction" makes bupropion tempting for the SSRI patient with a bulimia history, but the eating-disorder contraindication is absolute. Screen for a current or past eating disorder before any bupropion prescription.

INDIA

Bupropion (Bupron) and mirtazapine (Mirtaz) are both widely available in India. The Indian Psychiatric Society guidance on bipolar disorder notes that where an antidepressant must be used, bupropion is preferred over paroxetine (IPS guidelines); the Indian Psychiatric Society depression CPG (Gautam et al.) endorses second-generation antidepressants including these agents as first-line, though a mirtazapine- or bupropion-specific first-line row for depression could not be confirmed from the guideline database and is stated here at class level only.

GOOD TO REMEMBER

- **Bupropion (Bupron), mechanism:** NDRI, blocks noradrenaline and dopamine reuptake, activating, no serotonergic action, a CYP2D6 inhibitor.
- **Bupropion, signature caveat:** dose-dependent lowering of the seizure threshold, contraindicated in seizure disorders, eating disorders and abrupt alcohol/sedative withdrawal.
- **Bupropion, one to hold:** 150 to 300 mg/day, CANMAT first-line for depression and adjunct for SSRI-induced sexual dysfunction and fatigue; licensed (SR) for smoking cessation, started 1 to 2 weeks before the quit date.

HOLD THIS

Mirtazapine (NaSSA, alpha-2 antagonist) sedates and grows appetite with clean sexual and GI tolerability, best for depression with insomnia and weight loss; bupropion (NDRI) activates with no sexual dysfunction or weight gain, best for fatigue and SSRI-induced sexual dysfunction and for smoking cessation, but its dose-dependent lowering of the seizure threshold forbids it in seizure and eating disorders.

7 . Newer and multimodal antidepressants

A compact fold covering the agents that sit outside the SSRI, SNRI, TCA and MAOI classes yet keep appearing in exams because each carries one signature receptor mechanism and one signature caveat. The theme is **receptor engineering beyond simple reuptake**: two **multimodal** agents that add direct receptor actions to serotonin reuptake block, one melatonergic agent that resets the body clock, one sedating serotonin modulator repurposed for sleep, and one frankly atypical drug with a glutamate-and-opioid mechanism. Learn each as mechanism plus the one adverse effect the examiner is hunting for.

Framing. These are the "others" beside the SSRI and SNRI monographs; for how each slots into the guideline-anchored selection algorithm see the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes. For the serotonin receptor subtypes and CYP metabolism these agents act on, see the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes. Two facts are CRITICAL and verified below: agomelatine needs scheduled liver function monitoring, and trazodone causes priapism.

7.1 Vortioxetine and vilazodone: the multimodal serotonin modulators

An SSRI backbone plus direct receptor actions. Both are serotonin modulator antidepressants that block the serotonin transporter (SERT), the same pump the SSRIs act on, but add clinically meaningful action at specific 5-HT receptor subtypes (Stahl 2021, K&S 2024). Vortioxetine

(generic vortioxetine) is the fuller **multimodal** agent: SERT reuptake inhibitor, full agonist at 5-HT1A, partial agonist at 5-HT1B, and antagonist at 5-HT3, 5-HT7 and 5-HT1D (K&S 2024). Vilazodone (generic vilazodone) is narrower: an SSRI combined with 5-HT1A partial agonism, the same 5-HT1A property that makes buspirone anxiolytic, which is why Stahl files it as a SPARI (serotonin partial agonist reuptake inhibitor) (Stahl 2021). The added receptor actions are what differentiate the tolerability and, for vortioxetine, the cognitive signal.

RULE **Reuptake plus receptor.** A multimodal serotonin modulator does two things at once, block SERT and directly hit a named 5-HT receptor; the direct receptor action is what sets its side-effect profile apart from a plain SSRI.

7.2 Vortioxetine: dose, the pro-cognitive signal, and dose-dependent nausea

10 to 20 mg once daily, a first-line multimodal agent. CANMAT lists vortioxetine **10 to 20 mg/day** as a Level-1 first-line antidepressant for major depression (CANMAT 2016). PET occupancy of SERT reaches about 80% only at the 20 mg dose, so 10 to 20 mg is the effective band (K&S 2024). Its distinctive claims: a **pro-cognitive signal**, an improvement in processing speed, attention and executive function that trials suggest is partly independent of the antidepressant effect (attributed to its 5-HT7 and 5-HT3 antagonism and 5-HT1A agonism); a comparatively **lower rate of sexual dysfunction** than SSRIs; and a favourable cardiac profile with no meaningful effect on QT (Maudsley 2021, K&S 2024). The dominant adverse effect is **dose-dependent nausea**, driven by its serotonergic load, usually early and transient. It is a CYP2D6 substrate with a long **66-hour** half-life, so a strong 2D6 inhibitor roughly doubles levels and calls for a dose reduction, and a 14-day gap is needed before starting an MAOI (Stahl 2021, K&S 2024).

WORKED EXAMPLE

A depressed accountant with prominent complaints of "brain fog", slowed thinking and SSRI-related anorgasmia is a rational fit for vortioxetine 10 mg/day, uptitrated to 20 mg: the pro-cognitive signal targets the cognitive complaint and the lower sexual-dysfunction rate addresses the anorgasmia. Warn about early nausea and take it after food if needed (Stahl 2021, K&S 2024).

7.3 Vilazodone: dose, titration and the GI trade-off

20 to 40 mg once daily, titrated slowly with food. CANMAT places vilazodone **20 to 40 mg/day** as a second-line antidepressant, started at 10 mg and titrated up over about 2 weeks, taken **with food** to ensure absorption (CANMAT 2016, K&S 2024). The 5-HT1A partial agonism gives a relatively lower rate of sexual dysfunction and weight gain than pure reuptake blockers, but the price is **gastrointestinal**: diarrhoea and nausea are the commonest adverse effects, which is exactly why the slow titration and food rule exist, to blunt the GI burden (K&S 2024). It has no clinically significant effect on cardiac conduction. Head-to-head network meta-analyses find no clear efficacy advantage of vilazodone or vortioxetine over older antidepressants, which keeps vilazodone in the second line (Maudsley 2021).

10 to 20	20 to 40	66
VORTIOXETINE (MG/DAY)	VILAZODONE (MG/DAY)	VORTIOXETINE HALF-LIFE (HOURS)

GOOD TO REMEMBER

- **Vortioxetine, mechanism:** multimodal serotonin modulator, SERT reuptake inhibitor plus 5-HT1A agonist and 5-HT3/5-HT7 antagonist; a pro-cognitive signal.
- **Vortioxetine, signature effect and one to hold:** dose-dependent nausea and lower sexual dysfunction; CANMAT first-line 10 to 20 mg/day, CYP2D6 substrate, 66-hour half-life.
- **Vilazodone, mechanism:** an SSRI plus 5-HT1A partial agonism (SPARI); lower sexual dysfunction, but GI diarrhoea and nausea.
- **Vilazodone, one to hold:** CANMAT second-line 20 to 40 mg/day, titrate from 10 mg over 2 weeks and take with food.

7.4 Agomelatine: the melatonergic agonist that resets the body clock, and its liver caveat

An MT1/MT2 agonist and 5-HT2C antagonist. Agomelatine (generic agomelatine) is the uniquely **melatonergic** antidepressant: it is an agonist at the melatonin receptors **MT1** (mt1) and **MT2** (mt2), using the older M1/M2 nomenclature in some texts, and an antagonist at the serotonin **5-HT2C** (5-ht2c) receptor (K&S 2024, Stahl 2021). The MT1/MT2 agonism resynchronises circadian rhythm, restoring sleep architecture, while the 5-HT2C antagonism disinhibits frontocortical noradrenaline and dopamine, giving the antidepressant effect. CANMAT lists agomelatine **25 to 50 mg/day** at bedtime as a first-line agent, singled out for depression **with sleep disturbance**, and it has a low rate of sexual dysfunction, weight gain and discontinuation symptoms (CANMAT 2016). The defining caveat is **hepatotoxicity**: dose-related transaminase rises, and rare hepatitis and hepatic failure, mostly in the first months (Maudsley 2021).

The one monitoring rule. Agomelatine mandates **liver function monitoring**: check LFTs at baseline and again at 3, 6, 12 and 24 weeks after starting, and at every dose increase, then as clinically indicated; **stop the drug if transaminases rise above 3 times the upper limit of normal**; and it is **contraindicated in hepatic impairment** including cirrhosis and active liver disease (Maudsley 2021). It is a CYP1A2 substrate, so a strong 1A2 inhibitor such as fluvoxamine or ciprofloxacin markedly raises levels and is contraindicated.

25 to 50	0, 3, 6, 12, 24	3x ULN
AGOMELATINE (MG/DAY)	LFT WEEKS AFTER STARTING	TRANSAMINASE STOP THRESHOLD

RULE **Agomelatine needs baseline and follow-up liver function tests.** LFTs at baseline, then 3, 6, 12 and 24 weeks and at each dose increase; stop if transaminases exceed 3 times the upper limit of normal.

TRAP **Forgetting the LFTs.** Starting agomelatine without baseline liver function monitoring, or omitting the follow-up bloods, is the classic error; the same trap in reverse is missing high-dose trazodone priapism below.

GOOD TO REMEMBER

- **Agomelatine, mechanism:** melatonergic MT1 and MT2 agonist plus 5-HT2C antagonist that resynchronises circadian rhythm; CANMAT first-line 25 to 50 mg/day, especially with sleep disturbance.
- **Agomelatine, signature caveat and one to hold:** hepatotoxicity, so liver function monitoring at baseline and 3, 6, 12, 24 weeks; stop if transaminases exceed 3x ULN; contraindicated in hepatic impairment.

7.5 Trazodone: the sedating SARI, and the priapism caveat

A serotonin antagonist/reuptake inhibitor used low-dose for sleep. Trazodone (generic trazodone) is a SARI serotonin modulator: a potent 5-HT2A antagonist with weak serotonin reuptake inhibition and, crucially, **alpha-1 adrenergic** and H1 histamine antagonism (K&S 2024). At full antidepressant doses CANMAT rates it a second-line agent at **150 to 300 mg/day**, but in practice it is used far more often at **low dose (25 to 100 mg at night) for insomnia**, where the H1 and 5-HT2A block deliver sedation without the dependence of a benzodiazepine (CANMAT 2016, K&S 2024). The signature caveat is priapism: the alpha-1 antagonism that also causes its orthostatic hypotension can produce prolonged, painful erection, a urological emergency requiring immediate attention (K&S 2024). It is a CYP3A4 substrate, so a strong 3A4 inhibitor raises levels.

TRAP **The priapism warning omitted.** Prescribing trazodone, even low-dose for sleep, without counselling a male patient that a prolonged or painful erection is a medical emergency needing urgent care is the classic trazodone error.

PEARL

Trazodone's alpha-1 antagonism is the common thread: it explains the orthostatic hypotension AND the priapism. The mnemonic is that trazodone can "drop the pressure and raise the wrong thing" (K&S 2024).

GOOD TO REMEMBER

- **Trazodone, mechanism:** SARI serotonin modulator, 5-HT2A antagonist with weak SERT block plus alpha-1 and H1 antagonism; sedating, hence widely used low-dose (25 to 100 mg) for insomnia.
- **Trazodone, signature caveat and one to hold:** priapism (alpha-1 antagonism), a urological emergency; antidepressant dose 150 to 300 mg/day, CANMAT second-line.

7.6 Tianeptine: the glutamatergic, opioid-modulating atypical antidepressant

A mechanism unlike any other antidepressant. Tianeptine (generic tianeptine) is a genuinely atypical antidepressant whose action is **glutamatergic** rather than classically monoaminergic: it potentiates AMPA-receptor function and promotes synaptic plasticity, reversing stress-induced hippocampal remodelling, and (paradoxically for an antidepressant) it enhances rather than blocks serotonin reuptake (New Oxford 2020). More recently it has been shown to act as a **mu-opioid receptor agonist**, which is now thought to underlie much of its acute effect (New Oxford 2020). It is dosed at **25 to 50 mg/day** and is not marketed in many countries, including the UK

and USA (Maudsley 2021). The examinable concern that flows directly from the opioid mechanism is **abuse potential**: at supratherapeutic doses tianeptine behaves as an opioid, and misuse and dependence have been reported.

RULE **Glutamate and opioid, not just monoamine.** Tianeptine's antidepressant action rests on AMPA/glutamatergic modulation plus mu-opioid agonism; that opioid action is exactly why it carries abuse potential.

GOOD TO REMEMBER

- **Tianeptine, mechanism:** atypical glutamatergic antidepressant, AMPA-receptor potentiator that promotes synaptic plasticity and enhances serotonin reuptake, plus mu-opioid receptor agonism.
- **Tianeptine, signature concern and one to hold:** abuse potential from its opioid action; dose 25 to 50 mg/day; not marketed in many countries.

INDIA

Among these agents, agomelatine and vortioxetine are marketed in India; low-dose trazodone is in routine use for insomnia. A specific Indian brand for vortioxetine (sometimes cited as Vortioxa) could not be confirmed from the parsed reference library, so the generic name is used here rather than an unverified brand. The Indian Psychiatric Society depression CPG (Gautam et al.) endorses newer second-generation antidepressants as first-line at class level, but an IPS agent-specific first-line row for these particular molecules could not be confirmed from the guideline database and is stated at class level only.

COMMON TRAP

Treating this whole group as interchangeable SSRIs. They are not: agomelatine demands scheduled LFTs, trazodone risks priapism, and tianeptine has genuine abuse liability. Each carries a caveat an SSRI does not.

HOLD THIS

Vortioxetine (multimodal, SERT plus 5-HT1A agonism and 5-HT3/5-HT7 antagonism, pro-cognitive, dose-dependent nausea, 10 to 20 mg/day first-line) and vilazodone (SSRI plus 5-HT1A partial agonism, GI-heavy, 20 to 40 mg/day) are the multimodal serotonin modulators; agomelatine (melatonergic MT1/MT2 agonist and 5-HT2C antagonist, 25 to 50 mg/day) resets the body clock but needs liver function monitoring at baseline and 3, 6, 12, 24 weeks with a stop at transaminases above 3x ULN; trazodone (sedating SARI) is used low-dose for insomnia and can cause priapism; tianeptine is a glutamatergic, mu-opioid-agonist atypical with abuse potential.

8 . Serotonin syndrome and the NMS differential

Of all the complications an antidepressant can cause, **serotonin syndrome** is the one the exam asks about most reliably, because it is the drug-safety story that ties the whole antidepressant syllabus together: it is what happens when serotonergic drive is pushed too hard, usually by a combination of agents, and the single most dangerous combination, an MAOI plus a serotonergic drug, is exactly the interaction taught in the monoamine oxidase inhibitor topic. A resident must

be able to recite the triad, name the diagnostic criteria (the **hunter criteria**), give the first management step, and, above all, separate it cleanly from **neuroleptic malignant syndrome**, its dopamine-blocker mimic.

Why the differential is the whole point. Serotonin syndrome and neuroleptic malignant syndrome are both hyperthermic, rigid, autonomically unstable, altered-consciousness emergencies, and they are constantly confused. The examiner rewards the candidate who can name the one discriminator that tells them apart. The pharmacology of the serotonergic and dopaminergic pathways is in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the wider acute management of both syndromes (cooling, sedation, restraint, the medical emergency frame) is set out in the Perinatal/women's mental health and emergency psychiatry notes. Here the teaching is recognition, criteria, first management and the differential.

Discriminator	Serotonin syndrome serotonergic excess	Neuroleptic malignant syndrome dopamine blockade
Onset speed	over hours, rapid	over days, slower
Trigger drug	a serotonergic drug or combination SSRI plus MAOI, tramadol, linezolid	a dopamine blocker (antipsychotic), or abrupt dopamine-agonist withdrawal
Neuromuscular the pivot	**clonus, hyperreflexia, tremor, myoclonus**	**lead-pipe rigidity, bradyreflexia**
Bowel sounds	hyperactive	normal or reduced
Pupils	dilated (mydriasis)	normal
Course	resolves within about a day if stopped	evolves over days, slow recovery
Specific drug	cyproheptadine	dantrolene, bromocriptine
First step	**stop the serotonergic agent**	**stop the antipsychotic**

Fig 12.4 Serotonin syndrome versus neuroleptic malignant syndrome. The pivot is the neuromuscular sign: clonus and hyperreflexia point to serotonin syndrome, lead-pipe rigidity with hyporeflexia to NMS. Serotonin syndrome comes on over hours from a serotonergic combination, resolves fast once the drug is stopped and responds to cyproheptadine; NMS comes on over days from a dopamine blocker, evolves slowly and is treated with dantrolene or bromocriptine.

8.1 Pathophysiology: serotonergic excess, usually from a combination

The mechanism. Serotonin syndrome is a state of excessive serotonergic activity at central and peripheral serotonin receptors, chiefly the postsynaptic 5-HT2A and 5-HT1A receptors, produced by drugs that raise synaptic serotonin (Shorter Oxford 2018, Stahl 2021). It is extremely rare with a single agent at a recommended dose and is almost always the product of a **combination** of serotonergic drugs, or of an overdose (Kaplan and Sadock 2024). **The most dangerous combination.** The classic and most lethal pairing is an **MAOI plus a serotonergic drug**: the MAOI blocks serotonin breakdown while the second agent, an SSRI, an SNRI, clomipramine, tramadol or pethidine, drives serotonin higher, and together they produce runaway 5-HT toxicity (Shorter Oxford 2018, Stahl 2021). Other precipitants added to an SSRI

include a second serotonergic antidepressant, lithium, tryptophan, triptans, linezolid, methylene blue and the recreational drug ecstasy.

RULE **Serotonin syndrome is usually a combination, and MAOI-plus-serotonergic is the deadliest.** A single serotonergic drug at a normal dose rarely does it; two together, above all an MAOI, is the danger.

8.2 The clinical triad: neuromuscular, autonomic, mental-state

The three-part picture. Serotonin syndrome presents as a triad, and holding the triad is the fastest route to recognition (Shorter Oxford 2018, Stahl 2021). The first arm is **neuromuscular excitation**: clonus (spontaneous, inducible and ocular clonus, the single most characteristic sign), hyperreflexia, myoclonus, tremor and rigidity, and the neuromuscular findings are typically more prominent in the lower limbs. The second arm is **autonomic instability**: hyperthermia, tachycardia, diaphoresis, **mydriasis** (dilated pupils) and hyperactive bowel sounds with diarrhoea. The third arm is **altered mental state**: agitation, restlessness, anxiety and, in severe cases, confusion progressing to coma. Onset is **rapid, over hours** of the offending exposure.

clonus	hours	3
MOST CHARACTERISTIC NEUROMUSCULAR SIGN	TYPICAL ONSET AFTER THE TRIGGER	ARMS OF THE TRIAD (NEUROMUSCULAR, AUTONOMIC, MENTAL)

MNEMONIC

The three A's plus the clonus

Think Agitation (mental state), Autonomic instability (hyperthermia, tachycardia, diaphoresis, mydriasis, hyperactive bowel sounds) and Augmented neuromuscular activity (clonus, hyperreflexia, tremor, rigidity). The one sign that clinches it and that NMS does not share is clonus with hyperreflexia.

8.3 Diagnostic criteria: the hunter criteria and the older Sternbach criteria

The Hunter criteria. The hunter criteria (the Hunter Serotonin Toxicity Criteria, Dunkley et al. 2003) are the more specific and now-preferred diagnostic rule. In a patient who has taken a serotonergic agent, the diagnosis is made if any one of the following is present: spontaneous clonus; inducible clonus plus agitation or diaphoresis; ocular clonus plus agitation or diaphoresis; tremor plus hyperreflexia; or hypertonia plus a temperature above 38 degrees Celsius plus ocular or inducible clonus (Kaplan and Sadock 2024). The recurring anchors, clonus, agitation, diaphoresis, tremor and hyperreflexia, are why clonus and hyperreflexia are the exam discriminators. **The older Sternbach criteria.** The **Sternbach criteria** (Sternbach 1991) are the original, broader rule: a recent addition or dose increase of a serotonergic agent plus at least three of a list of features (agitation, myoclonus, hyperreflexia, diaphoresis, shivering, tremor, diarrhoea, incoordination, fever, mental-state change), with other causes and a recent neuroleptic excluded. Sternbach is more sensitive but less specific than Hunter.

TRAP **Treating serotonin syndrome as a diagnosis of exclusion only.** It is a clinical diagnosis anchored on clonus in a patient on a serotonergic drug; there is no confirmatory blood test, so waiting for one wastes time.

8.4 Management: stop the drug, support, benzodiazepines, cyproheptadine

The first and most important step. Stop all serotonergic agents immediately; if a 5-HT syndrome develops, all serotonergic medication should be withdrawn at once (Shorter Oxford 2018). **Supportive care.** Give supportive care with intravenous fluids, continuous monitoring and active **cooling** for hyperthermia, which is the feature that kills; the wider acute emergency frame, aggressive cooling, sedation and the management of severe hyperthermia, is set out in the Perinatal/women's mental health and emergency psychiatry notes. **Benzodiazepines.** Use a benzodiazepine (for example lorazepam or diazepam) to control agitation, tremor and the neuromuscular hyperactivity and to reduce the hyperadrenergic state. **The specific antidote.** In moderate-to-severe cases give cyproheptadine, a 5-HT2A antagonist, as the serotonin-antagonist antidote (Maudsley 2021, Kaplan and Sadock 2024); it is given orally, a common regimen being an initial 12 mg then 2 mg every two hours if symptoms continue, to a ceiling around 32 mg in 24 hours. Most cases resolve within about 24 hours of stopping the trigger and starting supportive care.

WORKED EXAMPLE

A patient on phenelzine is inadvertently started on tramadol for back pain and within hours becomes agitated and sweaty, with a temperature of 39 degrees Celsius, dilated pupils, a tachycardia of 130, brisk reflexes and sustained ankle clonus. This is serotonin syndrome from an MAOI-serotonergic combination. Stop both drugs at once, cool the patient and give intravenous fluids, sedate with a benzodiazepine, and give cyproheptadine as the serotonin antagonist. The Hunter criteria are met by the spontaneous clonus alone.

GOOD TO REMEMBER

- **Serotonin syndrome (the feature):** serotonergic excess, usually a combination and most dangerously an MAOI plus a serotonergic drug; the triad is neuromuscular excitation (clonus, hyperreflexia, tremor, rigidity), autonomic instability (hyperthermia, tachycardia, diaphoresis, mydriasis, hyperactive bowel sounds) and altered mental state (agitation); onset is rapid over hours.
- **Hunter criteria (the discriminator):** in a patient on a serotonergic agent, diagnose on clonus (spontaneous, inducible or ocular) with agitation or diaphoresis, or tremor plus hyperreflexia; clonus and hyperreflexia are the signs that separate it from NMS.
- **Cyproheptadine (the first management after stopping the drug):** a 5-HT2A antagonist used as the serotonin-antagonist antidote in moderate-to-severe cases; the management sequence is stop the serotonergic agents, support and cool, benzodiazepine for agitation, then cyproheptadine.

8.5 The differential from neuroleptic malignant syndrome

Why they are confused. Serotonin syndrome and neuroleptic malignant syndrome share hyperthermia, muscular rigidity, autonomic instability and altered consciousness, and 5-HT neurotoxicity is occasionally confused with NMS at the bedside (Shorter Oxford 2018, Maudsley

2021). What separates them is the **trigger, the neuromuscular sign and the tempo**. Serotonin syndrome follows a serotonergic drug, comes on **rapidly over hours**, and is defined by **clonus** and **hyperreflexia** with hyperactive bowel sounds and mydriasis. Neuroleptic malignant syndrome follows a **dopamine-blocker** (an antipsychotic or another dopamine antagonist such as metoclopramide), comes on **slowly over days**, and is defined by **lead-pipe rigidity** with **hyporeflexia**, normal-to-sluggish bowel sounds, and a marked rise in creatine kinase, often above 1000 units per litre (Maudsley 2021). The one discriminator to carry into the exam is **clonus and hyperreflexia (serotonin syndrome) versus lead-pipe rigidity and hyporeflexia (NMS).**

FEATURE	SEROTONIN SYNDROME	NEUROLEPTIC MALIGNANT SYNDROME
Trigger	a serotonergic drug (SSRI, SNRI, MAOI combination, tramadol)	a dopamine-blocker (antipsychotic, metoclopramide)
Onset / tempo	rapid, over hours	slow, over days
Neuromuscular sign (the discriminator)	**clonus and hyperreflexia**	**lead-pipe rigidity and hyporeflexia**
Pupils	mydriasis	normal
Bowel sounds	hyperactive, diarrhoea	normal or reduced
Creatine kinase	usually mild rise	marked rise, often above 1000 units per litre
Resolution	fast, often within about 24 hours of stopping the drug	slow, over days to weeks
Specific agent	cyproheptadine (5-HT2A antagonist)	bromocriptine and dantrolene

The serotonin-syndrome versus NMS grid: clonus and hyperreflexia against lead-pipe rigidity is the one discriminator (Shorter Oxford 2018, Maudsley 2021).

RULE **Clonus and hyperreflexia point to serotonin syndrome; lead-pipe rigidity points to NMS.** A serotonergic trigger over hours with brisk clonus is serotonin syndrome; a dopamine-blocker over days with lead-pipe rigidity and a high CK is NMS.

TRAP **Missing serotonin syndrome after an MAOI-serotonergic combination, or confusing it with NMS.** The commonest errors are failing to recognise 5-HT toxicity when an MAOI meets a serotonergic drug, and mislabelling clonus-with-hyperreflexia as NMS.

INDIA

Tramadol and pethidine are widely and casually co-prescribed for pain in Indian practice, so the highest-risk everyday scenario is a patient on an antidepressant (or, worse, an MAOI) who is given tramadol for a musculoskeletal complaint. Cyproheptadine is freely available in India as an oral antihistamine (commonly stocked as Ciplactin or Practin), which makes the antidote easy to obtain when moderate-to-severe serotonin syndrome is recognised.

GOOD TO REMEMBER

- **The one discriminator:** clonus and hyperreflexia mean serotonin syndrome; lead-pipe rigidity and hyporeflexia mean neuroleptic malignant syndrome.
- **Serotonin syndrome:** serotonergic trigger, rapid onset over hours, clonus, hyperreflexia, mydriasis, hyperactive bowel sounds, usually mild CK rise; first step stop the drug, then support/cool, benzodiazepine, cyproheptadine.
- **Neuroleptic malignant syndrome:** dopamine-blocker trigger, slow onset over days, lead-pipe rigidity, hyporeflexia, marked CK rise (often above 1000 units per litre); stop the antipsychotic, support, benzodiazepine, then bromocriptine and dantrolene.

HOLD THIS

Clonus and hyperreflexia after a serotonergic drug (rapid, over hours) is serotonin syndrome; lead-pipe rigidity and hyporeflexia after a dopamine-blocker (slow, over days) with a high CK is neuroleptic malignant syndrome, and the first step in serotonin syndrome is to stop the serotonergic agents and give cyproheptadine.

9 . Antidepressant discontinuation syndrome

When an antidepressant taken continuously for at least a few weeks is stopped or reduced, a recognisable cluster of somatic and psychological symptoms can emerge within a few days. This is **antidepressant discontinuation syndrome**, and the examiner tests three things: that you can name the cluster (the **finish** mnemonic), that you can predict who is at risk (the short-half-life agents), and that you can tell it apart from a true relapse of depression. Getting the last point wrong is the classic clinical error, because the fix for discontinuation is a slower taper and reassurance, whereas the fix for relapse is restarting treatment.

The framing that scores. Discontinuation symptoms are a pharmacological withdrawal phenomenon from an abrupt fall in synaptic serotonin availability, not a sign of addiction or drug dependence: there is no craving, no compulsive use and no dose escalation, and the syndrome is self-limiting. The organising fact is that onset, severity and duration all track the **half-life** of the agent, so paroxetine and venlafaxine are the worst offenders and fluoxetine the least (Maudsley 2021; Kaplan 2024). The receptor and cytochrome background sits in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the perinatal analogue is cross-referred to the Perinatal/women's mental health and emergency psychiatry notes.

9.1 The syndrome and the FINISH cluster

The setup. The patient has usually been on the antidepressant for a month or more, and symptoms begin within a few days of stopping, halving the dose, or even missing doses in a poor adherer (Kaplan 2024). The symptoms are typically mild and **self-limiting over one to two weeks**, though for some patients and some agents they last longer.

The cluster. The high-yield handle is **finish** (use "finish"): **F**lu-like symptoms (lethargy, myalgia, sweating), **I**nsomnia (often with vivid dreams), **N**ausea, **I**mbalance (dizziness, lightheadedness, vertigo), **S**ensory disturbances (paraesthesiae and the classic **electric-shock** or "brain-zap"

sensations), and **H**yperarousal (anxiety, irritability, agitation). The sensory "brain zaps", brief intracranial electric-shock feelings often triggered by eye movement, are close to pathognomonic and rarely feature in a depressive relapse (Maudsley 2021; Kaplan 2024).

MNEMONIC

FINISH

Flu-like, Insomnia, Nausea, Imbalance, Sensory disturbances (the electric-shock "brain zaps"), Hyperarousal/anxiety. The six-symptom cluster of antidepressant discontinuation syndrome, coming on within days of stopping and settling over one to two weeks.

RULE **Taper antidepressants slowly, especially the short-half-life agents.** A gradual reduction over weeks, or a switch to fluoxetine to taper, prevents most discontinuation symptoms.

9.2 Risk factors: half-life drives everything

The agent. Onset and severity correlate inversely with half-life. Paroxetine (Pexep) and venlafaxine (Venlor) are the worst because both have short half-lives with no meaningful active metabolite, and paroxetine adds a high serotonin-transporter affinity and anticholinergic rebound; short-half-life agents produce symptoms within a day or two of stopping (Maudsley 2021). Fluoxetine (Fludac) is the least likely to cause a discontinuation syndrome because its parent drug (2 to 3 days) and its active metabolite norfluoxetine (about 2 weeks) mean the drug effectively **self-tapers**; when symptoms do occur they may be delayed by 2 to 6 weeks (Maudsley 2021).

The other two levers. A **longer duration** of treatment and, above all, **abrupt cessation** raise the risk; a higher dose and a rapid taper method compound it (Maudsley 2021). Discontinuation is reported to some degree with every antidepressant class, including SNRIs, TCAs and MAOIs, not just the SSRIs.

AGENT (INDIAN BRAND)	HALF-LIFE	DISCONTINUATION RISK
Paroxetine (Pexep)	Short (~21 h), no active metabolite	**Worst: fast onset, prominent brain-zaps**
Venlafaxine (Venlor)	Short (~5 h; ODV ~11 h)	**Worst: notoriously severe, dizziness prominent**
Most other SSRIs/SNRIs	Intermediate	Moderate, dose- and taper-dependent
Fluoxetine (Fludac)	Long (norfluoxetine ~2 wk)	**Least: self-tapers; onset may be delayed**

Discontinuation risk tracks half-life inversely: shortest-half-life agents (paroxetine, venlafaxine) are the worst, the long-half-life fluoxetine the least (Maudsley 2021; Kaplan 2024).

9.3 Distinguishing discontinuation from relapse, and management

The discriminator. Two features separate **discontinuation** (use "discontinuation") from a depressive relapse. First, **timing**: discontinuation symptoms appear fast, within a few days of

stopping or reducing, and resolve over one to two weeks, whereas a genuine relapse builds gradually over weeks and does not remit on its own. Second, the **somatic and sensory quality**: the flu-like malaise, imbalance and electric-shock paraesthesiae of discontinuation are not part of a depressive syndrome, and a fast, dramatic improvement within hours of a single reinstated dose points firmly to discontinuation rather than relapse (Maudsley 2021; Kaplan 2024).

Management. The core intervention is a slow **taper** (use "taper") over weeks (in practice, weeks to months for a short-half-life agent, with hyperbolic small reductions near the bottom of the dose range), plus reassurance that the symptoms are self-limiting and are not a sign of addiction. If symptoms are already troublesome, reinstate the original antidepressant (or switch to fluoxetine and taper from there, exploiting its long half-life) until stable, then reduce more gradually. Reassurance and forewarning at the outset prevent much of the distress (Kaplan 2024).

TRAP **Mistaking discontinuation symptoms for a depressive relapse.** Restarting or escalating on the wrong call keeps the patient on a drug they were coming off; use timing and the somatic/sensory quality to tell them apart.

9.4 The perinatal analogue: neonatal adaptation syndrome

A related phenomenon follows late-pregnancy antidepressant exposure. The neonate, having been exposed transplacentally, can show a self-limiting **neonatal adaptation syndrome** after delivery, with jitteriness, irritability, feeding and respiratory difficulty and, occasionally, tremor, that mirrors an adult discontinuation picture and settles within days. The examiner's point is that abrupt withdrawal of the antidepressant before delivery is usually the wrong response, because it exposes the mother to relapse and postpartum depression; the fuller perinatal handling belongs to the Perinatal/women's mental health and emergency psychiatry notes.

1 to 2 wk	1 to 2 days	2 to 6 wk
TYPICAL DURATION, SELF-LIMITING	ONSET WITH SHORT-HALF-LIFE AGENTS	DELAYED ONSET WITH FLUOXETINE

HOLD THIS

Discontinuation symptoms come on within days, are captured by FINISH (with the "brain-zap" as the near-pathognomonic clue), are worst with paroxetine and venlafaxine and least with fluoxetine, and are treated by a slower taper and reassurance, not by treating a relapse.

GOOD TO REMEMBER

- **The cluster (FINISH):** Flu-like, Insomnia, Nausea, Imbalance, Sensory (electric-shock "brain zaps"), Hyperarousal, within days of stopping, self-limiting over **1 to 2 weeks**.
- **The discriminator:** fast onset plus somatic/sensory quality (brain-zaps, imbalance) mark discontinuation; a slow-building, purely mood picture marks relapse.
- **Worst agents:** paroxetine (Pexep) and venlafaxine (Venlor), short half-lives; fluoxetine (Fludac) least because it self-tapers.
- **First step:** taper slowly (or switch to fluoxetine to taper) and reassure; reinstate the agent if symptoms are severe. It is not addiction.

10 . Ketamine and esketamine

This is the glutamatergic corner of the antidepressant map, and it is a high-yield one because it breaks two things every resident is taught about depression. The first is the **monoamine model**: ketamine and esketamine do not touch the serotonin, noradrenaline or dopamine pumps as their primary act; they antagonise the glutamate NMDA (nmda) receptor. The second is the **therapeutic lag**: where a monoamine antidepressant is said to take weeks, these **rapid-acting** agents lift depressive symptoms and suicidal ideation within hours (K&S 2024, Maudsley 2021). That combination, a novel target and a rapid onset, is exactly what examiners probe, alongside the safety scaffolding the rapidity forces on you.

Framing. Treat this topic as two agents on one mechanism: racemic ketamine (intravenous, off-label) and esketamine, the S-enantiomer (intranasal, brand Spravato, licensed). For the receptor systems and the wider glutamate story, see the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; for where these agents sit in the treatment-resistant depression ladder and the CANMAT algorithm, see the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes; for the acute-suicidality assessment that flanks the licensed indication, see the Somatic-symptom, sexual, impulse-control disorders and suicide notes. Two facts are CRITICAL and verified below: the licensed indication is add-on esketamine for treatment-resistant depression (and for major depression with acute suicidal ideation), and it must be given under observation for dissociation and blood pressure.

10.1 The mechanism: NMDA antagonism, an AMPA burst and synaptogenesis

Block the brake, trigger a glutamate surge, grow synapses. Ketamine is a non-competitive (uncompetitive) antagonist at the NMDA receptor (K&S 2024, Maudsley 2021). The current model is a disinhibition cascade: NMDA blockade falls preferentially on GABAergic inhibitory interneurons, which normally suppress glutamate output; taking that brake off produces an acute cortical **glutamate surge** onto the pyramidal neuron (K&S 2024, Maudsley 2021). That surge activates postsynaptic **AMPA** (ampa) receptors, and the AMPA-throughput step drives brain-derived neurotrophic factor (BDNF) release, TrkB and mTOR activation, and downstream **synaptogenesis** and synaptic potentiation (K&S 2024). Because the antidepressant effect is carried by rapid neuroplasticity rather than by slow receptor down-regulation, it appears within hours, which is the direct **glutamatergic** reframing of depression: a disorder of impaired synaptic plasticity that a glutamate modulator can rapidly reverse.

RULE **NMDA off, AMPA on.** Ketamine works by antagonising NMDA receptors on inhibitory interneurons, which disinhibits a glutamate surge onto AMPA receptors and drives synaptogenesis; that plasticity, not monoamine reuptake block, is why the effect is rapid.

TRAP **Calling it a monoamine drug.** Ketamine has weak serotonergic, dopaminergic and opioid actions, but its rapid antidepressant effect is glutamatergic; framing it as "just another reuptake inhibitor" misses both the mechanism and the therapeutic-lag contrast the examiner wants.

10.2 The two agents: racemic ketamine and the S-enantiomer esketamine

Same target, different enantiomer, different regulatory status. Ketamine is a racemic mixture of two mirror-image enantiomers, (S)-ketamine and (R)-ketamine (arketamine); the S-enantiomer, esketamine, binds the NMDA receptor with roughly four times the affinity of the R-enantiomer (K&S 2024). Racemic ketamine is given **intravenously** and remains an **off-label** treatment for depression, drawing on its long licence as a dissociative anaesthetic (K&S 2024, Maudsley 2021). Esketamine was developed as an **intranasal** spray (brand Spravato) and is the licensed molecule (K&S 2024). A point of contrast worth holding: because esketamine is the more potent NMDA binder, it was the enantiomer taken to licence, yet head-to-head evidence suggests intravenous racemate is possibly at least as effective as intranasal esketamine (Maudsley 2021).

Ketamine (racemic)

50:50 S and R enantiomer mixture; intravenous, off-label for depression, anaesthetic licence.

Esketamine

the S-enantiomer, four-fold higher NMDA affinity; intranasal, brand Spravato, the licensed antidepressant.

Arketamine

the R-enantiomer; lower NMDA affinity, still investigational for depression.

10.3 The licensed indication and the treatment-resistant depression context

Add-on esketamine for treatment-resistant depression, and for major depression with acute suicidal ideation. Intranasal esketamine (Spravato) is licensed as an add-on to an oral antidepressant for **treatment-resistant depression**, defined by failure of at least two adequate antidepressant trials in the current episode, and separately for **major depression with acute suicidal ideation or behaviour** (K&S 2024, Maudsley 2021). It is not a monotherapy: the licence is as an add-on to an SSRI or SNRI. Racemic ketamine itself carries no depression licence and is used off-label (K&S 2024). At guideline level, CANMAT places **add-on intranasal esketamine** as a second-line adjunct for patients failing at least two adequate antidepressant trials, and **add-on intravenous racemic ketamine** as a second-line adjunct for a rapid antidepressant effect including rapid reduction of suicidal ideation, both with blood-pressure and dissociation monitoring (CANMAT 2023). Non-esketamine racemic ketamine by oral, intramuscular or intranasal route is reserved third-line given variable protocols (CANMAT 2023).

The other guidelines. The **Indian Psychiatric Society** depression guideline (Gautam et al.) endorses second-generation antidepressants first-line and reserves novel and specialist strategies for later steps; a specific IPS guidelines agent-level first-line row for esketamine could not be confirmed from the parsed reference library and is therefore not stated. The BAP TRD framework favours augmenting with quetiapine, aripiprazole or lithium first-line for treatment-resistant depression rather than naming esketamine as a first step (BAP). NICE recognises nasal esketamine as a licensed treatment for treatment-resistant major depression but, as of the parsed edition, had not approved it for routine NHS use in the UK, while it is used elsewhere (Maudsley 2021).

2	within hours	2
FAILED ANTIDEPRESSANT TRIALS DEFINING TRD	ONSET OF ANTIDEPRESSANT EFFECT	POST-DOSE OBSERVATION (HOURS)

10.4 The dosing schedule and why the benefit needs maintenance

Induction twice weekly, then step down; the effect is transient and must be scheduled. The intranasal esketamine dose is either **56 mg** or **84 mg** (K&S 2024). In the **induction phase** (weeks 1 to 4) dosing is **twice weekly**, starting at 56 mg after the first administration, titratable up to 84 mg as indicated. In the **maintenance phase** the schedule reduces to **once weekly for 4 weeks**, then continues once weekly or steps down to once every 2 weeks (K&S 2024). Intravenous racemic ketamine in the antidepressant setting is **0.5 mg/kg** infused over **40 minutes**, up to twice weekly, and not exceeding 6 weeks (K&S 2024, Maudsley 2021).

Why a schedule at all. A single ketamine infusion produces a rapid response that peaks around 24 hours but is short-lived: improvement typically lasts about 3 days and symptoms return toward baseline by around 7 days (K&S 2024). That transience is the whole reason for a repeated-dose induction and then a maintenance schedule; the drug is a bridge whose effect decays, not a one-off cure. This is the pharmacological basis of the topic RULE below.

WORKED EXAMPLE

A patient with treatment-resistant depression, already on an adequately dosed SSRI after two prior failed trials, is started on intranasal esketamine 56 mg twice weekly for the 4-week induction, titrated to 84 mg for tolerability, then moved to weekly and later fortnightly dosing while the oral antidepressant continues. Each session is given in the clinic with 2 hours of post-dose observation. The rapid lift in weeks 1 to 2 is real, but the oral antidepressant and the maintenance schedule are what hold it (K&S 2024).

10.5 Adverse effects: dissociation, blood pressure, sedation and abuse potential

The neuropsychiatric signature is dissociation. The hallmark adverse effect of ketamine and esketamine is dissociation and perceptual change: perceptual disturbances, vivid or abnormal sensory experiences, derealisation and depersonalisation, reported by over 70 percent of patients with intravenous ketamine (K&S 2024). These are experienced at the time of administration, are transient, and typically resolve within about 2 hours (K&S 2024). Related short-term effects include sedation, dizziness, confusion, memory disturbance and, particularly in those with a schizophrenia history, **psychotomimetic** (nondissociative psychotic) symptoms. The commonest intranasal esketamine adverse events are dissociation, dizziness, nausea, sedation, vertigo and increased blood pressure (K&S 2024).

The cardiovascular effect is a transient blood-pressure rise. At antidepressant doses both agents cause **transient hypertension and tachycardia** (K&S 2024). Rarely, hypotension, bradycardia, arrhythmias and cardiac decompensation are reported. Both are **contraindicated in uncontrolled significant hypertension**, and esketamine additionally in aneurysmal vascular disease, arteriovenous malformation and intracerebral haemorrhage (K&S 2024). Gastrointestinal nausea and vomiting are common enough to warrant antiemetic readiness.

Abuse potential and other cautions. Ketamine is a Schedule III controlled substance with recognised recreational misuse (the high-dose "K-hole"), and repeated use can produce tolerance and dependence (K&S 2024). Long-term chronic use is associated with a ketamine-induced **cystitis** (dysuria, frequency, haematuria, reduced bladder capacity), which is why longer-term ketamine or esketamine use attracts periodic urinalysis for cystitis (K&S 2024, CANMAT 2023). Esketamine carries a boxed warning for sedation, dissociation, abuse and misuse potential, availability only through the REMS programme, and increased suicidal thoughts in young people. Concomitant benzodiazepines or lamotrigine may attenuate the antidepressant response, and combining ketamine with opioids or other CNS depressants risks profound sedation and respiratory depression (K&S 2024).

TRAP **Giving it to a hypertensive patient unmonitored.** Both agents raise blood pressure transiently and are contraindicated in uncontrolled significant hypertension; administering without a baseline check and post-dose monitoring, or in a psychotic-prone patient without weighing the psychotomimetic risk, is the classic error.

10.6 The monitoring: in-clinic administration and the REMS-style observation

Because it dissociates and raises blood pressure, it is given under observation. The rapidity and the dissociative and cardiovascular effects force a supervised model. In the United States esketamine is dispensed and administered only in a certified, medically supervised setting under a **risk evaluation and mitigation strategy** (REMS), with the patient monitored for at least **2 hours** post-administration (K&S 2024). Practically this means the drug is self-sprayed under direct observation of a healthcare provider, with blood pressure checked before and after, and the patient not driving on the day of dosing or until the following morning (K&S 2024). For intravenous racemic ketamine, the Maudsley advises a pretreatment physical examination with baseline blood pressure and a pretreatment ECG, blood-pressure monitoring before and after the infusion, and observation during and for at least 1 hour after the infusion by a clinician trained in life support (Maudsley 2021). This is the REMS-style monitoring an examiner expects you to name.

PEARL

The monitoring headline maps to the two dangerous effects: observe for **dissociation** (neuropsychiatric) and for the **blood-pressure rise** (cardiovascular). Both are transient and settle within about 2 hours, which is exactly why the observation window is 2 hours for intranasal esketamine (K&S 2024).

RULE **Esketamine works within hours for treatment-resistant depression but must be given under observation for dissociation and blood pressure.** In-clinic administration, blood pressure before and after, and at least 2 hours of post-dose observation.

10.7 India, availability and cost

INDIA

Racemic ketamine is widely available in India as an injectable anaesthetic and is a controlled drug; its use for depression is off-label and confined to specialist and academic settings. Intranasal esketamine (Spravato) is a high-cost, cold-chain, REMS-gated product, and a specific Indian brand or routine Indian availability could not be confirmed from the parsed reference library, so no Indian brand is asserted here and the international brand Spravato is named only as the licensed innovator product. For Indian postgraduate answers, the practical position is that these are rapid-acting glutamatergic agents used in tertiary and research centres rather than routine practice, that the guideline to cite first is the Indian Psychiatric Society depression guideline (Gautam et al.), and that where a rapid response to severe or suicidal depression is needed in Indian teaching hospitals, ECT remains the widely available and heavily used option (see the ECT and neurostimulation notes).

MNEMONIC

"RAPID KETAMINE": Receptor NMDA, AMPA burst, Plasticity, In-clinic, Dissociation and blood pressure, Keeps needing repeats.

Receptor target is NMDA; the effect runs through an AMPA burst driving synaptic Plasticity; it is given In-clinic under observation; watch Dissociation and the blood-pressure rise; and because the benefit is transient it Keeps needing repeats on a maintenance schedule.

HOLD THIS

Esketamine (S-ketamine, intranasal, Spravato) is an NMDA antagonist licensed as an add-on to an oral antidepressant for treatment-resistant depression and for major depression with acute suicidal ideation; it works within hours, dose is 56 or 84 mg twice weekly at induction then stepped down, and it must be given in-clinic with blood-pressure checks and at least 2 hours of post-dose observation for dissociation.

GOOD TO REMEMBER

- **Ketamine, mechanism:** non-competitive NMDA-receptor antagonist producing a glutamate surge onto AMPA receptors and rapid synaptogenesis; a glutamatergic, not monoamine, antidepressant.
- **Ketamine, signature effect and one to hold:** dissociation and a transient blood-pressure rise, with abuse potential and chronic-use cystitis; racemic, intravenous, off-label, 0.5 mg/kg over 40 minutes, up to twice weekly.
- **Esketamine, mechanism:** the S-enantiomer with four-fold higher NMDA affinity, intranasal spray (brand Spravato).
- **Esketamine, indication and one to hold:** licensed add-on to an oral antidepressant for treatment-resistant depression and for major depression with acute suicidal ideation; 56 or 84 mg, twice weekly induction then stepped down, given under REMS-style observation with at least 2 hours of post-dose monitoring for dissociation and blood pressure.
- **The transience rule:** the response is rapid but short-lived (peaks about 24 hours, fades by about 7 days after a single dose), so it is a bridge needing a maintenance schedule and an ongoing oral antidepressant, not a cure.

11 . Choosing an antidepressant

Once the diagnosis of a depressive episode is settled and pharmacotherapy is indicated, the next decision the examiner tests is not *whether* to prescribe but *which* agent, and the reasoning behind it. **Choosing an antidepressant** is a selection topic, and the single organising principle the board rewards is that the first-line antidepressants are broadly equal in antidepressant efficacy, so the choice is driven not by presumed potency but by the adverse-effect profile, the **comorbidity**, past response, drug interactions, safety in overdose and cost (Kaplan & Sadock 2024; Maudsley 2021). This topic teaches **antidepressant selection** in clinical practice as a guideline-anchored algorithm; the pharmacology of each agent lives in its own topic and the deep treatment-resistance ladder is the treatment-resistance topic.

Ground the algorithm in the guidelines. Lead with **CANMAT**: the Canadian Network for Mood and Anxiety Treatments recommends a second-generation antidepressant as the first-line pharmacological treatment for major depression, individualising the choice to patient and medication factors under measurement-based monitoring (CANMAT 2016). Then state the **Indian Psychiatric Society** position, and what NICE and the BAP recommend. Every dose, interval and first-line recommendation below is verified against the CANMAT and IPS guideline rows and the Maudsley (CANMAT 2016; IPS 2017; Maudsley 2021).

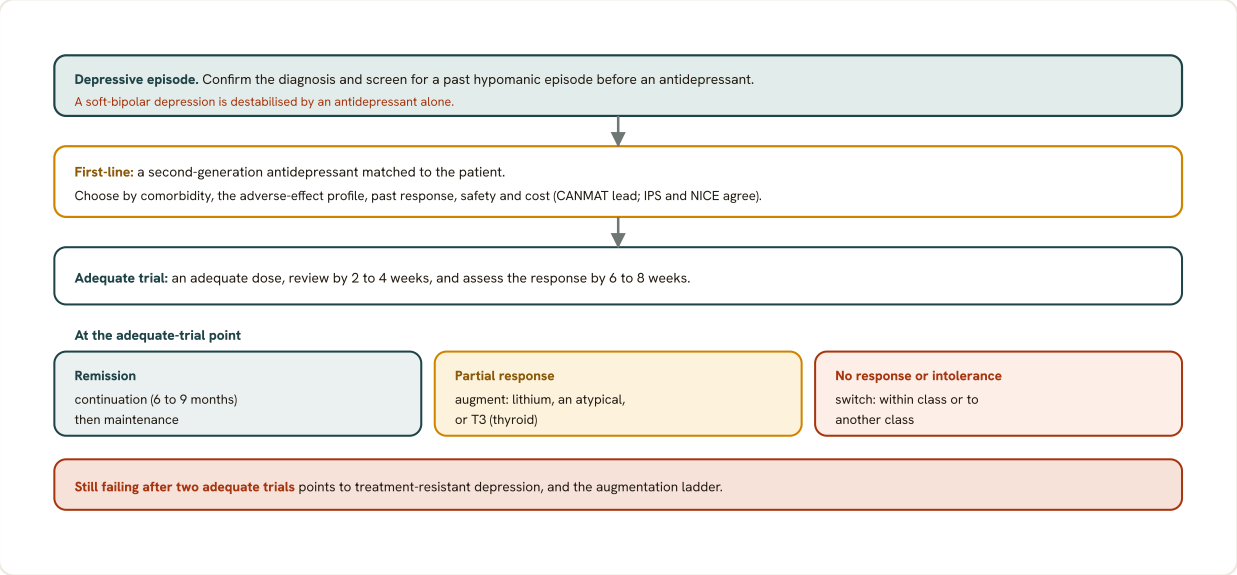


Fig 12.5 Choosing and sequencing an antidepressant. After confirming the diagnosis and screening for past hypomania, choose a second-generation antidepressant matched to the patient (the first-line agents are broadly equal in efficacy, so comorbidity and the adverse-effect profile drive the choice). Run an adequate trial, then act on the response: continue a remission, augment a partial response, switch a non-response. Two failed adequate trials define treatment resistance.

11.1 The governing principle: equal efficacy, so choose by profile

Efficacy is broadly equal. Head-to-head, no first-line antidepressant is convincingly more effective than another for the average patient with major depression, so the whole art of **choosing an antidepressant** is matching the drug to the individual patient rather than ranking drugs by strength (Kaplan & Sadock 2024; Maudsley 2021). A handful of agents (escitalopram, sertraline, venlafaxine, mirtazapine) carry a modest efficacy edge in network meta-analyses and

are worth preferring where maximising response is paramount, but this edge is small and never overrides tolerability.

So the choice is driven by six things. The adverse-effect and tolerability profile; the **comorbidity** (a coexisting condition the drug can help or harm); the patient's past response and any family response; drug interactions with existing medication; safety in overdose; and cost and availability (Kaplan & Sadock 2024; Maudsley 2021). Hold these six as the answer to almost any "which antidepressant and why" viva.

RULE **Choose the antidepressant by the adverse-effect and comorbidity match, not by presumed potency.** First-line agents are broadly equal in efficacy; the fit to the patient is what differs.

11.2 The CANMAT first-line list (lead guideline)

Second-generation antidepressants, first-line. CANMAT names the following as Level-1 first-line agents for major depression, all broadly equal and chosen by profile (CANMAT 2016): the SSRIs, the SNRIs, mirtazapine, bupropion, vortioxetine and agomelatine. The tricyclics and irreversible MAOIs are held back to second and third line because of their adverse-effect burden and danger in overdose.

CANMAT FIRST-LINE AGENT (INDIAN BRAND)	CLASS	DOSE (MG/DAY)	PROFILE NOTE THAT DRIVES SELECTION
Escitalopram (Nexito, S-Citadep)	SSRI	**10 to 20**	Cleanest, fewest interactions; dose-dependent QTc ceiling
Sertraline (Serta, Daxid)	SSRI	50 to 200	Broadest first choice; safe in pregnancy and post-MI
Fluoxetine (Fludac)	SSRI	20 to 60	Long half-life, activating, self-tapering
Paroxetine (Pexep)	SSRI	20 to 50	Anticholinergic, worst discontinuation; avoid in pregnancy
Venlafaxine (Venlor)	SNRI	**75 to 225**	Efficacy edge; monitor blood pressure at higher dose
Duloxetine (Duzela)	SNRI	60	First choice when depression coexists with neuropathic pain
Mirtazapine (Mirtaz)	NaSSA	15 to 45	Sedating, promotes appetite; for insomnia and weight loss
Bupropion (Bupron)	NDRI	150 to 300	No sexual dysfunction, no weight gain, activating; lowers seizure threshold

CANMAT FIRST-LINE AGENT (INDIAN BRAND)	CLASS	DOSE (MG/DAY)	PROFILE NOTE THAT DRIVES SELECTION
Vortioxetine (Vortioxa)	Multimodal	10 to 20	Low sexual dysfunction; possible pro-cognitive benefit
Agomelatine	Melatonergic	25 to 50	For sleep disturbance; monitor liver function tests

The CANMAT 2016 Level-1 first-line antidepressants with verified adult dose ranges and the one profile feature that drives selection; the Indian brand leads the generic. The highlighted cells are the two workhorse first steps.

GOOD TO REMEMBER

- **Escitalopram (Nexito or S-Citadep):** SSRI, cleanest and fewest interactions, dose-dependent QTc; first-line, **10 to 20 mg/day**.
- **Sertraline (Serta or Daxid):** SSRI, broadest first choice, safe post-MI and in pregnancy; first-line, **50 to 200 mg/day**.
- **Venlafaxine (Venlor):** SNRI, efficacy edge, dose-dependent hypertension; first-line, **75 to 225 mg/day**.
- **Duloxetine (Duzela):** SNRI, dual antidepressant and analgesic action; first-line when pain is comorbid, **60 mg/day**.
- **Mirtazapine (Mirtaz):** NaSSA, sedating and appetite-promoting; first-line for insomnia with weight loss, **15 to 45 mg/day**.
- **Bupropion (Bupron):** NDRI, no sexual dysfunction, activating, lowers seizure threshold; first-line, **150 to 300 mg/day**.

11.3 The Indian Psychiatric Society position

SSRIs first. The **indian psychiatric society** Clinical Practice Guidelines for depression (Gautam et al.) make the SSRIs the first-line antidepressant for major depression given their favourable side-effect and safety profile, with the TCAs, mirtazapine, bupropion and venlafaxine as the other preferred options (IPS 2017). For moderate to severe depression the **ips guidelines** name escitalopram 10 to 20 mg, sertraline 50 to 200 mg or fluoxetine 20 to 60 mg as the initial choice, matching the CANMAT list at guideline level.

The IPS reassessment and next-step rule. The IPS advises reviewing pharmacotherapy response at 4 to 6 weeks; if at least a moderate improvement is not seen, reappraise and adjust, by optimising the dose to the maximum tolerated, switching within class (one SSRI to another), or switching across class to an SNRI such as venlafaxine 75 to 225 mg or duloxetine 60 mg (IPS 2017). After acute-phase response the same dose is continued for a total of 6 to 9 months from initiation to prevent relapse. This IPS position is verified against the guideline rows; where a finer IPS specific cannot be confirmed it is flagged under gaps rather than invented.

INDIA

The IPS first-line choice mirrors CANMAT but is calibrated to Indian practice and cost: escitalopram (Nexito or S-Citadep) and sertraline (Serta or Daxid) are the outpatient workhorses because they are cheap generics, well tolerated, and safe in the medically complex and largely out-of-pocket patient. A month of a generic SSRI costs a small fraction of a single private consultation, which matters for adherence. The TCAs remain in wide use in India for comorbid pain and for cost, but their overdose danger keeps them off first line.

11.4 What NICE and the BAP recommend

NICE. When an antidepressant is used, NICE holds that the SSRIs are generally well tolerated, have a good safety profile and should be the first choice for most people; it warns that the TCAs are dangerous in overdose, with lofepramine having the best safety profile of the class (NICE 2022). NICE does not routinely offer an antidepressant first-line for less severe depression, preferring the least intrusive option such as guided self-help, and reviews symptoms and side effects usually within 2 weeks of starting (within 1 week in those aged 18 to 25 or where there is particular suicide concern).

BAP. The British Association for Psychopharmacology likewise directs, in the absence of special factors, to choose antidepressants that are better tolerated and safer in overdose, so the SSRIs and other newer antidepressants are the first-line choices, reserving older TCAs and MAOIs for when first-line treatment has failed (BAP 2015). Where maximising efficacy is paramount in a more severely ill patient, the BAP lists clomipramine, venlafaxine at 150 mg or more, escitalopram 20 mg, sertraline, amitriptyline or mirtazapine in preference to other agents (BAP 2015).

RULE **Every major guideline puts second-generation antidepressants (led by the SSRIs) first.** CANMAT, the IPS, NICE and the BAP all cite tolerability and overdose safety as the reason.

11.5 Practical matching: fit the agent to the comorbidity

The examinable skill is turning "equal efficacy" into a concrete choice by reading the patient. Match a favourable adverse effect or a coexisting condition to the drug that helps it, and avoid the drug that would harm it.

CLINICAL SITUATION	PREFERRED AGENT	WHY (THE PROFILE MATCH)
Comorbid chronic or neuropathic pain	**An SNRI (duloxetine) or a TCA (amitriptyline)**	Dual serotonin-noradrenaline action treats depression and pain with one drug
Insomnia and weight loss	**Mirtazapine**	H1-antihistamine sedation aids sleep; appetite stimulation restores weight
Fatigue or sexual dysfunction	**Bupropion**	Activating dopaminergic agent; no sexual dysfunction, no weight gain

CLINICAL SITUATION	PREFERRED AGENT	WHY (THE PROFILE MATCH)
Cardiac disease or overdose-risk patient	Avoid a TCA; use an SSRI (sertraline)	TCAs are cardiotoxic and lethal in overdose; SSRIs are safe post-MI
The elderly	An SSRI, watch hyponatraemia	Avoid TCA anticholinergic and orthostatic load; SSRIs risk SIADH/hyponatraemia
A woman planning pregnancy	Sertraline	Lowest infant exposure in breastfeeding; avoid paroxetine

The high-yield comorbidity-and-adverse-effect matches for antidepressant selection (Maudsley 2021; CANMAT 2016; IPS 2017). Read the situation, pick the agent whose profile fits, and avoid the agent whose profile harms.

Turn a side effect into an advantage. The sedating, weight-gaining mirtazapine is a liability in an obese sleeper but an asset in the thin, anorexic insomniac; the activating bupropion is wrong for the anxious patient but ideal for the fatigued patient with SSRI-induced sexual dysfunction. This inversion (one drug's adverse effect is another patient's indication) is the crux of the topic.

WORKED EXAMPLE

A 58-year-old man with diabetic peripheral neuropathy presents with a moderate depressive episode, poor sleep and low appetite. Rather than a default SSRI, duloxetine (Duzela) 60 mg is the pragmatic choice: one drug treats both the depression and the neuropathic pain, sparing a second prescription. Had the dominant problem instead been early insomnia with marked weight loss and no pain, mirtazapine (Mirtaz) 15 to 45 mg would be the better fit, using its sedation and appetite stimulation as therapeutic, not merely tolerated, effects.

PEARL

Ask two questions before writing the prescription: "what else does this patient have that a drug could help?" and "what must I not make worse?" The first points you to duloxetine for pain, mirtazapine for insomnia and weight loss, or bupropion for fatigue; the second steers you away from a TCA in cardiac or overdose risk and away from paroxetine in a woman planning pregnancy.

11.6 Safety in overdose and interactions as tie-breakers

Safety in overdose. Because depressed patients are at risk of self-harm, the toxicity of the drug in overdose is a genuine selection factor. The SSRIs and other second-generation agents are far safer in overdose than the tricyclic antidepressants, whose overdose is cardiotoxic (QRS widening, arrhythmia), proconvulsant and frequently fatal; this is a principal reason the guidelines put SSRIs first and hold TCAs back (NICE 2022; BAP 2015). Where a TCA is unavoidable, lofepramine is the least dangerous in overdose (NICE 2022).

Interactions. Existing medication narrows the field. In a polypharmacy or medically complex patient, prefer the clean agents (escitalopram, sertraline) over the potent cytochrome inhibitors (fluoxetine, paroxetine and fluvoxamine); never co-prescribe with an MAOI. The receptor and CYP metabolism that underlie these interactions belong to the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

TRAP **Reaching for a TCA in a patient with cardiac disease or overdose risk.** TCAs are cardiotoxic and lethal in overdose; an SSRI is the safer first-line choice.

11.7 The reassessment rule: review by 2 to 4 weeks

Review early. Having chosen the agent, the guidelines converge on reviewing the patient by 2 to 4 weeks. The BAP directs an initial review every 1 to 2 weeks after starting, noting that a lack of significant improvement by 2 to 4 weeks substantially reduces the chance of eventual sustained response (BAP 2015). CANMAT frames the same window as measurement-based care: for non-improvers at 2 to 4 weeks, increase the dose if tolerated, and switch if tolerability is the problem, with early improvement defined as roughly a 20 to 30 percent reduction on a depression rating scale (CANMAT 2016).

Then step up or switch. If there is no early improvement trajectory, act: optimise the dose to the maximum tolerated, then switch (within or across class, the outcome is similar) after an adequate trial. The BAP assesses response formally at 4 weeks and again at 6 to 8 weeks, switching or moving to a next-step treatment if there is no trajectory by 4 weeks (BAP 2015). The full next-step and augmentation ladder for the patient who fails an adequate trial is the treatment-resistance topic.

TRAP **Switching too early, or persisting past 4 weeks with no trajectory.** Give an adequate trial before declaring failure, but do not sit on a non-responder beyond 4 weeks hoping it will turn.

2 to 4 wk	4 wk	6 to 9 mo
FIRST REVIEW AFTER STARTING	ACT IF NO IMPROVEMENT TRAJECTORY	CONTINUATION AFTER REMISSION

GOOD TO REMEMBER

- **The selection principle:** first-line antidepressants are equal in efficacy, so choose by adverse effects, comorbidity, past response, interactions, overdose safety and cost.
- **CANMAT first-line:** the SSRIs, SNRIs, mirtazapine, bupropion, vortioxetine and agomelatine, individualised to the patient (CANMAT 2016).
- **Comorbidity match:** pain to an SNRI or TCA, insomnia with weight loss to mirtazapine, fatigue or sexual dysfunction to bupropion, cardiac or overdose risk away from a TCA, the elderly to an SSRI watching hyponatraemia, pregnancy planning to sertraline.
- **Reassessment:** review by 2 to 4 weeks; switch or step up if there is no early improvement trajectory by 4 weeks.

MNEMONIC

PICO-SC

What drives the choice when efficacy is equal: **P**ast response, **I**nteractions, **C**omorbidity, **O**verdose safety, **S**ide-effect profile, **C**ost. Run the list and the "which antidepressant and why" answers itself.

HOLD THIS

First-line antidepressants are broadly equal in efficacy, so choose by the adverse-effect and comorbidity match, not by presumed potency: CANMAT leads with the SSRIs, SNRIs, mirtazapine, bupropion, vortioxetine and agomelatine, the IPS and NICE and the BAP agree the SSRIs come first for tolerability and overdose safety, and you review by 2 to 4 weeks and switch or step up if there is no early improvement trajectory by 4 weeks.

12 . Managing an acute depressive episode: the phases

Managing an **acute depressive episode** is not a drug list, it is a sequence: decide **where** to treat, then work through the **phases of treatment** in order, choosing the mode of treatment each phase asks for. This is the mood-block closer, and a high-yield theory question: the examiner rewards the LOCUS to FOCUS to MODUS spine and the exact phase durations, not a recitation of side effects. The deep drug pharmacology, dosing and adverse-effect profiles are owned by the earlier topics in these notes; the augmentation and treatment-resistance ladder is owned by the treatment-resistance topic. This topic carries the phased plan and the durations.

Lead the guideline answer with CANMAT (CANMAT 2016), then give the Indian Psychiatric Society position, now carried by the 2025 IPS depression update (IPS 2025, Tripathi et al., which supersedes the 2017 Gautam guideline), BAP (BAP 2015) and NICE positions. Across all four the single organising principle the exam tests is one instruction, not two: **treat to remission, then continue at the acute dose.** Response is not remission, and remission is not the end point.

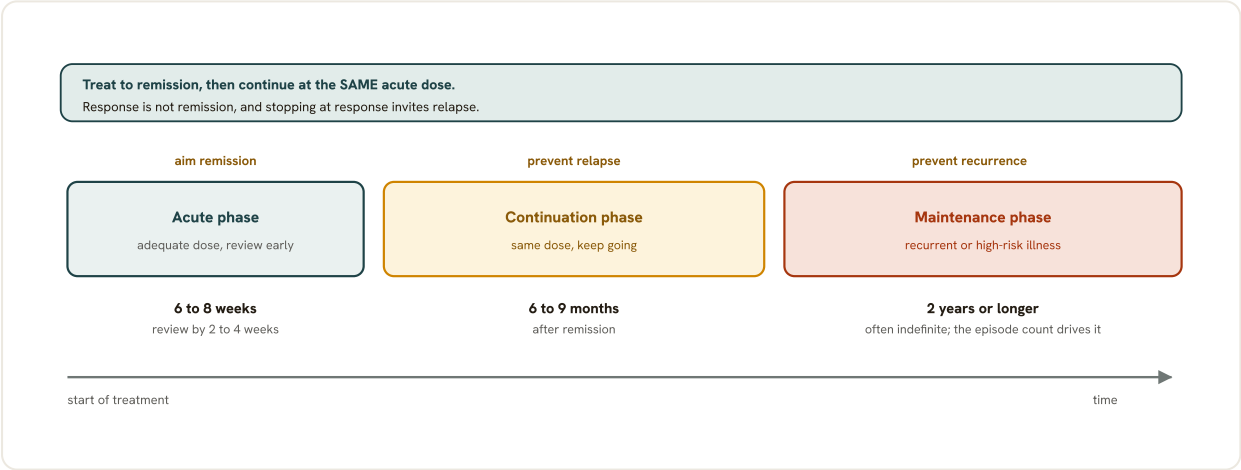


Fig 12.6 The phases and duration of treating an acute depressive episode. The acute phase runs about 6 to 8 weeks to remission, with an early review by 2 to 4 weeks; the continuation phase keeps the same acute dose for 6 to 9 months to prevent relapse; the maintenance phase extends to 2 years or longer, often indefinitely, for recurrent or high-risk depression. The cardinal rule is to treat to remission and continue at the acute dose, never to stop at response.

12.1 LOCUS: where to treat, and when to admit

Outpatient is the default. Most patients with an acute depressive episode are managed in the outpatient or the day care centre setting from the outset. Admission is reserved for a defined set of high-risk situations: **high suicide risk**, depression with **psychotic features**, severe **self-neglect** (not eating or drinking, dehydration), or the need for inpatient-level treatment such as ECT. The full clinical suicide risk assessment and safety planning that set the admission

threshold are owned by the Somatic-symptom, sexual, impulse-control disorders and suicide notes; the ECT technique itself is owned by the ECT and neurostimulation notes. Whatever the locus, care is delivered as **measurement-based care**: CANMAT specifies regular, frequent monitoring of clinical and functional outcomes with a validated scale such as the PHQ-9 or HAM-D, not clinical impression alone (CANMAT 2016; IPS 2017).

RULE **Admit for high suicide risk, psychosis, severe self-neglect, or the need for ECT.** Everything else is outpatient with measurement-based follow-up.

12.2 The ACUTE phase: aim remission, not response

The target of the acute phase is **remission**, the near-complete resolution of symptoms, not merely a partial **response** (conventionally a 50 percent symptom reduction). Stahl frames the whole plan around this: continue treatment until all symptoms are gone, that is remission, because residual symptoms predict relapse (Stahl 2021). Give an **adequate trial at an adequate dose**: a first-line antidepressant titrated to a therapeutic dose and continued for **6 to 8 weeks** before it can be called a failure. Review early: CANMAT and BAP advise reviewing the patient every **1 to 2 weeks** after starting (BAP 2015). Judge response on a trajectory. A lack of significant improvement by **2 to 4 weeks** substantially reduces the chance of eventual sustained response, so for a non-improver at 2 to 4 weeks you increase the dose if tolerated, or switch if tolerability is the problem (CANMAT 2016). BAP frames the same checkpoint as assessing response at 4 weeks and again at **6 to 8 weeks**, switching or stepping up if there is no improvement trajectory by 4 weeks or only minimal improvement by 6 to 8 weeks (BAP 2015). The IPS reappraises at 4 to 6 weeks (IPS 2017).

TRAP **Do not combine two antidepressants at initiation.** CANMAT states this explicitly: start one first-line agent, monitor, then optimise or switch. Combination belongs to the treatment-resistance step, not the start.

12.3 The CONTINUATION phase: protect the remission at the SAME dose

Once remission is achieved, do not stop. The **continuation** phase continues the antidepressant at the **same acute treatment dose** (not a reduced "maintenance" dose) for **6 to 9 months** after symptomatic remission, to prevent early relapse (CANMAT 2016). The IPS is explicit that the dose achieving response is continued and not reduced through the continuation phase, which the 2025 IPS update now sets at **4 to 9 months** (IPS 2025). BAP frames the lower bound as at least 1 year for anyone with an increased relapse risk (BAP 2015); NICE frames it as at least 6 months after symptoms remit (NICE 2022). This is the phase most often failed in practice: the patient feels well at week 8 and stops, and the relapse that follows is a continuation-phase relapse, not a genuinely new episode.

RULE **Continue at the acute dose through continuation; do not drop the dose or stop at response.** Continuation is 6 to 9 months at the same dose after remission (CANMAT 2016; IPS 2017).

12.4 The MAINTENANCE phase: prevent recurrence, and let the episode count set the duration

For recurrent, severe or high-risk depression the plan extends into a **maintenance** phase. CANMAT extends antidepressant treatment to **2 years or more** for patients with risk factors for recurrence (CANMAT 2016). The key examinable principle is that the number of prior episodes drives the **duration**: Stahl states that after a first episode you continue for about 1 year, but for a second and subsequent episodes treatment may need to be indefinite (Stahl 2021). The 2025 IPS update sets the maintenance phase at **6 to 24 months**, extended long-term for recurrent depression, with the probability of recurrence and the frequency and severity of past episodes driving the decision to continue (IPS 2025). BAP names the higher-risk group as, for example, more than five lifetime episodes or two episodes in recent years, and recommends at least 2 years and often long-term (BAP 2015). The maintenance-phase psychological options are CBT or mindfulness-based cognitive therapy (MBCT) to prevent relapse (CANMAT 2016); the technique of these therapies is owned by the Psychotherapies, clinical assessment, MSE and nosology notes.

MNEMONIC

FINISH

When the maintenance phase does end, taper slowly over several weeks to limit antidepressant discontinuation symptoms, which CANMAT summarises as FINISH: **F**lu-like symptoms, **I**nsomnia, **N**ausea, **I**mbalance, **S**ensory disturbances, **H**yperarousal (CANMAT 2016). Taper short half-life drugs (for example paroxetine, venlafaxine) more slowly. The discontinuation syndrome detail is owned by the discontinuation topic in these notes.

12.5 The MODUS: which mode of treatment each phase asks for

At guideline level the mode is an antidepressant, an evidence-based psychotherapy, or both. The **first-line** pharmacological agent is a **second-generation antidepressant**, individualised to the patient with measurement-based monitoring (CANMAT 2016). CANMAT's first-line agents (verified) include the SSRIs escitalopram (Nexito or S-Citadep; 10 to 20 mg/day), sertraline (Serta or Daxid; 50 to 200 mg/day), fluoxetine (Fludac; 20 to 60 mg/day) and the SNRI venlafaxine (Venlor; 75 to 225 mg/day), with bupropion (Bupron), mirtazapine (Mirtaz) and vortioxetine (Vortioxa) also first-line; the full per-agent dosing, mechanism and adverse-effect detail live in the earlier topics of these notes. The IPS names the SSRIs as first-line on grounds of tolerability and overdose safety (IPS 2017), NICE treats SSRIs as the first choice for most people, and BAP prefers newer antidepressants for tolerability and overdose safety (BAP 2015). The first-line psychotherapies for the acute phase are CBT, interpersonal therapy (IPT) and behavioural activation (BA); where feasible, combining a psychotherapy with an antidepressant is superior to either alone (CANMAT 2016; IPS 2017). The receptor-level pharmacology and CYP metabolism that underlie agent selection are cross-referred to the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

RULE **First-line = one second-generation antidepressant, individualised, or an evidence-based psychotherapy.** Combination is superior for many, especially the more severe presentations.

12.6 The MODUS: the psychotic-depression rule

Psychotic depression is the one presentation with a fixed combination rule. Treat it with an **antidepressant plus an antipsychotic** from the outset, in preference to either drug alone, or use ECT (BAP 2015; IPS 2017). An antidepressant alone is inadequate here. The mood-with-psychotic-features entity itself is owned by the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes, and the ECT technique by the ECT and neurostimulation notes. One more selection rule sits behind the whole plan: a treatment-emergent switch to mania or hypomania on antidepressant monotherapy reclassifies the diagnosis as bipolar; stop or reduce the antidepressant and add a mood stabiliser (IPS 2017). Giving an antidepressant alone in what is really a bipolar depression is the classic error, and it is owned in full by the bipolar-management topics.

TRAP **Treating psychotic depression with an antidepressant alone.** The rule is antidepressant plus an antipsychotic from the outset, or ECT.

12.7 Putting the phases together: the phase-by-phase plan

The four phases and the locus decision assemble into one table. Learn the highlighted cell in each row: it is the fact the examiner tests.

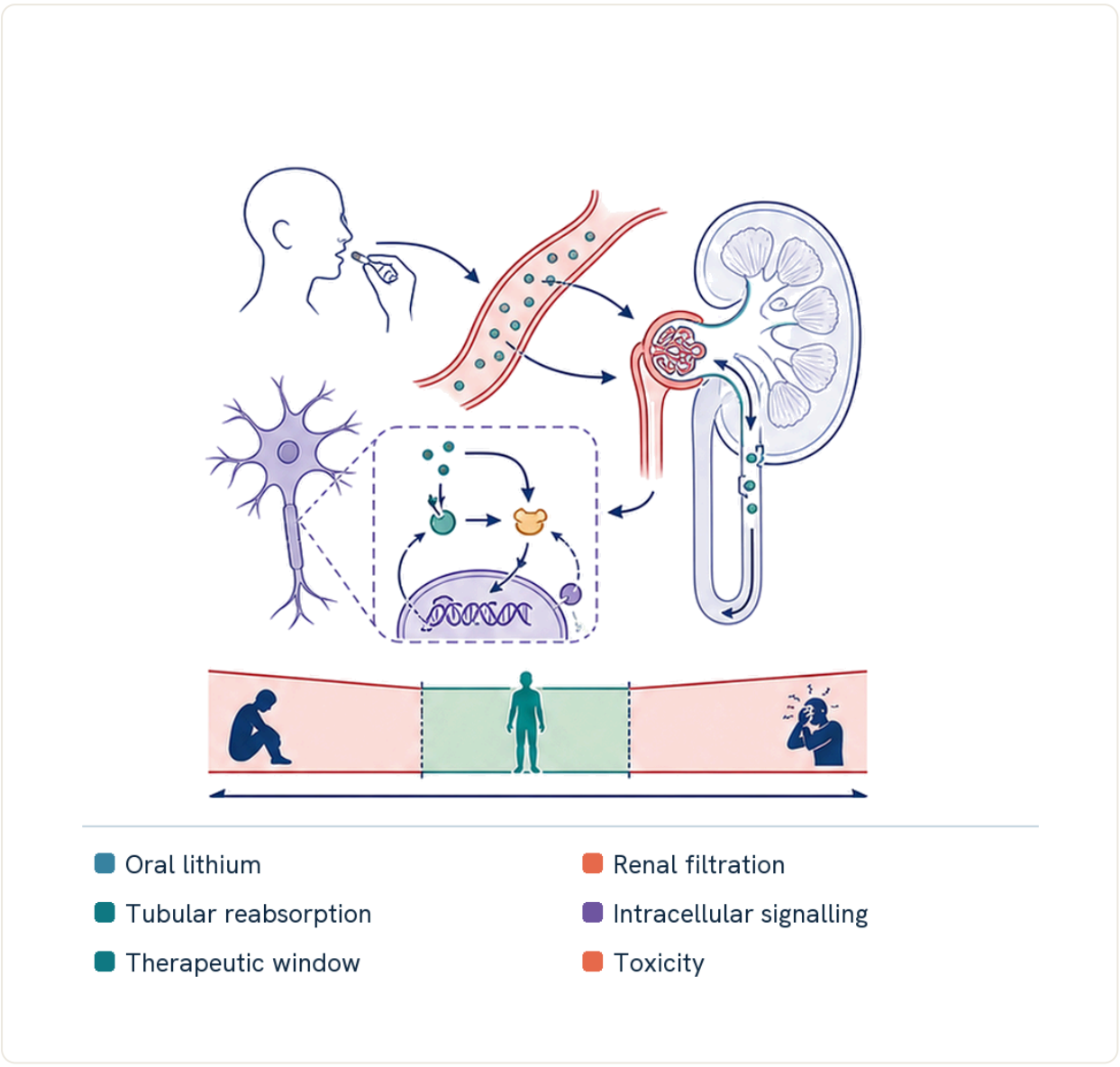


Fig 12.7 Lithium is filtered and substantially reabsorbed by the kidney while acting on intracellular signalling pathways. Its narrow therapeutic window makes changes in renal handling clinically consequential.

6 to 8 wk ADEQUATE ACUTE TRIAL	**2 to 4 wk** NON-IMPROVER REVIEW POINT	**6 to 9 mo** CONTINUATION AT THE ACUTE DOSE	**2 years+** MAINTENANCE IF RECURRENT

PHASE	TARGET	DURATION / CHECKPOINT	GUIDELINE-FIRST MODE
Locus decision	Choose the safest adequate setting	**Admit for high suicide risk, psychosis, severe self-neglect, or the need for ECT**	Outpatient default; measurement-based care throughout (CANMAT 2016)
Acute	Remission (not just response)	**Adequate dose for 6 to 8 weeks; review every 1 to 2 weeks; judge by 2 to 4 weeks and switch or step up if no trajectory**	One second-generation antidepressant, individualised, and/or CBT, IPT or BA; combination superior for many (CANMAT 2016)

PHASE	TARGET	DURATION / CHECKPOINT	GUIDELINE-FIRST MODE
Continuation	Protect the remission	**Continue at the same acute dose for 6 to 9 months after remission**	Same acute-phase agent at the same dose; do not down-titrate (CANMAT 2016; IPS 2017)
Maintenance	Prevent recurrence	**Extend to 2 years or longer (often indefinite) for recurrent, severe or high-risk depression; the number of prior episodes drives the duration**	Continue antidepressant; CBT or MBCT to prevent relapse; taper slowly (FINISH) at stop (CANMAT 2016)
Psychotic depression	Remission with psychosis control	From the outset	**Antidepressant plus an antipsychotic, or ECT (BAP 2015)**
Inadequate response	Optimise, then augment or switch	Optimise dose first, then reassess	Augmentation or switch; the full ladder is owned by the treatment-resistance topic in these notes

The acute depressive episode managed by the phases of treatment on the LOCUS to FOCUS to MODUS spine; durations verified against CANMAT 2016, IPS 2017 and BAP 2015. Drug detail is cross-referred to the earlier topics in these notes.

INDIA

The Indian Psychiatric Society Clinical Practice Guideline for depression has been updated: the 2025 IPS depression update (IPS 2025, Tripathi et al., Indian J Psychiatry 2026;68:68-93) supersedes the 2017 Gautam guideline and is now the current examinable Indian reference. It sets the treatment phases as acute **8 to 16 weeks** (achieve remission), continuation **4 to 9 months** (consolidate remission, prevent relapse) and maintenance **6 to 24 months** (prevent recurrence, restore functioning), extended long-term for recurrent depression. It selects the initial treatment by severity: for mild low-risk depression, psychotherapy is preferred (pharmacotherapy is acceptable in the Indian setting given limited access to psychologists); for moderate depression, pharmacotherapy or psychotherapy, with pharmacotherapy slightly more efficacious, quicker and more cost-effective; for severe depression without psychosis, combined pharmacotherapy and psychotherapy; for severe depression with psychosis, an antidepressant plus an antipsychotic as first-line; and for life-threatening presentations, ECT with admission. The first-line SSRIs and their doses are unchanged (escitalopram 10 to 20 mg, sertraline 50 to 200 mg, fluoxetine 20 to 60 mg), and the update names vilazodone, vortioxetine and agomelatine among the newer options. All the first-line agents are inexpensive Indian brands: escitalopram (Nexito or S-Citadep), sertraline (Serta or Daxid), fluoxetine (Fludac), venlafaxine (Venlor), duloxetine (Duzela), mirtazapine (Mirtaz), bupropion (Bupron), vortioxetine (Vortioxa). ECT is widely available across Indian teaching hospitals and remains a mainstream option for severe, psychotic, suicidal or treatment-resistant depression rather than a last resort.

GOOD TO REMEMBER

- **LOCUS:** outpatient default; admit for high suicide risk, psychosis, severe self-neglect, or the need for ECT; measurement-based care throughout.
- **Acute phase:** aim **remission**, not response; adequate dose for **6 to 8 weeks**; review every 1 to 2 weeks; switch or step up if no trajectory by 2 to 4 weeks (CANMAT 2016; BAP 2015).
- **Continuation phase:** continue at the **same acute dose** for **6 to 9 months** after remission; do not down-titrate (CANMAT 2016; IPS 2017).
- **Maintenance phase: 2 years or longer** (often indefinite) for recurrent, severe or high-risk depression; the number of prior episodes drives the duration (Stahl 2021; IPS 2017).
- **MODUS:** one second-generation antidepressant, or an evidence-based psychotherapy (CBT, IPT, BA), or both; combination superior for many.
- **Psychotic depression:** antidepressant plus an antipsychotic from the outset, or ECT (BAP 2015).
- **Do-not-combine rule:** two antidepressants are not combined at initiation (CANMAT 2016).

WORKED EXAMPLE

A 38-year-old man with a second moderate-to-severe depressive episode, no psychosis and no active suicidal plan, is managed as an outpatient. He is started on a single first-line SSRI, escitalopram (Nexito or S-Citadep), titrated to a therapeutic dose, and offered CBT alongside because combination is superior to either alone. He is reviewed at 2 weeks and again at 4 weeks: there is a partial improvement trajectory, so the dose is optimised rather than switched, and the adequate trial is allowed to run to 6 to 8 weeks. He reaches remission by month 3. The escitalopram is continued at the same acute dose for 6 to 9 months in the continuation phase, not reduced. Because this is his second episode, the recurrence-risk conversation supports a maintenance phase of at least 1 to 2 years rather than stopping at the end of continuation.

PEARL

"Remission then continuation at the acute dose" is a single instruction. The dose that achieved remission is the dose that maintains it: the continuation phase is the acute-phase drug at the acute-phase dose for 6 to 9 months. Reducing the dose the moment the patient feels well is a common and avoidable cause of relapse.

TRAP **Stopping the antidepressant as soon as the patient feels better.** Response is not remission, and remission is not the end point; early cessation invites relapse.

HOLD THIS

Treat the acute depressive episode to remission on an adequate 6-to-8-week trial, continue at the same acute dose for 6 to 9 months after remission, and extend to 2 years or longer for recurrence, with the number of prior episodes setting the duration.

Mood stabilisers and lithium

13 . Lithium: mechanism and pharmacokinetics

Why this leads the block. Lithium is a monovalent cation with no receptor, no enzyme it was designed for, and no metabolism, yet it remains the gold-standard mood stabiliser and the only agent with a genuine anti-suicide signal (Maudsley 2021). The examiner reward here is mechanistic: two intracellular **mechanism of action** hypotheses that also explain the neuroprotective story, and a **pharmacokinetics** profile so unusual that the drug is effectively a sodium mimic cleared entirely by the kidney. Get the pharmacokinetics right and the interactions, the monitoring schedule and the toxicity all fall out of it; get them wrong and a stable patient tips into toxicity from nothing more than a stomach bug.

This fragment teaches the molecular targets, then the four pharmacokinetic facts a resident must hold, then the bridge that makes lithium's kinetics the source of its danger. The therapeutic ranges, the monitoring intervals and the drug interactions themselves are developed in the sibling topics; the deep monoamine and second-messenger anatomy sits in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

13.1 A drug with no obvious target

The framing problem. Lithium has "practically no acute effects in normal individuals" and is neither sedative nor euphoriant; the mood-stabilising action appears only on prolonged administration (KDT 2019). It does not bind a classical receptor. Instead it acts inside the cell on two enzymes that sit on second-messenger and signalling cascades, and it does so at the low millimolar concentrations reached therapeutically. The two dominant, exam-relevant hypotheses are **inositol** depletion and GSK-3 inhibition. Both converge on dampening an over-active signalling state and on downstream neurotrophic or neuroprotective effects (Stahl 2021).

RULE **Two targets, one theme.** Lithium works intracellularly on inositol monophosphatase and GSK-3 beta, not on a membrane receptor: it turns down an over-active signalling cascade and switches on neuroprotective genes.

13.2 The inositol depletion hypothesis

Inositol monophosphatase and the phosphatidylinositol cycle. Gq-coupled receptors activate phospholipase C, which hydrolyses membrane phosphatidylinositol to the second messengers inositol trisphosphate (IP3) and diacylglycerol. To regenerate the signalling lipid, the cell must recycle inositol, and the enzyme that liberates free **inositol** from inositol monophosphate is inositol monophosphatase (IMPase). Lithium is a powerful inhibitor of IMPase, so the phosphatidylinositol second-messenger cascade runs down as the cell is depleted of inositol (Berridge 1982; New Oxford 2020). Because the brain crosses the blood brain barrier poorly for inositol and is therefore uniquely dependent on recycling, it is selectively sensitive to this depletion (New Oxford 2020).

Uncompetitive inhibition is the elegant part. Lithium inhibits IMPase *uncompetitively*, meaning the block deepens as substrate rises. Lithium therefore acts most where a pathway is hyperfunctional and barely touches pathways ticking over at basal rates, which is exactly the selectivity you want in an anti-manic drug (New Oxford 2020). This "inhibition of inositol monophosphatase dampening the phosphatidylinositol second-messenger cascade" is the phrase to reproduce. Supporting the class relevance, valproate and carbamazepine also deplete brain inositol, though largely by inhibiting a synthetic enzyme rather than IMPase (New Oxford 2020).

MNEMONIC

"I MP-ede the cycle"

IMPase is the enzyme lithium blocks; blocking it *impedes* the phosphatidylinositol cycle by starving it of recycled inositol. Uncompetitive means the busier the pathway, the harder lithium hits.

13.3 GSK-3 beta inhibition and the neurotrophic story

The second target. Glycogen synthase kinase 3 beta (glycogen synthase kinase 3, GSK-3) is a constitutively active kinase that phosphorylates and inactivates a wide set of substrates. Lithium robustly inhibits GSK-3 beta, both directly and indirectly through the beta-arrestin 2 / Akt pathway that dopamine D2 signalling recruits (Companion 2010; Lithium Handbook 2023). Inhibiting GSK-3 releases its downstream substrates from suppression: Wnt / beta-catenin signalling, the cytoskeletal and tau proteins, and the transcription factors CREB and AP-1 (jun) (Companion 2010).

Downstream neurotrophic and neuroprotective effects. The net consequence is upregulation of neurotrophic and cytoprotective programmes, notably brain-derived neurotrophic factor (BDNF) and the anti-apoptotic protein bcl-2 (Kaplan 2024). This is the molecular basis usually invoked for lithium's neuroprotective and putative anti-dementia signal (Lithium Handbook 2023). GSK-3 also phosphorylates core clock proteins, so its inhibition feeds into the **circadian** and signalling pathways that are disordered in bipolar illness, one proposed route by which lithium lengthens and re-entrains the circadian period (Stahl 2021).

TARGET	WHAT LITHIUM DOES	DOWNSTREAM CONSEQUENCE
Inositol monophosphatase (IMPase)	**Uncompetitive inhibition**	Inositol depletion, phosphatidylinositol / IP3 cascade damped, most in hyperactive pathways
GSK-3 beta	**Direct and Akt/beta-arrestin inhibition**	Wnt/beta-catenin, CREB, BDNF, bcl-2 up; neuroprotection; circadian re-entrainment

The two dominant mechanism-of-action hypotheses for lithium and their downstream signalling effects.

PEARL

Both mood-stabiliser mechanisms fit a single idea: lithium quietens an over-active intracellular signal (inositol/PI cycle) while switching on survival and plasticity genes (via GSK-3 inhibition). This "dampen the noise, protect the cell" dual action distinguishes it from receptor-blocking drugs.

13.4 Absorption and distribution

A small ion that behaves like body water plus sodium. Lithium is well absorbed orally with peak plasma levels at **2 to 3 hours** for immediate-release salts, and it is not protein bound (KDT 2019). It first enters the extracellular water, then slowly crosses into cells, giving an apparent **volume of distribution** around **0.8 L/kg**, close to total body water and narrow compared with lipophilic psychotropics (KDT 2019). The slow intracellular equilibration matters clinically: after an acute overdose the plasma level can be alarmingly high while the patient is still asymptomatic, then deteriorate over hours as lithium loads into cells, which is why the serum level and the clinical picture can dissociate early (Kaplan 2024).

2 to 3	0.8	18 to 24
TIME TO PEAK, IR (HOURS)	VOLUME OF DISTRIBUTION (L/KG)	ELIMINATION HALF-LIFE (HOURS)

13.5 Not metabolised: entirely renal excretion

The single most important pharmacokinetic fact. Lithium is not metabolised by the liver and is not protein bound; it undergoes **renal excretion** essentially in its entirety, cleared unchanged by the kidney (KDT 2019; Kaplan 2024). It is filtered at the glomerulus and then handled by the proximal tubule "in much the same way as sodium," where roughly 80% of the filtered load is reabsorbed alongside sodium; its renal clearance is about one fifth of creatinine clearance (KDT 2019). The elimination half-life is of the order of **18 to 24 hours** in a patient with normal renal function, described by Kaplan as "about a day," which is what makes once-daily dosing feasible and why steady state and a valid trough level are reached only after several days at a fixed dose (Kaplan 2024).

WORKED EXAMPLE

A euthymic patient stable for years on a fixed lithium dose develops gastroenteritis, eats little, and becomes volume-deplete over a weekend. Sodium and water avidity rise, the proximal tubule reabsorbs more filtered sodium and therefore more lithium, renal lithium clearance falls, and the serum level climbs even though the dose has not changed. The stable patient is now heading into toxicity with no prescribing error at all.

13.6 The sodium link is the whole game

Why the kinetics drive the toxicity and the interactions. Because lithium is handled like sodium and cleared only by the kidney, anything that lowers total-body sodium or reduces renal clearance raises the level. Sodium depletion, dehydration and a low-salt diet all increase proximal reabsorption of lithium; renal impairment and a falling glomerular filtration rate reduce its excretion (Kaplan 2024; KDT 2019). This is the mechanistic root of the classic interactions developed in the interaction and monitoring topics: thiazide diuretics deplete sodium and raise

levels; NSAIDs and ACE inhibitors or ARBs cut renal perfusion or clearance and raise levels; sodium loading or osmotic diuresis lowers them. There is no hepatic escape route and no protein reservoir to buffer swings, so kinetic changes translate directly into level changes.

RULE **Lithium follows sodium and the kidney.** Lithium is renally cleared and sodium-linked, so anything that lowers sodium or lowers renal clearance raises the level. That single sentence predicts nearly every lithium interaction and every toxicity trigger.

TRAP **The "nothing changed" toxicity.** Forgetting that dehydration, a vomiting or diarrhoeal illness, a heat wave or a new low-salt diet can push a long-stable patient into toxicity with the dose untouched. The level moved because sodium and water moved, not because the prescription did.

13.7 Narrow therapeutic index: why monitoring is mandatory

The margin is thin and individual. Lithium has a **narrow therapeutic index**: therapeutic maintenance levels sit around **0.6 to 1.0 mEq/L** while toxicity appears not far above, with early features from roughly **1.5 mEq/L** and serious toxicity higher still (Meyer and Stahl / Lithium Handbook 2023; CANMAT 2018). Guideline targets are level-defined rather than dose-defined: CANMAT sets maintenance at 0.6 to 1.0 mEq/L and an acute-mania target of 0.8 to 1.2 mEq/L, and the Indian Psychiatric Society (IPS guidelines) similarly anchor maintenance around 0.6 to 1.0 mmol/L with acute targets up to about 1.2 mEq/L (CANMAT 2018; Shah, Grover et al. 2017). Because the same oral dose produces widely different levels between patients (large inter-individual variation in renal clearance) and the same patient's level moves with sodium and hydration, therapeutic drug monitoring of the serum level is not optional, it is the drug (Kaplan 2024; Lithium Handbook 2023). This is the bridge into the initiation, monitoring and toxicity topics.

INDIA

Lithium carbonate is widely available in India as immediate-release and sustained-release tablets, commonly branded Licab and Intalith CR (generic lithium carbonate stays primary in the prose). The narrow-index and sodium-link teaching is especially load-bearing in Indian practice: hot-climate dehydration, gastroenteritis, fasting and low-salt diets are common real-world triggers for a stable patient to drift into toxicity between clinic visits.

HOLD THIS

Lithium is not metabolised and is cleared entirely by the kidney where it is handled like sodium, so with a narrow therapeutic index any fall in sodium, hydration or renal clearance raises the level toward toxicity.

GOOD TO REMEMBER

- **Mechanism (inositol):** inhibits inositol monophosphatase, uncompetitively, depleting inositol and dampening the phosphatidylinositol / IP3 second-messenger cascade, most in hyperactive pathways.
- **Mechanism (GSK-3):** inhibits GSK-3 beta, releasing Wnt/beta-catenin, CREB, BDNF and bcl-2, giving downstream neurotrophic, neuroprotective and circadian effects.
- **Pharmacokinetics:** not protein bound, not metabolised, renal excretion entirely; handled like sodium (proximal reabsorption ~80%); Vd ~0.8 L/kg; half-life ~18 to 24 hours; peak at 2 to 3 hours (IR).
- **The clinical rule:** narrow therapeutic index (maintenance ~0.6 to 1.0 mEq/L) makes serum monitoring mandatory; sodium depletion, dehydration and renal impairment raise the level.

14 . Lithium: indications, initiation, dosing and range

Lithium is the oldest and still the single most important mood stabiliser, and the examiner treats it as a set-piece: the indications, the baseline work-up before the first tablet, the starting dose, and above all the **serum lithium** therapeutic range that differs between acute mania and maintenance. It is the gold-standard prophylactic agent in bipolar disorder and carries the strongest anti-suicidal evidence of any psychotropic (Maudsley 2021; CANMAT 2018), so a resident is expected to prescribe it correctly and to know its numbers cold. A wrong serum level or a skipped renal or thyroid baseline is the classic marked error.

Organise the topic around one idea: **aim high for acute mania, aim lower for maintenance**, and never start without a baseline renal, thyroid and calcium screen. The ranges below are verified against the Maudsley and the CANMAT and Indian Psychiatric Society guideline rows (Maudsley 2021; CANMAT 2018; IPS 2017); the neurobiology of mood and the wider guideline-anchored management PLAN belong to the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes, and the deep antimanic-antipsychotic detail to the Schizophrenia: management, antipsychotics and adverse effects notes.

14.1 Mechanism: a monovalent cation with intracellular targets

The molecular target. Lithium is a monovalent cation with no single agreed mechanism; the best-supported candidates are inhibition of glycogen synthase kinase 3 (GSK3-beta) and interference with the phosphatidylinositol second-messenger cycle through inhibition of inositol monophosphatase, together with effects on CREB and on neuronal sodium and calcium handling (Maudsley 2021; Stahl 2021). It also promotes hippocampal neurogenesis and has putative neuroprotective effects.

Why the narrow window matters. Lithium is not metabolised; the ion is handled entirely by the kidney and excreted with a half-life of about 24 hours, so anything that alters sodium handling or renal function moves the serum level directly (Kaplan and Sadock 2024). That renal-only clearance, and the fact that the therapeutic and toxic ranges nearly abut, is why serum monitoring is non-negotiable.

14.2 Lithium indications: mania, maintenance and augmentation

The core indications. The set of **lithium indications** a resident must recite: **acute mania** (a first-line antimanic agent), bipolar maintenance and **prophylaxis** (the gold-standard mood stabiliser for preventing both manic and depressive recurrence), augmentation of an antidepressant in treatment-resistant unipolar depression, and prophylaxis of recurrent unipolar depression (Maudsley 2021; CANMAT 2018).

Acute mania

First-line, alone or combined with an antipsychotic; a faster antimanic onset is gained by adding a dopamine antagonist (Maudsley 2021; CANMAT 2018).

Bipolar maintenance / prophylaxis

The best-performing single agent for long-term relapse prevention; in 2024 it remains the gold-standard maintenance treatment (Maudsley 2021).

Unipolar antidepressant augmentation

A first-choice augmenting agent in treatment-resistant depression, most effective at a serum level of 0.6 to 1.0 mmol/L (Maudsley 2021).

Recurrent unipolar depression

Prophylaxis is indicated after two depressive episodes in five years, or after one severe episode with strong suicide risk (Maudsley 2021).

The anti-suicidal signal. Lithium is the one psychotropic with dedicated anti-suicide evidence: a meta-analysis of clinical trials concluded it reduced attempted and completed suicide by roughly 80 percent in bipolar illness, and this protection extends to unipolar depression (Maudsley 2021; IPS 2017). About 15 percent of people with bipolar disorder die by suicide, which frames why this matters. The full clinical suicide risk assessment and safety planning belong to the Somatic-symptom, sexual, impulse-control disorders and suicide notes.

RULE **Lithium is the anti-suicidal mood stabiliser.** In a bipolar patient with suicidality it is the preferred long-term agent for its specific, class-unique anti-suicide evidence.

14.3 Initiation: the baseline work-up before the first tablet

The pre-lithium screen. Because clearance is renal and the drug is a putative teratogen with thyroid, parathyroid and cardiac effects, a baseline work-up is mandatory before **initiation** (Maudsley 2021; IPS 2017). As a minimum, check: renal function (estimated GFR with urea and electrolytes), thyroid function (TSH), serum calcium, a baseline weight, and a pregnancy test with contraceptive counselling in women of child-bearing potential. An ECG is recommended in those with cardiovascular risk factors or established cardiac disease.

BASELINE TEST	WHY
Renal function (eGFR, U and Es)	Lithium is cleared only by the kidney; sets the safety floor and the interaction baseline
Thyroid function (TSH)	Lithium causes hypothyroidism (up to ~20 percent in middle-aged women over time)
Serum calcium	Hyperparathyroidism with hypercalcaemia occurs in about 4 percent
ECG (if cardiovascular risk)	Recommended where cardiac risk factors or disease exist
Weight / BMI	Weight gain is a common, adherence-limiting adverse effect
Pregnancy test / contraception	Putative teratogen (Ebstein anomaly with first-trimester exposure)

The pre-lithium baseline work-up (Maudsley 2021; IPS 2017). Renal, thyroid and calcium are the non-negotiable trio; ECG is conditional on cardiac risk. The perinatal detail is cross-referred.

TRAP **Starting lithium without baseline renal and thyroid function.** You lose the safety baseline, miss pre-existing renal impairment or hypothyroidism, and cannot later attribute change to the drug.

14.4 Dosing: starting dose and titration to the target level

Starting and titrating. The standard **dosing** approach: start lithium carbonate at **400 mg at night** in an adult, or **200 mg at night** in the elderly, then titrate against the serum level, not against a fixed milligram target (Maudsley 2021). Check the first plasma level after 7 days, and again 7 days after every dose change, until the desired level is reached; once stable it is checked every 6 months (Maudsley 2021; IPS 2017).

Timing the sample. The blood sample must be taken 12 hours after the last dose (the standardised 12-hour trough), because a sample drawn too early reads falsely high (Maudsley 2021). The usual maintenance dose lands around 600 to 1200 mg daily, but the number that matters is the serum level, not the dose.

RULE **Titrate to the level, and take the sample at 12 hours.** A lithium level drawn before the 12-hour trough overreads and can trigger a wrongful dose cut.

WORKED EXAMPLE

A 34-year-old man in acute mania is started on lithium carbonate 400 mg nocte after a normal baseline eGFR, TSH and calcium. A level after one week, drawn 12 hours post-dose, reads 0.6 mmol/L. Because the target for acute mania is higher, the dose is increased and a repeat level 7 days later reaches 0.9 mmol/L, within the 0.8 to 1.0 mmol/L acute band, with good tolerability. Had the day-7 sample been taken at 3 hours post-dose it would have read spuriously high and prompted an inappropriate dose reduction.

14.5 The therapeutic range: aim high for mania, lower for maintenance

The two targets. This is the single highest-yield fact of the topic. The **therapeutic range** is phase-dependent. For **acute mania** aim for a serum lithium of **0.8 to 1.0 mmol/L**, extending up to 1.2 mmol/L in difficult-to-treat mania (Maudsley 2021; CANMAT 2018; IPS 2017). For maintenance and prophylaxis aim lower, at **0.6 to 0.8 mmol/L**, with the option to go up to 1.0 mmol/L for insufficient response and good tolerance, or down to 0.4 to 0.6 mmol/L for good response but poor tolerance (Maudsley 2021; CANMAT 2018).

The elderly and the augmentation targets. In older adults a lower maintenance target of about **0.4 to 0.6 mmol/L** is often used, starting low (for example 150 to 200 mg at night) because renal clearance falls with age (Maudsley 2021; CANMAT 2018). For unipolar antidepressant augmentation the effective serum level is 0.6 to 1.0 mmol/L. The minimum effective prophylactic level is probably about 0.4 mmol/L, but the practical prophylaxis target remains 0.6 to 0.8 mmol/L (Maudsley 2021).

INDICATION / PHASE	SERUM LITHIUM TARGET (MMOL/L)	SOURCE
Acute mania	**0.8 to 1.0 (up to 1.2 in difficult mania)**	Maudsley 2021; CANMAT 2018; IPS 2017
Maintenance / prophylaxis (bipolar)	**0.6 to 0.8 (up to 1.0)**	Maudsley 2021; CANMAT 2018
Maintenance in the elderly	0.4 to 0.6	Maudsley 2021; CANMAT 2018
Unipolar antidepressant augmentation	0.6 to 1.0	Maudsley 2021
Toxicity threshold	above 1.5 (seizures usually above 2.0)	Maudsley 2021

Verified serum lithium targets by phase (mmol/L; for lithium, 1 mmol/L equals 1 mEq/L). The two highlighted rows are the must-hold numbers: higher for acute mania, lower for maintenance. Toxicity begins reliably above 1.5 mmol/L.

0.8 to 1.0	0.6 to 0.8	above 1.5
ACUTE MANIA TARGET (MMOL/L)	MAINTENANCE TARGET (MMOL/L)	TOXICITY THRESHOLD (MMOL/L)

TRAP **Using the maintenance range to treat acute mania.** A 0.6 to 0.8 mmol/L level undertreats an acute manic episode; the acute target is higher, 0.8 to 1.0 (up to 1.2) mmol/L.

14.6 The Indian brands and continued front-line use

What is prescribed here. In Indian practice lithium is prescribed as lithium carbonate, and remains a genuine first-line mood stabiliser rather than a legacy drug, endorsed as first-line for acute mania and as the primary maintenance agent in the Indian Psychiatric Society guidelines (the IPS guidelines; IPS 2017). Its low cost and the strength of the maintenance and anti-suicide evidence keep it front-line in a largely out-of-pocket health system.

INDIA

Lithium carbonate is marketed in India as Licab and as Intalith (both lithium carbonate), available as standard and sustained-release tablets. It stays a genuine front-line agent: the Indian Psychiatric Society guidelines place lithium first-line for acute mania (target 0.8 to 1.2 mmol/L) and as the primary maintenance mood stabiliser for preventing both manic and depressive recurrence, at a maintenance level of 0.6 to 1.0 mmol/L, with its specific anti-suicide evidence explicitly noted (IPS 2017). Serum-level access is widely available in district and teaching hospitals, and the drug is inexpensive, both of which support its continued heavy use in Indian outpatient departments.

GOOD TO REMEMBER

- **Lithium (Licab or Intalith):** monovalent cation, GSK3-beta and inositol-cycle effects; renal clearance only; first-line for acute mania and the gold-standard maintenance agent with unique anti-suicide evidence.
- **Acute mania target:** serum lithium **0.8 to 1.0 mmol/L** (up to 1.2 in difficult mania).
- **Maintenance / prophylaxis target:** serum lithium **0.6 to 0.8 mmol/L** (up to 1.0; 0.4 to 0.6 in the elderly).
- **Initiation:** baseline renal (eGFR, U and Es), thyroid (TSH), calcium, weight, ECG if cardiac risk, pregnancy test; start **400 mg nocte** (200 mg elderly).
- **Monitoring:** level at 7 days and 7 days after each change, sampled 12 hours post-dose, then 6-monthly with eGFR and TFTs.

HOLD THIS

Lithium is first-line for acute mania and the gold-standard maintenance mood stabiliser with the strongest anti-suicidal evidence: aim for a serum level of 0.8 to 1.0 mmol/L in acute mania and 0.6 to 0.8 mmol/L in maintenance, always after a baseline renal, thyroid and calcium screen, sampling the level 12 hours post-dose.

15 . Lithium monitoring

lithium monitoring is examined more precisely than almost any other prescribing topic, because lithium has the narrowest therapeutic index in psychiatry: the gap between an effective and a toxic level is small, so the drug is unusable without a disciplined monitoring routine. The two things the board rewards are the **sampling rule** (how and when to draw the level) and the **investigation schedule** (what to check at baseline and how often afterwards). Get the timing of the blood sample wrong and the number is meaningless; let the renal or thyroid checks lapse and you miss the two organ toxicities that end lithium therapy.

The whole topic hangs on one physiological fact: lithium is renally cleared with a long distribution phase, so the plasma level is only interpretable at a standardised time after the dose. That time is twelve hours. Everything below, the target ranges, the check after a dose change, the six-monthly organ panel, is verified against the Maudsley Prescribing Guidelines, Stahl's Prescriber's Guide, the CANMAT guideline and the Indian Psychiatric Society clinical practice guideline (Maudsley 2021; Stahl 2021; Yatham 2018; Shah 2017). The lithium initiation and toxicity detail sits alongside this in the mood-block pharmacotherapy notes; the guideline-

anchored management PLAN that puts lithium first-line is set out in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes.

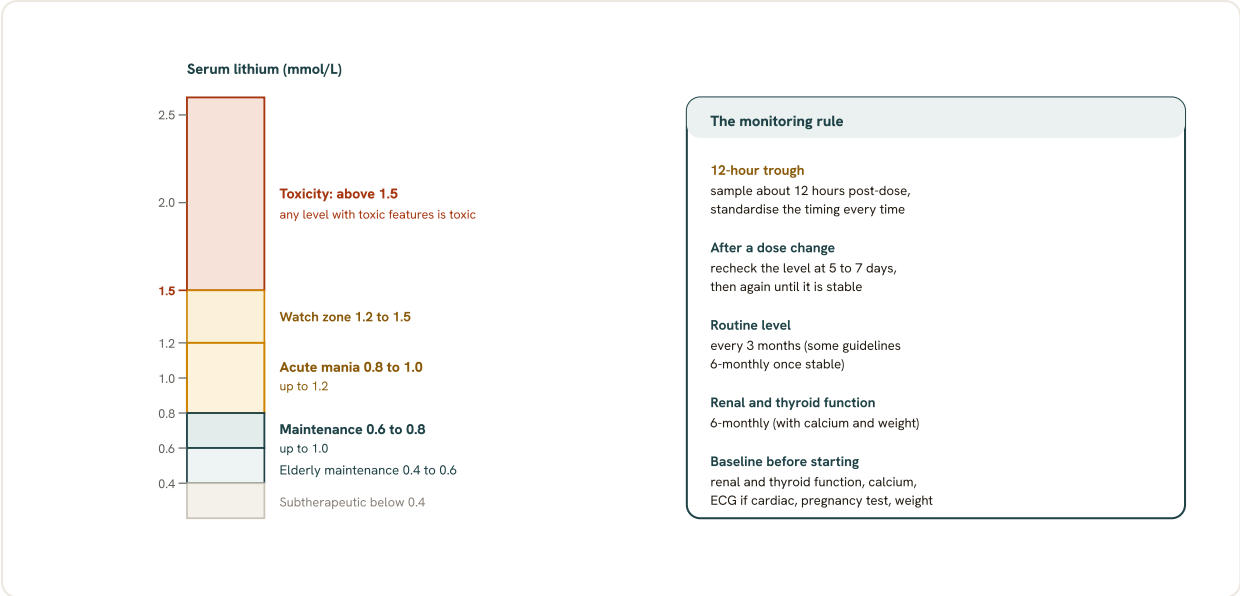


Fig 12.8 The lithium therapeutic window and the monitoring rule. The window is narrow: aim about 0.8 to 1.0 (up to 1.2) mmol/L for acute mania and 0.6 to 0.8 (up to 1.0) for maintenance, with a lower 0.4 to 0.6 target in the elderly; toxicity is expected above 1.5, though any level with toxic features counts as toxic. Sample as a 12-hour trough, recheck 5 to 7 days after any dose change, and monitor renal and thyroid function with the baseline work-up shown.

15.1 The sampling rule: the twelve-hour trough

Sample at the trough, twelve hours post-dose. The single most examined fact in **lithium monitoring** is when to draw the blood. Because lithium has a long distribution phase, an early sample catches the drug still redistributing and reads falsely high. The standard is the **twelve-hour trough**: the blood is taken as the **12-hour** post-dose sample, ideally 10 to 14 hours after the last dose, with 12 hours the target, in a patient on a once-daily bedtime regimen (Maudsley 2021). This is the **serum level** that every published target range refers to. In practice, for a patient who takes lithium at night, the sample is drawn the next morning before the day's dose.

Standardise the timing. Because the level changes across the dosing interval, the timing must be held constant from one sample to the next, so that a change in the number reflects a change in the patient and not a change in when you took the blood. A CANMAT and the Indian Psychiatric Society both anchor drug-level sampling to this trough point (Yatham 2018; Shah 2017).

RULE **Draw the lithium level as a twelve-hour trough.** The 12-hour post-dose sample, timed the same way each time, is the only interpretable serum level.

TRAP **Taking a random, non-trough level and acting on it.** A sample drawn a few hours after the dose reads spuriously high and invites a wrong dose cut, or a spuriously reassuring number if drawn late; always standardise to 12 hours.

15.2 The target ranges the level is read against

What number you are aiming for. The trough **serum level** is only useful against a target. For maintenance and prophylaxis in bipolar disorder the accepted range is **0.6 to 1.0 mmol/L**

(CANMAT keeps maintenance at 0.6 to 1.0 mEq/L; the Maudsley narrows the prophylactic optimum to 0.6 to 0.8 mmol/L) (Yatham 2018; Maudsley 2021). In acute mania a slightly higher level of **0.8 to 1.2 mmol/L** is targeted, and for lithium augmentation of an antidepressant in unipolar depression the target is **0.6 to 1.0 mmol/L**, the same as maintenance (Maudsley 2021). Toxic effects reliably appear above **1.5 mmol/L**, which is why the trough discipline matters so much.

0.6 to 1.0	0.8 to 1.2	1.5
MAINTENANCE LITHIUM (MMOL/L)	ACUTE MANIA TARGET (MMOL/L)	TOXICITY THRESHOLD (MMOL/L)

15.2b Checking the level after a dose change

Recheck 5 to 7 days after every dose change. Lithium reaches a new steady state roughly five half-lives after any change in dose, which is about 5 to 7 days in an adult with normal renal function. So after starting lithium or altering the dose you draw the next twelve-hour trough about 5 to 7 days later, and you repeat this after each successive change until the level is stable in the target range (Maudsley 2021; Shah 2017). The Maudsley states the interval as a level after 7 days and then 7 days after every dose change; the Indian Psychiatric Society states it as 5 to 7 days after a dose change, and CANMAT applies the same 5 to 7 day rule after any dose or interacting-drug change in older adults (Maudsley 2021; Shah 2017; Yatham 2018). Practically, hold 5 to 7 days.

RULE **After any dose change, recheck the trough level in 5 to 7 days.** Steady state is about five half-lives; repeat after each change until stable.

15.3 The frequency of level monitoring once stable

Frequent during titration, then every 3 months. During titration the level is checked every few days to a week as the dose is adjusted (each check 5 to 7 days after the preceding change). Once the patient is established on a stable dose with the level in range, routine **serum level** monitoring settles to **every 3 months** in the Indian Psychiatric Society schedule, while some guidelines including the Maudsley move to **6-monthly** lithium levels once the patient is stable (Shah 2017; Maudsley 2021). CANMAT sits between these, repeating levels every 3 to 6 months after two consecutive therapeutic acute-phase readings (Yatham 2018).

Check more often in the vulnerable. The interval shortens in the **elderly**, in anyone starting or stopping an interacting drug (see 15.6), in renal impairment or other relevant physical illness, and whenever toxicity is suspected clinically (Maudsley 2021). In these groups a routine 6-monthly level is not enough.

15.4 Baseline investigations before starting lithium

The pre-lithium work-up. The **baseline investigations** exist to establish the two organ functions lithium threatens and to flag cardiac risk. Before prescribing, check **renal function** (estimated glomerular filtration rate, that is eGFR, with urea and electrolytes and serum creatinine) and **thyroid function** (thyroid-stimulating hormone, that is TSH), together with a baseline serum calcium, a baseline weight or body mass index, and an ECG where the patient has

risk factors for or established cardiovascular disease (Maudsley 2021; Yatham 2018). Because lithium is a putative human teratogen, a woman of child-bearing potential should be counselled on reliable contraception and a pregnancy test considered at baseline (Maudsley 2021).

Renal function
eGFR, serum creatinine, urea and electrolytes; the organ that clears lithium and the one at long-term risk.

Thyroid function
TSH (with free T4 if abnormal); lithium causes hypothyroidism, up to about 20% in middle-aged women over time.

Calcium
baseline serum calcium; lithium can cause hyperparathyroidism and hypercalcaemia.

ECG
at baseline where cardiovascular risk factors or disease exist.

Weight / BMI
baseline, because lithium causes weight gain.

15.5 The follow-up panel: renal and thyroid roughly 6-monthly

Repeat renal and thyroid at 6 months. The on-treatment organ panel mirrors the baseline one. **Renal function** (eGFR and creatinine) and **thyroid function** (TSH) are rechecked roughly 6-monthly, along with serum calcium and weight, and at least annually thereafter or as clinically indicated; the Maudsley checks plasma lithium, eGFR, U&Es, TFTs and calcium every 6 months, CANMAT assesses thyroid and renal function and plasma calcium at 6 months and at least annually, and the Indian Psychiatric Society specifies baseline and 6-monthly TSH, creatinine, eGFR, calcium and weight (Maudsley 2021; Yatham 2018; Shah 2017). Thyroid function is often checked more frequently in the first year, when hypothyroidism most commonly emerges (Maudsley 2021).

Note that the follow-up level (15.3) and the follow-up organ panel run on slightly different clocks: the trough level is checked 3-monthly (some guidelines 6-monthly once stable), while the renal and thyroid panel is checked roughly 6-monthly. Both intervals shorten in the elderly and with interacting drugs.

INVESTIGATION	BASELINE	TITRATION	ONCE STABLE (INTERVAL)	NOTE
Serum lithium (12-hour trough)	not applicable	**5 to 7 days after each dose change**	**every 3 months (some guidelines 6-monthly)**	Draw 12 h post-dose; standardise timing
Renal function (eGFR, creatinine)	yes	if concern	**roughly 6-monthly**	More often in the elderly / interacting drugs / CKD
Thyroid function (TSH)	yes	if concern	**roughly 6-monthly**	Consider more often in first year

INVESTIGATION	BASELINE	TITRATION	ONCE STABLE (INTERVAL)	NOTE
Serum calcium	yes	if concern	roughly 6-monthly	Hyperparathyroidism / hypercalcaemia
Weight / BMI	yes	monitor	roughly 6-monthly	Lithium causes weight gain
ECG	where CV risk	not routine	as clinically indicated	Baseline if cardiovascular risk factors or disease

Lithium monitoring schedule: the twelve-hour trough serum level after each dose change and then 3-monthly (some guidelines 6-monthly), with renal and thyroid function roughly 6-monthly, plus calcium, weight and ECG where indicated (Maudsley 2021; Yatham 2018; Shah 2017). Highlighted cells are the board-critical intervals.

TRAP **Letting renal or thyroid monitoring lapse.** A patient stable for years still needs the roughly 6-monthly renal and thyroid panel; silent hypothyroidism or a creeping fall in eGFR is missed when the panel is dropped.

15.6 Interacting drugs that force closer monitoring

Anything that raises the lithium level tightens the schedule. Lithium sits on the renal sodium-handling system, so drugs that alter that system change its level and mandate more frequent checks. The classic culprits are thiazide diuretics, ACE inhibitors and angiotensin-receptor blockers, and NSAIDs, each of which raises the lithium level and can precipitate toxicity (Maudsley 2021). Whenever one of these is started, stopped or dose-adjusted, recheck the twelve-hour trough 5 to 7 days later and monitor renal function more closely; in the elderly, ACE inhibitors raise the risk of lithium-toxicity hospitalisation several-fold (Maudsley 2021).

COMMON TRAP

A stable lithium patient develops hypertension and is started on a thiazide or an ACE inhibitor by another clinician. Without a repeat trough level 5 to 7 days later, the rising lithium level goes unnoticed until the patient presents with tremor, ataxia and confusion. Any new interacting drug is a trigger to recheck the level, not to wait for the next routine appointment.

INDIA

Lithium is cheap, freely available and heavily prescribed in Indian practice; the generic is lithium carbonate, marketed as Licab and as the controlled-release Intalith CR. The serum level assay is inexpensive and widely available, but the twelve-hour trough discipline is easily lost in a busy outpatient department, so counsel the patient to attend fasting in the morning before the day's dose and to note the time of the last tablet. The Indian Psychiatric Society schedule (serum level 5 to 7 days after a dose change, then 3-monthly when stable, with baseline and 6-monthly TSH, creatinine, eGFR, calcium and weight) is the practical standard to memorise for Indian exams (Shah 2017).

MNEMONIC

TRoTTeR

What lithium monitoring turns on: **T**welve-hour trough (the sample timing), **R**echeck at 5 to 7 days after a dose change, **o**ngoing level every 3 months once stable, **T**hyroid (TSH) roughly 6-monthly, **T**ests of renal function (eGFR/creatinine) roughly 6-monthly, and **R**emember calcium, weight and ECG where indicated.

GOOD TO REMEMBER

- **Serum level timing:** twelve-hour trough, the 12-hour post-dose sample (ideally 10 to 14 hours), standardised each time.
- **After a dose change:** recheck the trough level in 5 to 7 days (about five half-lives to steady state), repeat until stable.
- **Routine level once stable:** every 3 months (some guidelines 6-monthly), more often in the elderly or with interacting drugs.
- **Renal function (eGFR/creatinine):** at baseline then roughly 6-monthly; the organ that clears lithium and the long-term risk.
- **Thyroid function (TSH):** at baseline then roughly 6-monthly (often more in the first year); lithium causes hypothyroidism.
- **Also:** baseline and 6-monthly calcium and weight; baseline ECG where cardiovascular risk exists.
- **Target ranges the level is read against:** maintenance **0.6 to 1.0 mmol/L**, acute mania **0.8 to 1.2 mmol/L**, toxicity above **1.5 mmol/L**.

HOLD THIS

Sample lithium as a standardised twelve-hour trough, recheck 5 to 7 days after every dose change until stable, then run the level 3-monthly (some guidelines 6-monthly) and the renal and thyroid panel roughly 6-monthly, checking more often in the elderly or on interacting drugs.

16 . Lithium toxicity

lithium toxicity is the one lithium emergency the board expects you to recognise on sight, grade, and manage in the right order. Lithium has the narrowest therapeutic index in psychiatry, so a patient sitting comfortably in the maintenance range of **0.6 to 1.0 mmol/L** can be pushed into toxicity by an ordinary intercurrent event: a bout of gastroenteritis, a hot spell with poor fluid intake, a new diuretic, or an NSAID bought over the counter. The examinable core is the **graded picture keyed to the serum level** and the **stepwise management**, because both are scored precisely and both save lives.

Everything below is keyed to the twelve-hour trough **serum level** and verified against the Maudsley Prescribing Guidelines, with the guideline-level counselling and threshold cross-checked against CANMAT and the Indian Psychiatric Society clinical practice guideline (Maudsley 2021; Yatham 2018; Shah 2017). The Maudsley states that toxic effects reliably occur at levels above **1.5 mmol/L**, that disorientation and seizures usually appear above 2 mmol/L progressing to coma and death, and that dialysis is often used above 3 mmol/L (Maudsley 2021). The sampling rule, target ranges and organ monitoring sit alongside this in the lithium initiation

and monitoring notes; the wider emergency frame for acute management and the perinatal picture is set out in the Perinatal/women's mental health and emergency psychiatry notes.



Fig 12.9 Lithium toxicity graded by serum level. Mild toxicity from 1.5 to 2.0 mmol/L gives coarse tremor, GI upset and lethargy; moderate toxicity (2.0 to 2.5) adds confusion, ataxia and dysarthria; severe toxicity above 2.5 brings seizures, coma and renal failure and needs haemodialysis. Any level with toxic features counts as toxicity, and dehydration or an interacting drug is the usual precipitant.

16.1 Why toxicity happens: the precipitants

Anything that raises the lithium level or the brain's exposure to it. Lithium is handled by the kidney exactly like sodium, so most precipitants act by changing sodium balance or renal clearance. The examinable list is: **dehydration** (vomiting, diarrhoea, fever, hot climate, reduced intake), **sodium loss** or a low-salt diet, **renal impairment** (which lowers clearance), **drug interactions**, and **overdose** (deliberate or accidental) (Maudsley 2021). The Maudsley notes that most risk factors involve a fall in sodium or a change in how the body handles sodium, for example low-salt diets, dehydration, drug interactions and uncommon illnesses such as Addison's disease (Maudsley 2021).

The interacting drugs to hold. Three classes raise the level and precipitate toxicity: thiazide diuretics, ACE inhibitors and angiotensin-receptor blockers, and NSAIDs (Maudsley 2021). Each reduces renal lithium clearance, so a stable patient started on any of them needs a repeat level and can tip into toxicity within days.

RULE **Any coarse tremor, ataxia or confusion in a patient on lithium is toxicity until the level proves otherwise.** Check the level before you look for another cause.

TRAP **Continuing lithium through an intercurrent illness with vomiting or dehydration.** Fluid loss concentrates the drug; the level climbs even though the dose has not changed. Withhold lithium and rehydrate.

16.2 The graded picture: mild, moderate, severe

Read the features against the level. Toxicity follows a **mild moderate severe** gradient that tracks the rising **serum level**, and the board rewards you for stating the **grading** with the

matching level band. The Maudsley anchors the two hard thresholds: toxic effects reliably occur above **1.5 mmol/L** (gastrointestinal upset plus early CNS signs), and above 2 mmol/L disorientation and seizures usually occur, progressing to coma and death (Maudsley 2021). The widely taught three-band scheme places mild toxicity from 1.5 to 2.0 mmol/L, moderate from 2.0 to 2.5 mmol/L, and severe above 2.5 mmol/L, consistent with the Maudsley anchors above (serious neurotoxicity and seizures usually appear above 2, and dialysis is often needed above 3).

Mild (1.5 to 2.0 mmol/L)
coarse **tremor** (the fine physiological tremor becomes coarse), gastrointestinal upset (anorexia, nausea, diarrhoea), lethargy and mild drowsiness.

Moderate (2.0 to 2.5 mmol/L)
confusion, **ataxia**, dysarthria, myoclonus and muscle twitching, worsening coarse tremor, marked drowsiness.

Severe (above 2.5 mmol/L)
seizure, coma, cardiovascular collapse, and renal failure; ultimately death.

The level is only a guide. The Maudsley cautions that these plasma levels are a guide only and individuals vary in susceptibility, and that neurotoxicity has been described even at normal plasma levels because brain lithium may not be reflected in the plasma concentration (Maudsley 2021). Treat the patient in front of you, not the number alone.

1.5 to 2.0	2.0 to 2.5	above 2.5
MILD TOXICITY (MMOL/L)	MODERATE TOXICITY (MMOL/L)	SEVERE TOXICITY (MMOL/L)

16.3 The graded table of level, features and management

The one table to hold for the viva. Grade, features and the corresponding management step line up as follows (Maudsley 2021).

GRADE	SERUM LEVEL (MMOL/L)	CLINICAL FEATURES	MANAGEMENT
Mild	**1.5 to 2.0**	coarse tremor, GI upset (anorexia, nausea, diarrhoea), lethargy	Stop lithium; check level, renal function and electrolytes; rehydrate; recheck level
Moderate	**2.0 to 2.5**	confusion, ataxia, dysarthria, myoclonus, coarse tremor	Stop lithium; admit; intravenous normal saline to restore volume and sodium; serial levels and renal function; supportive care
Severe	**above 2.5**	seizure, coma, cardiovascular collapse, renal failure	Stop lithium; medical/ICU care; correct volume; **haemodialysis** for severe features or renal failure, usually at levels above 2.5 to 3.0 mmol/L

Lithium toxicity grading: features and management keyed to the twelve-hour trough serum level, mild 1.5 to 2.0, moderate 2.0 to 2.5, severe above 2.5 mmol/L; haemodialysis is reserved for severe toxicity (Maudsley 2021). Highlighted cells are the board-critical level bands.

16.4 Management: stop, assess, rehydrate, dialyse if severe

Four steps in order. The management of **lithium toxicity** is a fixed sequence. First, **stop lithium** immediately. Second, **check the level and renal function and electrolytes** (serum lithium, creatinine and eGFR, urea and electrolytes) and repeat serially, because the level can keep rising as the drug redistributes. Third, **rehydrate with saline**: intravenous normal (0.9%) saline restores intravascular volume and sodium and promotes renal excretion of lithium. Fourth, use **haemodialysis** for severe toxicity, that is high levels, renal failure, or severe clinical features such as seizures, coma or haemodynamic collapse (Maudsley 2021). The Maudsley states that above 3 mmol/L peritoneal or haemodialysis is often used, and that in more severe symptomatic cases osmotic or forced alkaline diuresis has historically been used in a medical facility (Maudsley 2021).

Why dialysis, and why it may need repeating. Lithium is a small, non-protein-bound ion that dialyses readily, so haemodialysis rapidly clears it from plasma. But lithium leaves the intracellular and brain compartments slowly, so the plasma level can rebound after a session ends, and dialysis may need to be repeated until the post-dialysis rebound level stays below the toxic threshold. This is why serial levels continue after the first run.

RULE **Stop lithium, give saline, and dialyse the severe.** Haemodialysis is indicated for very high levels, renal failure, or severe neurological or cardiovascular features, regardless of the exact number.

16.5 The silent sequel: delayed and irreversible neurotoxicity

Recovery is not always complete. A minority of patients who survive significant neurotoxicity are left with persistent, sometimes permanent, cerebellar and other neurological deficits: the **silent** picture, described as the syndrome of irreversible lithium-effectuated neurotoxicity (SILENT). The hallmark is a persisting cerebellar syndrome, most often ataxia and dysarthria, that outlasts the acute episode and the fall in serum level. The teaching point is that lithium neurotoxicity is not always a fully reversible event, which is a further reason to act quickly and not to let a moderate picture drift toward the severe. Delayed neurotoxic sequelae can persist after the plasma level has normalised, consistent with the Maudsley observation that brain lithium is not reflected in the plasma (Maudsley 2021).

INDIA

Lithium is cheap, freely available and heavily prescribed in Indian practice, marketed as lithium carbonate (Licab, and the controlled-release Intalith CR). The commonest real-world precipitants here are summer dehydration, gastroenteritis with vomiting and diarrhoea, and over-the-counter NSAIDs bought without a prescription, so counsel every patient at initiation to withhold lithium and increase fluids during any vomiting, diarrhoea or febrile illness and to attend for a level. Serum lithium, creatinine and electrolyte assays are inexpensive and widely available; the practical management chain to hold is stop lithium, send a stat level with renal function and electrolytes, start intravenous normal saline, and refer for **haemodialysis** if the level is high, renal function is failing, or the patient has seizures or coma (Maudsley 2021; Shah 2017). Where dialysis is not immediately available, transfer the severely toxic patient to a centre that has it rather than waiting.

PEARL

The discriminator between a therapeutic tremor and toxicity is its character: lithium normally causes a fine physiological tremor, but a **tremor** that has become coarse, especially with any GI upset, ataxia or confusion, signals toxicity and demands a level. Do not attribute new ataxia or confusion in a lithium patient to age, alcohol or a virus until the level is back.

MNEMONIC

SALT loss climbs the level; STOP-SALINE-DIALYSE brings it down

Precipitants act through **SALT** and water: dehydration, sodium loss, NSAIDs and diuretics, renal impairment, overdose. Management is **STOP** lithium, check the level and renal function and electrolytes, **SALINE** (rehydrate with normal saline), and **DIALYSE** if severe (high level, renal failure or severe features).

GOOD TO REMEMBER

- **Mild toxicity (around 1.5 mmol/L):** coarse tremor, GI upset and lethargy; the earliest and commonest feature.
- **Moderate toxicity (around 1.5 to 2.5 mmol/L):** ataxia, dysarthria, confusion and myoclonus; the patient is now clearly encephalopathic.
- **Severe toxicity (above 2.5 mmol/L):** seizures, coma and cardiovascular collapse; a medical emergency.
- **Precipitants:** dehydration and NSAIDs are the classic ones; also sodium loss, diuretics, ACE inhibitors/ARBs, renal impairment and overdose.
- **First management step:** stop lithium, check level plus renal function and electrolytes, rehydrate with saline; dialyse if severe.
- **Discriminator (silent sequel):** haemodialysis for severe toxicity; a persisting cerebellar syndrome (silent, irreversible neurotoxicity) can outlast the normalised level.

HOLD THIS

Coarse tremor and GI upset at ~1.5, ataxia/dysarthria/confusion at 1.5 to 2.5, seizures/coma above 2.5 mmol/L: stop lithium, check level with renal function and electrolytes, rehydrate with saline, and haemodialyse the severe (Maudsley 2021).

17 . Lithium and the kidney

The kidney is where lithium is cleared and where lithium does its most talked-about harm, so **lithium and the kidney** is a favourite examiner theme. Two effects sit at opposite ends of the time axis: an **early, common, largely reversible** concentrating defect that the patient feels as thirst and frequent urination, and a **slow, long-term** decline in filtration that only a monitoring trend will reveal. The board rewards you for separating the two, for naming the drug that treats the first, and for knowing that the second is managed by watching the eGFR trend and taking a measured nephrology-guided decision rather than stopping lithium on a single reading.

The whole topic follows from one physiological fact set out in the Mood disorders: pharmacotherapy renal-handling detail: lithium enters collecting-duct principal cells through the epithelial sodium channel (ENaC), competing with sodium, and its intracellular accumulation inhibits the renal response to antidiuretic hormone and, over years, drives interstitial fibrosis (Meyer and Stahl 2023; Maudsley 2021). Everything below, the polyuria, the amiloride, the eGFR trend, the CKD risk-benefit, derives from that. The initiation, dosing and toxicity detail sits in the mood-block pharmacotherapy notes; the twelve-hour trough and the full baseline and follow-up panel are in the lithium monitoring topic; the guideline-anchored PLAN that keeps lithium first-line is in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes. The receptor and channel background is in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

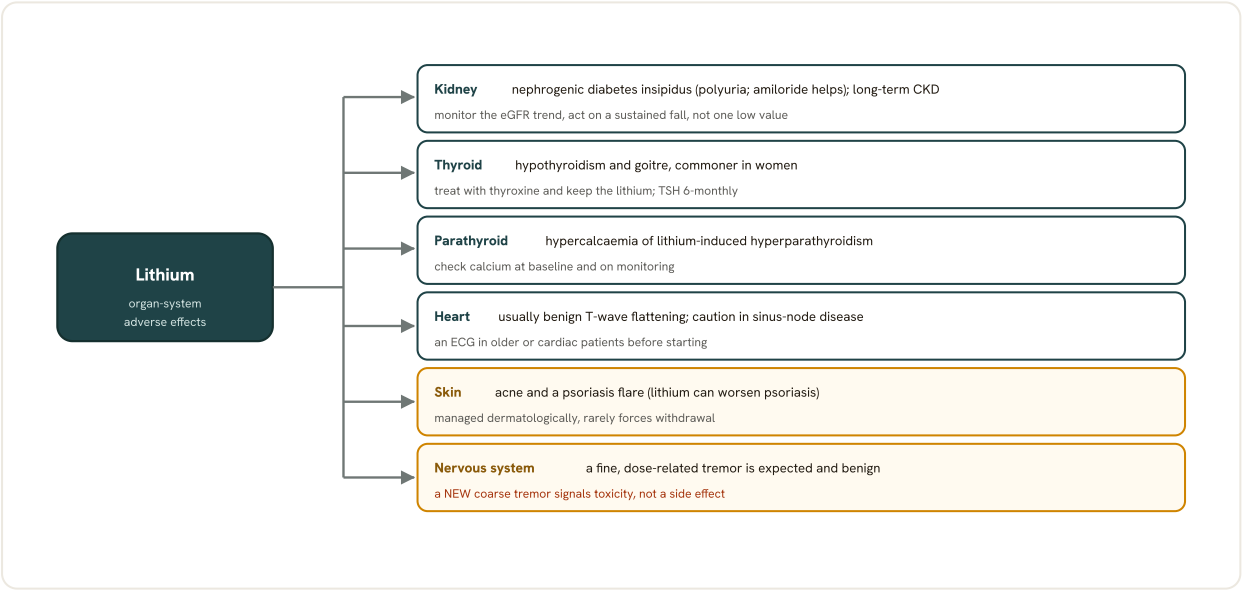


Fig 12.10 The organ-system adverse effects of lithium and their monitoring. The kidney (nephrogenic diabetes insipidus, long-term chronic kidney disease) and thyroid (hypothyroidism, goitre) are the load-bearing ones, caught by routine renal and thyroid monitoring; hypercalcaemia, benign cardiac T-wave changes, acne and psoriasis, and a fine dose-related tremor complete the picture. A new coarse tremor is the exception: it signals toxicity rather than a tolerable side effect.

17.1 Nephrogenic diabetes insipidus: the mechanism

Lithium blocks the renal response to ADH. The earliest and commonest renal effect is nephrogenic diabetes insipidus. Lithium entering the collecting-duct principal cell via ENaC accumulates intracellularly and, in roughly 20% of patients, produces insensitivity to antidiuretic

hormone (ADH, vasopressin) with downregulation of the water-absorbing aquaporin-2 channels on the apical surface (Meyer and Stahl 2023). The kidney can no longer concentrate the urine in response to ADH, so dilute urine is passed in large volume. The result is **polyuria** and, secondarily, **polydipsia** as the patient drinks to keep up. It is nephrogenic (the defect is at the kidney, the ADH itself is normal or high), which is why it is called nephrogenic diabetes insipidus rather than a central one.

Common, and usually reversible early. A reduction in urinary concentrating capacity is common on lithium and, in the short to medium term, is usually reversible on stopping or dose reduction; renal effects may become irreversible only after long-term treatment (Grierson and companion authors, Companion to Psychiatric Studies; Meyer and Stahl 2023). Polyuria is defined as a 24-hour urine output above **3 litres** (Meyer and Stahl 2023). It is the effect patients notice first and complain about most, and it is the single commonest cited reason for wanting to stop lithium, so recognising and treating it early forestalls unnecessary discontinuation.

RULE **Lithium polyuria is nephrogenic diabetes insipidus until proven otherwise.** ADH is normal, the kidney cannot respond, and the defect is usually reversible if caught early.

17.2 Assessing the polyuria

Ask at every visit, then quantify. Assessment of **polyuria** starts with routine inquiry at each office visit about excessive thirst and urination, because some patients underreport the functional impact (Meyer and Stahl 2023). Two office tools then quantify it. The 24-hour fluid intake record (FIR) is a simple screen the patient can keep: an intake below 2000 mL over 24 hours makes polyuria very unlikely, while an intake climbing towards 3000 to 3500 mL makes it likely. The early morning urine osmolality (EMUO) estimates concentrating ability directly and tracks response to treatment.

Polyuria (definition)
24-hour urine output above 3 litres; the standard threshold.

24-hour fluid intake record (FIR)
patient-kept screen; below 2000 mL/24 h makes polyuria unlikely, above 3500 mL/24 h makes it likely.

Early morning urine osmolality (EMUO)
direct measure of concentrating ability; normal exceeds about 850 mOsm/kg.

Full nephrogenic diabetes insipidus
EMUO below 300 mOsm/kg; treat regardless of how loudly the patient complains.

A normal EMUO is above about **850 mOsm/kg** after overnight water deprivation; a value below **300 mOsm/kg** represents full nephrogenic diabetes insipidus and warrants treatment whatever the patient reports, because it signals clear lithium accumulation in the principal cells (Meyer and Stahl 2023).

17.3 Managing nephrogenic diabetes insipidus: dose review, once-daily dosing, amiloride

First tighten the regimen, then add amiloride. Management of lithium-related **nephrogenic diabetes insipidus** proceeds in a logical order. First, review the dose and the serum level: keep the maintenance twelve-hour trough modest, and prefer once-daily dosing, because polyuria occurs more frequently with twice-daily than once-daily regimens and modern once-daily dosing lowers renal risk (Maudsley 2021; Meyer and Stahl 2023). Second, where polyuria persists, add amiloride.

Amiloride blocks lithium entry into the collecting duct. Amiloride is a potassium-sparing diuretic that specifically blocks ENaC, the very channel lithium uses to enter principal cells, so it reduces lithium's intracellular accumulation and improves urine concentrating ability (Meyer and Stahl 2023; Kortenoeven et al. 2009). It is the primary, best-evidenced treatment for lithium-related nephrogenic diabetes insipidus and should be started as soon as a concentrating problem is detected; the claim that the only option is to switch off lithium is simply untrue (Meyer and Stahl 2023). Importantly, amiloride is one of the diuretics whose effect on lithium clearance is clinically insignificant, so it does not itself push the lithium level up the way a thiazide does, though at least one repeat lithium level after starting it is prudent (Meyer and Stahl 2023).

TRAP **Reaching for a thiazide to treat lithium polyuria.** A thiazide reduces polyuria but raises the lithium level and risks toxicity; amiloride, an ENaC blocker, treats the concentrating defect at its mechanism without that hazard.

WORKED EXAMPLE

A patient stable on lithium complains of drinking constantly and passing urine through the night. You confirm a 24-hour fluid intake record above 3500 mL and an early morning urine osmolality of 250 mOsm/kg, which is full nephrogenic diabetes insipidus. You do not stop the lithium. You move the patient to once-daily bedtime dosing, keep the twelve-hour trough modest, and start amiloride, then track the early morning urine osmolality as it recovers. The patient stays on the drug that protects them from relapse.

17.4 The long-term risk: chronic kidney disease

A slow decline in eGFR over years. The second, separate concern is chronic kidney disease. Years of lithium exposure can be associated with a slow decline in the estimated glomerular filtration rate (eGFR), the histological substrate being a chronic interstitial nephropathy, that is proximal tubular atrophy and interstitial fibrosis driven by intracellular lithium inhibiting GSK-3-beta in principal cells (Meyer and Stahl 2023). Lithium can lead to a reduction in glomerular filtration rate, though the magnitude of the risk is uncertain; it is driven mainly by cumulative exposure, repeated episodes of toxicity, older multiple-daily dosing and comorbidity (hypertension, diabetes) rather than by any single therapeutic level (Companion to Psychiatric Studies; Meyer and Stahl 2023).

Lithium is not the whole story. The modern reframing matters for the exam. Much of the renal risk historically pinned on lithium alone actually reflects two things: old prescribing practices (multiple daily dosing, allowing trough levels to exceed 1.2 mEq/L) and the chronic kidney

disease risk factors, hypertension, metabolic syndrome, diabetes and smoking, that are disproportionately common in bipolar patients (Meyer and Stahl 2023). Having a bipolar diagnosis itself carries a roughly 3-fold increased CKD risk independent of drug treatment. With once-daily dosing and modest outpatient trough levels below about 1.0 mEq/L, progression to end-stage renal disease attributable to lithium has become very rare (Meyer and Stahl 2023). So chronic kidney disease is a real long-term risk that mandates monitoring, but not the near-inevitability it was once feared to be.

HOLD THIS

Lithium harms the kidney in two separable ways: an early, common, usually reversible nephrogenic diabetes insipidus (polyuria, treated with amiloride) and a slow, long-term chronic kidney disease seen as a declining eGFR trend, watched over time and never acted on from one low value.

17.5 Monitoring the eGFR trend, not a single value

Watch the trend. Because the long-term change is a gradual slope, the practical rule is to monitor the **eGFR trend** rather than react to any one reading. Renal function (eGFR and creatinine) is checked at baseline and then roughly 6-monthly on stable lithium, more often when eGFR is already reduced or an interacting drug is in play (Maudsley 2021; Meyer and Stahl 2023). What triggers action is not a value but a verified downward slope. The Lithium Handbook operationalises this: increase lab frequency to every 3 months when the eGFR is below **60 ml/min**, or when there is an initial decline of more than **2 ml/min over 6 months** or more than **4 ml/min over 12 months** confirmed on a repeat specimen (Meyer and Stahl 2023).

When to bring in nephrology. A nephrology review is warranted when the eGFR falls in a sustained way, not on a single blip: a second confirmed decline exceeding those thresholds, an eGFR below **45 ml/min** verified on repeat, progression of albuminuria to stage A3, or nephrogenic diabetes insipidus unresponsive to maximal amiloride plus adjunctive acetazolamide (Meyer and Stahl 2023). The point of the nephrology referral is a joint, measured decision, weighing the renal trajectory against lithium's mood-stabilising and anti-suicide benefit, rather than a reflex switch.

RULE **Monitor the eGFR trend on long-term lithium and act on a sustained fall, not a single value.** A confirmed decline (for example more than 4 ml/min over 12 months on repeat) triggers closer monitoring and nephrology review; one isolated low reading does not.

RENAL PARAMETER	BASELINE	STABLE FOLLOW-UP	ESCALATE FREQUENCY WHEN	REFER TO NEPHROLOGY WHEN
eGFR (with creatinine)	yes	**roughly 6-monthly**	**below 60 ml/min, or decline over 2 ml/min in 6 months / over 4 ml/min in 12 months (repeat-verified)**	**second confirmed decline, or eGFR below 45 ml/min on repeat**

RENAL PARAMETER	BASELINE	STABLE FOLLOW-UP	ESCALATE FREQUENCY WHEN	REFER TO NEPHROLOGY WHEN
Early morning urine osmolality (EMUO)	consider if over 50 years	if polyuria / on amiloride	new or increased polyuria, or EMUO below 300 mOsm/kg	full NDI unresponsive to maximal amiloride plus acetazolamide
Albumin-to-creatinine ratio (ACR)	as indicated	for CKD risk factors	progression from stage A1 to A2 (repeat-verified)	stage A3
24-hour fluid intake record (FIR)	not routine	periodic office screen	polyuria complaints	not a referral trigger by itself

Practical renal monitoring on long-term lithium: the eGFR trend is the spine, with EMUO and the fluid intake record tracking the concentrating defect and the ACR tracking glomerular injury from comorbid CKD risk factors (Meyer and Stahl 2023; Maudsley 2021). Highlighted cells are the trend-based triggers a resident must hold.

17.6 Do not stop abruptly: the rebound-mania trap

A low eGFR is not a reason to stop lithium overnight. The most dangerous reflex on this topic is to see one reduced eGFR and abruptly discontinue lithium. Abrupt cessation carries a much greater than expected incidence of manic relapse in the first few months, even in patients who have been symptom-free for years (Maudsley 2021). If a decision to withdraw lithium is genuinely reached, the dose should be reduced gradually over at least a month, preferably three, avoiding stepwise plasma-level reductions greater than 0.2 mmol/L, which lowers the relapse risk (Maudsley 2021). Where the concern is renal, the correct path is the eGFR trend and a nephrology-guided risk-benefit decision, continuing lithium unless the likelihood of progression to end-stage disease clearly outweighs its benefit (Meyer and Stahl 2023).

TRAP **Stopping lithium abruptly on one low eGFR.** That risks rebound mania; the measured move is to confirm the trend, involve nephrology, and if withdrawing at all, taper over at least a month.

3	60	45
POLYURIA THRESHOLD (LITRES/24 H)	ESCALATE LABS BELOW (EGFR ML/MIN)	NEPHROLOGY REVIEW BELOW (EGFR ML/MIN)

INDIA

Lithium carbonate (marketed as Licab and as the controlled-release Intalith CR) is cheap, freely available and heavily prescribed in Indian practice, so its renal monitoring falls to the psychiatrist. Serum creatinine and eGFR are inexpensive and widely available; amiloride is available and affordable. The Indian Psychiatric Society schedule builds the renal check into routine care: baseline and 6-monthly creatinine and eGFR alongside TSH, calcium and weight, with counselling on dehydration risk (Shah et al., Indian Psychiatric Society bipolar guideline). The practical Indian-exam point is that a falling eGFR trend, not a single value, drives escalation, and that amiloride, not switching off lithium, is the first answer to lithium polyuria.

MNEMONIC

PEAR-T

Lithium and the kidney: **P**olyuria and polydipsia are the early, common, usually reversible sign, **E**NaC entry drives it (so amiloride, an ENaC blocker, treats it), **A**miloride plus once-daily dosing and a dose review is the management, **R**enal trend (the eGFR slope) is what you watch long term for chronic kidney disease, and **T**aper never abruptly stop (rebound mania).

GOOD TO REMEMBER

- **Nephrogenic diabetes insipidus:** lithium blocks the renal response to ADH at the collecting duct (via ENaC entry, aquaporin-2 downregulation), causing polyuria and polydipsia; common (about 20%), usually reversible early.
- **Amiloride:** a potassium-sparing ENaC blocker that stops lithium entering the collecting duct; the first-line, best-evidenced treatment for lithium polyuria, alongside dose review and once-daily dosing, does not raise the lithium level.
- **Polyuria assessment:** ask at every visit; quantify with the 24-hour fluid intake record and early morning urine osmolality; polyuria is over 3 litres/24 h, full NDI is EMUO below 300 mOsm/kg.
- **Chronic kidney disease:** a slow, long-term eGFR decline (chronic interstitial nephropathy); real but modest with modern once-daily dosing and troughs below about 1.0 mEq/L, and partly driven by comorbid hypertension and diabetes.
- **Monitoring:** watch the eGFR trend, not a single value; escalate labs below eGFR 60 ml/min or a confirmed decline (over 4 ml/min in 12 months); nephrology review for a sustained fall or eGFR below 45 ml/min on repeat.
- **Do not stop abruptly:** one low eGFR is not grounds to stop; abrupt cessation risks rebound mania, so confirm the trend, involve nephrology, and if withdrawing, taper over at least a month.

18 . Lithium and the thyroid and parathyroid

Why it matters. lithium is the most effective long-term agent in bipolar disorder, yet clinician fear of its endocrine effects drives underuse (Meyer and Stahl 2020). The examinable point is that the two glandular effects, on the **thyroid** and the **parathyroid**, are common, detectable on routine bloods, and treatable without ever stopping the lithium. This is the topic where a resident must resist the reflex to withdraw an effective drug for a monitorable, correctable side effect.

Frame the whole topic around three verified truths: lithium accumulates in the thyroid and inhibits thyroid hormone release, producing **hypothyroidism** (often with a **goitre**) that is picked up by the routine TSH and corrected with levothyroxine; it also shifts the parathyroid calcium set point, producing hypercalcaemia of lithium-induced hyperparathyroidism, picked up by the routine serum calcium; and neither event, on its own, is a reason to discontinue lithium.

18.1 Mechanism at the thyroid follicle

Iodide trapping and hormone release. Lithium is a substrate for the sodium-iodide symporter (NIS) and concentrates in the thyroid gland at levels **3 to 4 times** those in plasma (Meyer and Stahl 2020). Its dominant action is **inhibition of T4 and T3 release** from the gland; it additionally alters thyroglobulin conformation so that coupling of iodinated tyrosine residues to form T4 and T3 is impaired. The net effect is a fall in circulating thyroid hormone, a

compensatory rise in TSH, and, over time, clinical hypothyroidism. Importantly, lithium is **not** associated with Hashimoto thyroiditis, Graves disease, an excess of antithyroid antibodies, or thyroid tumours (Meyer and Stahl 2020, Companion 2010).

RULE **Concentrate then throttle.** Lithium is trapped by the NIS and chiefly blocks thyroid hormone release, so TSH rises and hypothyroidism, not autoimmunity, is the signature.

18.2 Hypothyroidism: the common, treatable thyroid effect

Frequency and who is at risk. Slight falls in T4 with compensatory rises in TSH appear within a few months and usually stabilise within 12 months (Companion 2010). The annual incidence of new-onset **hypothyroidism** on lithium is about **1.5 percent**, and overt hypothyroidism occurs in roughly **8 to 19 percent** across long-term studies (Meyer and Stahl 2020). It is distinctly **commoner in women**, with female rates about three times those of men. The classic at-risk profile is a woman over 45 with circulating antithyroid antibodies and a slight but sustained TSH elevation (Companion 2010).

Detection and management. It is detected by the **routine TSH monitoring** already built into lithium follow-up: a sustained TSH elevation, even with a normal T4, is sufficient indication to supplement. It is managed with levothyroxine (L-thyroxine, Indian brand Thyronorm), titrated to the TSH, **without stopping lithium** (Meyer and Stahl 2020). A prior history of hypothyroidism is not a reason to withhold lithium, and new-onset hypothyroidism is not a reason to discontinue it.

HOLD THIS

Lithium hypothyroidism is a TSH diagnosis with a levothyroxine solution: supplement and keep the lithium, never stop the lithium to treat the thyroid.

18.3 The goitre, and the rarer hyperthyroidism

Goitre. Lithium-induced **goitre** is under-recognised on palpation but, on ultrasonography, is common, affecting over 50 percent of long-term users (Companion 2010). Most goitres are not palpable, and enlargement alone does not signify hypofunction. The mechanism reflects impaired iodine incorporation into thyroid hormone. Asymptomatic goitre, like biochemical or clinical hypothyroidism, is **not a contraindication** to continued lithium; only the rare multinodular goitre needing surgery is an exception, and long-term lithium does not increase thyroid carcinoma risk (Companion 2010).

Hyperthyroidism. Less commonly, patients may show hyperthyroidism, but on the best data this is rare and is likely **incidental** to lithium rather than caused by it (Meyer and Stahl 2020). In one large database analysis, lithium exposure was not significantly associated with hyperthyroidism after adjustment. The practical rule is unchanged: if TSH is low, continue lithium, confirm with T4 and T3, and work up Graves or Hashimoto disease on their own merits.

TRAP **Stopping the wrong drug.** Discontinuing an effective lithium to treat a hypothyroidism that levothyroxine would fully correct sacrifices the mood benefit for a problem that needed a second tablet, not withdrawal.

18.4 Hyperparathyroidism and hypercalcaemia: check calcium

Mechanism and picture. Lithium enters the parathyroid chief cell and, via GSK3-beta inhibition, disrupts the **calcium-sensing receptor** pathway, shifting the PTH set point to the right: a higher serum calcium is now required to suppress PTH. The earliest measurable change is therefore a rise in serum calcium, which is why routine monitoring includes **calcium** (Meyer and Stahl 2020). Chronic therapy in a subset unmasks a parathyroid adenoma or drives multiglandular hyperplasia; the clinical picture then is identical to primary **hyperparathyroidism**, is commoner in women, and may not reverse when lithium is stopped. A meta-analysis found total calcium raised by 0.09 mmol/L and PTH by 7.32 pg/mL on lithium (Meyer and Stahl 2020).

Detection and management. Sporadic elevated calcium is repeated in 3 to 6 months; persistent elevation is confirmed with an ionized calcium, then a PTH level, then endocrine referral. Because stopping lithium may not reverse established adenoma or hyperplasia, discontinuation is not the first move: symptomatic or criteria-meeting disease goes to parathyroid surgery, and calcimimetics such as cinacalcet allosterically activate the calcium-sensing receptor and offer a non-surgical option that lets lithium continue (Meyer and Stahl 2020).

GLAND	EFFECT	SCREENING TEST	MANAGEMENT (KEEP LITHIUM)
Thyroid	**Hypothyroidism, goitre (commoner in women)**	routine TSH	levothyroxine to TSH target
Thyroid	Hyperthyroidism (rare, usually incidental)	routine TSH (low)	confirm T4/T3, treat cause on merits
Parathyroid	**Hyperparathyroidism with hypercalcaemia**	routine serum calcium	surgery if criteria met, else cinacalcet

The two glandular effects of lithium, each caught by a routine test already in the monitoring panel, each treatable without withdrawing lithium.

18.5 Why this rarely forces lithium withdrawal, and where it sits in monitoring

The unifying principle. Thyroid and parathyroid dysfunction on lithium is **common, monitorable and treatable**, so it rarely forces lithium withdrawal. Hypothyroidism is not among the ten leading causes of lithium discontinuation and, in surveillance, accounts for only about a 2 percent discontinuation rate (Meyer and Stahl 2020). The guideline-anchored monitoring that catches both is standard: baseline TSH and calcium before starting, then thyroid and renal function plus plasma calcium checked at around 6 months and at least annually thereafter (CANMAT 2018). The Indian Psychiatric Society advises baseline and 6-monthly TSH, creatinine, eGFR and calcium, with TSH checked once or twice in the first 6 months then 6-monthly to yearly (IPS 2017); this could not be re-confirmed to the exact interval against the

primary IPS text here and is taken from the guideline digest. For the wider emergency frame around lithium and the perinatal frame, see the Perinatal/women's mental health and emergency psychiatry notes; for the initiation and toxicity detail, this note sits within the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes management thread.

8 to 19	1.5	6 to 12
OVERT HYPOTHYROIDISM ON LITHIUM (PERCENT)	ANNUAL INCIDENCE NEW HYPOTHYROIDISM (PERCENT)	TSH PLUS CALCIUM REVIEW INTERVAL (MONTHS)

GOOD TO REMEMBER

- **Lithium (thyroid):** concentrated by the NIS to 3 to 4 times plasma and inhibits T4/T3 release; signature effect is hypothyroidism with goitre, commoner in women; the one thing to hold is that a sustained TSH rise triggers supplementation, not withdrawal.
- **Hypothyroidism:** detected by routine TSH, managed with levothyroxine (Thyronorm) titrated to TSH; keep the lithium.
- **Goitre:** common on ultrasound (over 50 percent), usually impalpable and euthyroid; not a contraindication and no increase in thyroid carcinoma.
- **Hyperparathyroidism:** lithium shifts the parathyroid PTH set point rightward via the calcium-sensing receptor; discriminator on bloods is a rising serum calcium; confirm with ionized calcium then PTH, treat with surgery or cinacalcet, keep the lithium where possible.

INDIA

Lead with the Indian brand where you name one: lithium carbonate is Licab (Intas) or Intalith CR (Samarth); levothyroxine for the hypothyroidism is Thyronorm (Abbott) or Eltroxin. Generic names stay primary in prescribing; the brand is the parenthetical the patient will recognise on the strip.

PEARL

Both glandular effects are caught by tests you are already drawing: the TSH catches the thyroid, the serum calcium catches the parathyroid. Add calcium to the lithium panel and neither surprise you.

19 . Lithium: dermatological and cardiac effects

Two organ-system effects of **lithium** (Licab or Intalith; lithium carbonate) are examined less as reasons to stop the drug and more as things you must recognise, counsel about, and manage without reflex withdrawal. The **dermatological** effects are cosmetic and usually treatable topically, but they drive real-world non-adherence if missed; the **cardiac** effects are mostly benign ECG changes, with one genuine caution in sinus-node disease. The exam framing is: name the skin problems and the ECG changes, state that both are usually manageable, and know the single situation where the heart forces your hand (Maudsley 2021; Meyer and Stahl 2021).

Everything below is verified against the Meyer and Stahl Lithium Handbook for the detailed derm and cardiac profile, cross-checked against the Maudsley Prescribing Guidelines and Kaplan and Sadock for the class-level statements (Maudsley 2021; Meyer and Stahl 2021; Kaplan 2024).

The renal, thyroid, toxicity and monitoring picture sits alongside this in the lithium initiation and monitoring notes; the baseline pre-lithium ECG rule is set out there too.

19.1 Dermatological effects: acne, psoriasis, and hair thinning

Skin and hair problems are new-onset or an exacerbation of what was already there. The **dermatological** set that the board expects is: acne (an acneiform eruption, new or worsened), a **psoriasiform rash**, the **exacerbation of psoriasis** (lithium can worsen or unmask psoriasis), and diffuse hair thinning (alopecia). Folliculitis and a maculopapular rash also occur (Meyer and Stahl 2021). The Maudsley states plainly that some skin conditions such as psoriasis and acne can be aggravated by lithium therapy (Maudsley 2021). The true incidence is uncertain because the literature is mostly case reports, and controlled data have not clearly separated lithium from placebo, but the association is real enough that you counsel about it and ask at every visit (Meyer and Stahl 2021).

Managed dermatologically, rarely forcing withdrawal. The governing principle is that lithium discontinuation is not always necessary for these problems. Acne responds to topical benzoyl peroxide (2 to 10 percent) and, if needed, topical retinoids or a dermatology referral; a psoriasis flare is discussed honestly and co-managed with a dermatologist, and modern biologic therapy may let some patients stay on lithium; hair thinning is treated as any pattern hair loss, with topical minoxidil (5 percent), remembering that regrowth is slow, so early detection by routine inquiry is the real intervention (Meyer and Stahl 2021). Only a problem with no obvious option other than stopping, such as a persistent maculopapular rash, prompts a slow taper with dermatology input if you wish to rechallenge (Meyer and Stahl 2021).

RULE **Ask about skin eruptions and hair loss at every visit and manage them dermatologically, not by stopping lithium.** Most respond to topical treatment; discontinuation is the exception, not the rule.

TRAP **Stopping lithium reflexively for acne or a psoriasis flare in a patient it has stabilised.** You trade a treatable, cosmetic problem for a real relapse risk; treat the skin and keep the mood stabiliser.

19.2 Cardiac effects: benign T-wave changes, and the sinus-node caution

The common ECG changes are benign. The usual **cardiac** finding on the ECG is a benign, reversible **T-wave** flattening or inversion, reflecting an effect on ventricular repolarisation; long-term treatment can also produce benign PR-interval prolongation and U-waves that resemble those of hypokalaemia (Meyer and Stahl 2021; Kaplan 2024). These reflect the chronicity of lithium exposure and do not carry sudden-death risk, so a novel benign ECG finding is not a reason to stop the drug; any real impact on cardiac conduction is unlikely at therapeutic serum levels and becomes prominent mainly in toxicity (Meyer and Stahl 2021). Lithium, unlike antipsychotics, tricyclics, citalopram, escitalopram and lamotrigine, carries no routine QT-monitoring warning outside overdose (Meyer and Stahl 2021).

The one genuine caution: sinus-node dysfunction. Lithium can worsen or unmask sick sinus syndrome, so it is associated with bradycardia, **sinus node** dysfunction, sinus block and sinus arrest (Meyer and Stahl 2021; Kaplan 2024). The mechanism is not that lithium creates the pathology but that it hastens the appearance of an underlying, often age-related, degenerative sinus-node disease; the rare patient who develops symptomatic bradycardia at therapeutic levels represents unmasked sick sinus syndrome and may need lithium interrupted until a pacemaker is placed (Meyer and Stahl 2021). This is why a baseline ECG is advised in the older or cardiac patient, that is roughly above age 40 or with cardiovascular risk factors, syncope or a family history of sudden cardiac death, before starting lithium (Meyer and Stahl 2021).

toxic or chronic	above 40
EXPOSURE DRIVING ANY CONDUCTION EFFECT	BASELINE ECG ADVISED FROM THIS AGE (YEARS)

RULE **Lithium ECG changes are usually benign, but avoid lithium in sinus-node dysfunction.** Benign T-wave changes are no reason to stop; symptomatic sick sinus syndrome is.

TRAP **Starting lithium in significant conduction disease without a cardiology view.** In an older or cardiac patient, get a baseline ECG first; unmasked sinus-node disease can present with symptomatic bradycardia and near-syncope.

HOLD THIS

Lithium's skin effects (acne, psoriasis flare, hair thinning) are treated dermatologically and rarely force withdrawal; its ECG changes (T-wave flattening or inversion) are usually benign, and the one real caution is sinus-node disease, where lithium can unmask sick sinus syndrome, so get a baseline ECG in the older or cardiac patient.

GOOD TO REMEMBER

- **Dermatological (lithium):** acne, a psoriasiform rash and exacerbation of psoriasis, plus hair thinning; managed dermatologically (topical benzoyl peroxide, minoxidil, dermatology co-management), rarely forcing withdrawal (Meyer and Stahl 2021; Maudsley 2021).
- **Cardiac (lithium):** usually benign T-wave flattening or inversion on the ECG (a benign t-wave change on the ecg, plus benign PR prolongation and U-waves); not a reason to stop (Meyer and Stahl 2021; Kaplan 2024).
- **The discriminator to hold:** benign ECG change means continue; symptomatic bradycardia at therapeutic level means unmasked sick sinus syndrome, so interrupt lithium and involve cardiology.
- **The one caution:** caution with sinus node dysfunction; lithium can worsen sick sinus syndrome, so an ECG in the older or cardiac patient before starting (Meyer and Stahl 2021).

20 · Lithium drug interactions

Lithium is renally cleared, has a narrow therapeutic index and is handled by the kidney exactly like sodium. That single fact drives almost every clinically important interaction: any drug or state that makes the proximal tubule reabsorb more sodium, or that drops the glomerular filtration rate, drags lithium up with it and can tip a stable patient into toxicity. Because the safe window is so tight (**0.6 to 1.0 mmol/L** maintenance, toxicity from about **1.5 mmol/L**), a change

that would be trivial for most drugs is dangerous here. Examiners test this as a keyed direction question: does the drug **raise** or **lower** the level, and what do you do about it.

This note teaches the **lithium drug interactions** as a two-column split (drugs that raise versus drugs and states that lower the level), then the pharmacodynamic combinations that are dangerous even at a normal level, then the one practical monitoring rule that ties it together. Verify the direction of every interaction; a swapped direction is a critical error. For the wider prescribing frame, initiation and the toxicity syndrome, see the mood-block pharmacotherapy notes; for the renal and thyroid monitoring schedule and teratogenicity, cross to those; the receptor and CYP background sits in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

20.1 Why lithium interacts: the renal mechanism

Sodium mimicry. About 70 percent of filtered lithium is reabsorbed in the proximal tubule through the sodium/hydrogen exchanger (NHE3), where lithium competes with sodium for uptake (The Lithium Handbook 2023). When the body senses sodium or volume depletion it up-regulates proximal reabsorption, and lithium is reabsorbed alongside the sodium, so the serum level climbs. Anything that cuts the glomerular filtration rate does the same by reducing clearance. Lithium is not metabolised and not protein-bound, so there are essentially no cytochrome interactions: the interactions are pharmacokinetic-renal (level-changing) or pharmacodynamic (toxicity-adding at any level).

RULE **Sodium and lithium move together.** Volume depletion, a low-salt state, or any fall in GFR raises the lithium level, because the kidney reabsorbs lithium wherever it reabsorbs sodium.

20.2 Drugs that RAISE the level (the dangerous ones)

Reduced renal clearance. Three classes are the classic level-raisers a resident must hold, plus metronidazole. NSAIDs inhibit renal prostaglandins, constrict the afferent arteriole and cut renal blood flow, raising the level (Maudsley 2021); the effect is class-wide but aspirin and sulindac raise it less (The Lithium Handbook 2023). Thiazide diuretics deplete sodium, driving compensatory proximal reabsorption of lithium and a substantial rise. ACE inhibitors and ARBs limit angiotensin II mediated efferent arteriolar tone and cause volume depletion, both dropping GFR and raising the level. Metronidazole raises the level by reducing renal clearance.

CLASS / DRUG	DIRECTION	MECHANISM	PRACTICAL NOTE
NSAIDs (ibuprofen, diclofenac, indomethacin, naproxen, celecoxib)	**RAISE**	Inhibit renal prostaglandins, afferent vasoconstriction, reduced clearance	Includes over-the-counter ibuprofen; aspirin and sulindac raise it less
Thiazide diuretics (hydrochlorothiazide, chlorthalidone)	**RAISE**	Sodium depletion drives proximal lithium reabsorption	The strongest, most predictable diuretic riser
ACE inhibitors (enalapril, ramipril, lisinopril)	**RAISE**	Reduced efferent tone and volume depletion, lower GFR	Elderly especially vulnerable
ARBs (losartan, telmisartan, valsartan)	**RAISE**	Same efferent / volume mechanism as ACE inhibitors	Treat as equivalent to ACE inhibitors
Metronidazole	**RAISE**	Reduces renal lithium clearance	Recheck if a course is started

The four level-raisers to hold: NSAIDs, thiazides, ACE inhibitors and ARBs, plus metronidazole; each reduces clearance or depletes sodium.

TRAP **The over-the-counter NSAID.** A stable patient buys ibuprofen for backache, no prescriber is told, the level climbs over days and toxicity is precipitated. NSAID access is the commonest hidden riser.

20.3 A note on loop diuretics and potassium-sparing agents

Not all diuretics behave alike. Thiazides are the reliable, dangerous risers. Loop diuretics (furosemide) also reduce clearance and can raise the level, but the effect is more variable and less pronounced than with a thiazide. The safest rule for the exam and the clinic is to treat any diuretic start or stop as a level-changing event and recheck, rather than trusting one class to be neutral.

20.4 Drugs and states that LOWER the level

Increased clearance. The mirror image: anything that increases renal lithium clearance drops the level and risks loss of prophylaxis. Osmotic diuretics (mannitol) and, classically, the carbonic-anhydrase and osmotic agents increase lithium excretion. Theophylline and aminophylline increase renal clearance and lower the level. Caffeine, in the same way, modestly increases clearance, so a big swing in caffeine intake shifts the level. A high sodium intake competes lithium out of the proximal tubule and lowers the level, which is the flip side of the salt-restriction rule: a patient who suddenly increases dietary salt may lose efficacy, and one who crash-diets on salt may become toxic.

AGENT / STATE	DIRECTION	MECHANISM
Osmotic diuretics (mannitol)	**LOWER**	Increase lithium excretion
Theophylline / aminophylline	**LOWER**	Increase renal lithium clearance
Caffeine (sustained high intake)	**LOWER**	Increases clearance; abrupt cessation can raise the level
High sodium intake	**LOWER**	Sodium competes lithium out of proximal reabsorption
Low sodium intake / dehydration	RAISE	Volume/sodium depletion drives proximal lithium reabsorption

The level-lowering agents and the salt paradox: high salt lowers the level, low salt or dehydration raises it.

20.5 Pharmacodynamic interactions: toxicity added at a normal level

Danger without a level change. Some combinations are hazardous even when the serum level reads normal, because the toxicity is additive at the target rather than through clearance. First, the neurotoxicity risk with a high-dose antipsychotic: reports of lithium plus a high-dose antipsychotic (historically haloperidol) producing an encephalopathic, delirious, sometimes irreversible neurotoxic picture relate largely to the excessive antipsychotic doses used in earlier decades, and many such cases were actually neuroleptic malignant syndrome (The Lithium Handbook 2023). The practical message is caution and dose restraint, not absolute avoidance. Second, the serotonin-syndrome risk with serotonergic drugs: lithium is pro-serotonergic, so combining it with an SSRI, an SNRI (venlafaxine) or other serotonergic agents raises the risk of serotonin syndrome, and lithium augmentation of an antidepressant should be started low and titrated slowly (Shorter Oxford 2018). Third, the additive tremor: lithium tremor stacks with the tremor of an SSRI, valproate or a beta-agonist, worsening a benign but distressing side effect.

WORKED EXAMPLE

A woman stable at **0.7 mmol/L** on lithium and sertraline is prescribed hydrochlorothiazide for hypertension by her GP. Over the next week she develops a coarse tremor, nausea and unsteadiness. The thiazide has raised the lithium level; the additive serotonergic and tremor load with sertraline makes her more symptomatic. Withhold lithium, check the level and renal function, and rethink the antihypertensive.

20.6 The practical monitoring rule

Recheck around any interacting drug. The one rule that operationalises all of the above: whenever an interacting drug, especially an NSAID, a thiazide or an ACE inhibitor, is **started or stopped**, recheck the lithium level. Stopping a riser is as important as starting one, because a level that was in range only because of the interaction will fall. The verified interval is a trough (12 hours post-dose) level about **5 to 7 days** after any dose change or interacting-drug change (CANMAT 2018; Maudsley 2021). Counsel every patient not to buy over-the-counter NSAIDs, and to flag any new blood-pressure or water tablet, before it is dispensed.



Fig 12.11 Perinatal mood-stabiliser planning balances maternal relapse risk against fetal and neonatal exposure through shared specialist decisions, medication review, monitoring and an explicit postpartum and lactation plan.

0.6 to 1.0	1.5	5 to 7
MAINTENANCE LITHIUM (MMOL/L)	TOXICITY THRESHOLD (MMOL/L)	RECHECK AFTER INTERACTING-DRUG CHANGE (DAYS)

RULE **An NSAID, a thiazide or an ACE inhibitor raises the lithium level, so recheck it.** Recheck a trough level 5 to 7 days after any interacting drug is started or stopped.

HOLD THIS

NSAIDs, thiazides and ACE inhibitors / ARBs all RAISE the lithium level by cutting renal clearance; theophylline, caffeine and high sodium LOWER it; recheck a trough level 5 to 7 days after any interacting drug starts or stops.

MNEMONIC

NTA raises, CATS lowers

NSAID, **T**hiazide, **A**CE inhibitor (and ARB) RAISE the level. **C**affeine, **A**minophylline/theophylline, **T**oo much **S**alt LOWER it.

INDIA

Lithium carbonate is marketed in India as Licab (Torrent) and Intalith, among others; the generic stays primary in prescribing. The interaction trap is amplified here by easy over-the-counter access to NSAIDs (ibuprofen, diclofenac) and to combination analgesic and cold preparations, so explicit counselling to avoid self-medicated painkillers is essential.

PEARL

Caffeine cuts both ways: a heavy coffee drinker may run a lower level, and abruptly stopping caffeine (for example on admission) can nudge the level up. Ask about caffeine and salt habits when a level drifts without an obvious drug cause.

GOOD TO REMEMBER

- **NSAIDs:** inhibit renal prostaglandins and reduce clearance, so they RAISE the level; aspirin and sulindac raise it less; over-the-counter ibuprofen is the classic hidden precipitant.
- **Thiazide diuretics:** deplete sodium, drive proximal lithium reabsorption, RAISE the level; the strongest, most predictable diuretic riser.
- **ACE inhibitors / ARBs:** lower GFR via efferent tone and volume depletion, RAISE the level; the elderly are most vulnerable.
- **Metronidazole:** reduces renal clearance, RAISES the level; recheck if a course is started.
- **Theophylline / caffeine:** increase renal clearance, LOWER the level; a big change in caffeine intake shifts the level.
- **High sodium intake:** competes lithium out of the proximal tubule, LOWERS the level; low salt or dehydration does the opposite and RAISES it.
- **High-dose antipsychotic:** caution for a neurotoxic encephalopathy at a normal level; restrain the dose rather than avoid absolutely.
- **Serotonergic drugs (SSRI, venlafaxine):** additive serotonin-syndrome risk; start lithium augmentation low and titrate slowly.
- **The one rule:** recheck a trough lithium level 5 to 7 days after any interacting drug, especially an NSAID, thiazide or ACE inhibitor, is started or stopped.

21 . Lithium in pregnancy and lactation

Reproductive-age women make up a large share of the bipolar caseload, and **lithium in pregnancy** is the single most examined perinatal prescribing decision in psychiatry. The board wants three things from you: the specific **teratogenicity** signal (the first-trimester link with Ebstein anomaly), the way lithium pharmacokinetics shift across pregnancy and swing sharply at delivery, and the guideline-anchored logic of a planned risk-benefit discussion rather than a reflex stop. The whole topic is a study in numbers that are **small but raised**: the absolute risk to

the fetus is low, yet it is high enough that continuation demands fetal echocardiography and closer level monitoring.

Everything below is verified against the Maudsley Prescribing Guidelines and the Meyer and Stahl Lithium Handbook for the pharmacology and monitoring, with the class detail cross-checked against Kaplan and Sadock and the Companion to Psychiatric Studies (Maudsley 2021; Meyer 2023; Sadock 2024; Johnstone 2010). The wider perinatal frame, including relapse-prevention planning and postpartum psychosis, sits in the Perinatal/women's mental health and emergency psychiatry notes; the toxicity grading it references is in the lithium toxicity notes. Lithium is dispensed in Indian practice as lithium carbonate (Licab, and the controlled-release Intalith CR).

21.1 Teratogenicity: the Ebstein anomaly signal

The classic association is with a right-sided cardiac malformation. First-trimester **lithium in pregnancy** carries a well-known association with Ebstein anomaly, a malformation in which the tricuspid valve is displaced downward into the right ventricle (a right-sided cardiac lesion causing tricuspid regurgitation and a small, functionally impaired right ventricle) (Maudsley 2021; Sadock 2024). The historical Register of Lithium Babies vastly overstated this because uneventful pregnancies went unreported; corrected estimates put the risk of Ebstein anomaly with first-trimester exposure at roughly **0.05 to 0.1%**, a roughly 10- to 20-fold rise over the very low population baseline, but still an absolute risk well under 1% (Johnstone 2010).

Small but raised is the phrase to hold. The Maudsley notes that more recent data suggest the magnitude of the effect is much smaller than previously estimated, and that a surveillance study of 5.6 million births found Ebstein anomaly linked to maternal mental illness generally rather than specifically to lithium; the Lithium Handbook gives a number needed to harm of 37 for any major malformation from first-trimester exposure (Maudsley 2021; Meyer 2023). The overall risk of major malformation, and of atrial and ventricular septal defects, is raised but low. The period of maximum fetal risk is **2 to 6 weeks after conception**, before many women know they are pregnant (Maudsley 2021). Because the risk is real but small, the decision is a risk-benefit one, and if lithium is continued the woman is offered fetal echocardiography and high-resolution ultrasound in liaison with fetal-medicine obstetric services.

RULE **If lithium is continued in pregnancy, monitor the level closely and offer fetal echocardiography.** The first-trimester Ebstein signal is screened for with high-resolution ultrasound and fetal echocardiography in liaison with fetal medicine.

TRAP **Stopping lithium abruptly on discovering the pregnancy.** Abrupt discontinuation carries a very high relapse risk (postpartum relapse up to 70% in women who stop before conception); the correct move is a planned risk-benefit discussion, not a reflex stop (Maudsley 2021).

0.05 to 0.1	10 to 20	2 to 6
EBSTEIN RISK, FIRST-TRIMESTER LITHIUM (%)	FOLD RISE OVER BASELINE	WEEKS POST-CONCEPTION: PEAK FETAL RISK

21.2 Pharmacokinetic shifts across pregnancy

The level falls as pregnancy advances, then rebounds at delivery. Renal plasma flow and glomerular filtration rise across pregnancy and total body water expands, so lithium clearance increases and the serum level falls; an increasing dose is needed to hold the level in the therapeutic range, and the level must be monitored more often (Maudsley 2021; Sadock 2024). This is why the sample cannot be taken at pre-pregnancy intervals. NICE recommends checking the plasma lithium level **every 4 weeks**, then **weekly from week 36**, adjusting the dose to keep the level in the woman's therapeutic range while maintaining adequate fluid balance (Maudsley 2021).

At delivery the requirement snaps back to pre-pregnancy levels. The raised clearance reverses abruptly the moment the baby is delivered, so a dose that was correct in the third trimester becomes an overdose within a day, and the large intercompartmental electrolyte and fluid shifts around labour make sudden maternal toxicity possible (Maudsley 2021; Johnstone 2010). The dose is therefore adjusted around the birth: the woman delivers in hospital where fluid balance can be monitored, lithium is stopped during labour, and the plasma level is checked **12 hours after the last dose**; the pre-pregnancy dose is resumed post-delivery with a level check (Maudsley 2021).

RULE **Monitor levels more often in pregnancy and adjust the dose around delivery.** The level falls as renal clearance rises antenatally, then rebounds sharply postpartum; deliver in hospital, hold lithium in labour, and check the level 12 hours after the last dose.

21.3 The peripartum neonate: floppy baby and toxicity

Lithium equilibrates fully across the placenta, so the neonate is exposed. Lithium completely crosses the placenta, and peripartum exposure produces the **floppy baby** picture: neonatal hypotonia and lethargy, poor feeding and low Apgar scores, together with reported neonatal goitre, cardiac arrhythmia and respiratory symptoms (Maudsley 2021). Neonatal lithium toxicity is a real peripartum risk because the newborn's immature renal function clears lithium slowly; the Lithium Handbook notes that newborn reactivity is better when the maternal level at birth is below about **0.64 mEq/L**, which is one rationale for a modest dose reduction in the week before delivery (Meyer 2023).

Balance the neonatal risk against the maternal relapse risk. The counterweight is that lithium is the drug most likely to keep the mother well, and abrupt discontinuation drives a very high peripartum and postpartum relapse rate; lithium probably does not affect neonatal brain development (Maudsley 2021). The floppy, poorly feeding neonate is managed supportively with a neonatal lithium level and fluid attention, and typically resolves as the infant's renal function matures.

21.4 Lactation: passes into milk, generally cautioned

Lithium enters breast milk and is a relative contraindication in many guidelines. Lithium passes into breast milk and is renally cleared by an infant whose kidneys are still maturing, so **lactation** on lithium is generally cautioned; the Maudsley advises that lithium should be

continued in the mother but that breastfeeding should not be permitted, treating it as the exception among the mood stabilisers (Maudsley 2021). The Companion likewise states that because lithium passes into breast milk, breastfeeding should be avoided (Johnstone 2010).

The position is individualised, not absolute. Newer data soften the older blanket prohibition: a systematic review and the Lithium Handbook report that infant lithium levels fall significantly after the second week of life as renal function matures, and that breastfeeding while taking lithium does not pose a risk to the majority of infants under close monitoring, so lithium-treated women need not be automatically discouraged from breastfeeding provided infant growth and lithium-related bloods are tracked, especially in the early weeks (Meyer 2023). The exam-safe line is that lactation on lithium is a relative contraindication decided case by case; the wider perinatal decision frame is set out in the Perinatal/women's mental health and emergency psychiatry notes.

TRAP **Treating breastfeeding on lithium as absolutely forbidden or as freely permitted.** The Maudsley cautions against breastfeeding while newer monitored-cohort data are reassuring; the answer is an individualised, monitored decision, not a blanket rule either way.

21.5 The management algorithm: a planned risk-benefit decision

Guideline-level logic, not a reflex. The framework is consistent across sources (Maudsley 2021; NICE 2014; Yatham 2018). No mood stabiliser is clearly safe, and the decision turns on how well and how quickly the woman relapses off treatment.

SCENARIO	GUIDELINE-LEVEL ACTION
Planning pregnancy, long remission, low relapse risk	**Consider slow discontinuation before conception, or switch to a mood-stabilising antipsychotic; taper over about 4 weeks, never abruptly**
Becomes pregnant, well, lower risk	Consider stopping lithium gradually over 4 weeks; explain the postnatal relapse risk
Severe illness or rapid relapse off treatment	**Continue lithium after a documented risk-benefit discussion; offer fetal echocardiography and high-resolution ultrasound**
If lithium continued	Level every 4 weeks, then weekly from week 36; deliver in hospital; hold lithium in labour; check level 12 hours after last dose
Breastfeeding	Generally cautioned (relative contraindication); individualise with infant monitoring

Guideline-anchored algorithm for lithium in pregnancy and lactation: the decision keys to relapse risk, and continuation triggers fetal echocardiography plus intensified level monitoring (Maudsley 2021; NICE 2014). Highlighted cells are the board-critical branch points.

Where the guidelines converge. NICE advises considering a gradual stop over 4 weeks if the woman is well, switching to an antipsychotic or restarting in the second trimester if she is at higher risk, and continuing lithium where relapse risk is high and an antipsychotic is unlikely to work (Maudsley 2021; NICE 2014). CANMAT frames the perinatal period as one of very high bipolar relapse risk and prioritises maintaining prophylaxis in women who relapse quickly, with

lithium among the first-line maintenance options (Yatham 2018). The Indian Psychiatric Society bipolar clinical practice guideline (Shah et al.) similarly counsels a planned pre-conception risk-benefit discussion rather than abrupt cessation; the precise IPS wording on breastfeeding could not be confirmed from the parsed sources and is flagged under gaps.

WORKED EXAMPLE

A 29-year-old woman with bipolar I disorder, well on lithium for four years with two severe manic relapses whenever she has stopped it, presents at 7 weeks pregnant, having just found out. The wrong move is to stop lithium today. The right move is a documented risk-benefit discussion: her rapid, severe relapse pattern favours continuation; she is counselled on the small but raised Ebstein risk, referred for fetal echocardiography and high-resolution ultrasound, her level is checked every 4 weeks and weekly from week 36, she is booked to deliver in hospital with lithium held in labour and a level 12 hours after her last dose, and breastfeeding is discussed as a cautioned, individualised decision (Maudsley 2021).

INDIA

Lithium carbonate (Licab, Intalith CR) is cheap and widely used in Indian bipolar practice, and reproductive-age women are a large part of the caseload, so this decision is common. The practical points that matter here: many pregnancies are unplanned and present after the 2 to 6 week window of peak risk has already passed, so counsel women of childbearing potential about the plan at initiation, not at conception. Serum lithium, creatinine and TSH assays are inexpensive and available; fetal echocardiography and high-resolution anomaly scanning are available in most tertiary and many secondary obstetric units and should be arranged in liaison with the obstetric team if lithium is continued. Deliver in hospital, hold lithium in labour, and check a level after delivery because the dose requirement drops back to pre-pregnancy levels at once (Maudsley 2021; Shah 2017).

PEARL

The two numbers that decide the antenatal plan pull in opposite directions: the Ebstein absolute risk is tiny (well under 1%), while the postpartum relapse risk after abrupt discontinuation is huge (up to 70%). Stated side by side they explain why guidelines lean toward a planned continuation-with-monitoring in women who relapse quickly, rather than a reflex stop.

MNEMONIC

ECHO: Ebstein, Clearance rises, Hold in labour, Off breastfeeding (cautioned)

Ebstein anomaly is the first-trimester teratogenic signal (small but raised); **C**learance rises antenatally so the level falls and is checked more often, then rebounds at delivery; **H**old lithium in labour, deliver in hospital, check the level 12 hours after the last dose; breastfeeding is generally **O**ff / cautioned (relative contraindication, individualised). ECHO also cues the fetal echocardiography offered on continuation.

GOOD TO REMEMBER

- **Teratogenicity:** first-trimester lithium associates with Ebstein anomaly (a right-sided cardiac malformation); absolute risk about 0.05 to 0.1%, small but raised (10- to 20-fold over baseline).
- **If continued:** monitor the level closely and offer fetal echocardiography plus high-resolution ultrasound; peak fetal risk is 2 to 6 weeks post-conception.
- **Pharmacokinetics:** the level falls as renal clearance rises in pregnancy (check every 4 weeks, then weekly from week 36), then rebounds sharply at delivery; adjust the dose around the birth.
- **Peripartum neonate:** floppy baby (hypotonia, lethargy, poor feeding) and neonatal toxicity risk; deliver in hospital, hold lithium in labour, check the level 12 hours after the last dose.
- **Lactation:** lithium passes into breast milk and is generally cautioned (a relative contraindication in many guidelines, individualised with infant monitoring).
- **The trap:** do not stop lithium abruptly on discovering pregnancy (relapse up to 70%); make it a planned risk-benefit decision.

HOLD THIS

First-trimester lithium raises the risk of Ebstein anomaly (small but raised, about 0.05 to 0.1%): if continued, monitor levels closely and offer fetal echocardiography; the level falls as clearance rises antenatally and rebounds at delivery, so adjust the dose around the birth; breastfeeding is generally cautioned; never stop abruptly (Maudsley 2021).

22 . Valproate

Valproate is the second workhorse mood stabiliser after lithium, and the examiner treats it as a paired set-piece: a genuinely effective antimanic and maintenance agent that carries the single worst reproductive-safety profile of any mood stabiliser. The whole topic hangs on two axes, the drug pharmacology (mechanism, forms, dose, the serum range, the adverse-effect set and monitoring) and the **teratogenicity**, which is a marked-error magnet: neural-tube defects, a dose-related fall in IQ, and an autism signal (Maudsley 2021). A resident is expected to prescribe it competently in a man or a woman past childbearing, and to know that in a woman who could become pregnant it is effectively contraindicated unless a formal pregnancy-prevention programme is running.

Organise the topic around one idea: **valproate is anti-manic and a maintenance agent, not a bipolar-depression monotherapy, and it is the drug you do not give to a woman who could conceive without counselling and a pregnancy-prevention programme.** Every dose, serum level and teratogenicity fact below is verified against the Maudsley, the CANMAT and Indian Psychiatric Society rows and Stahl (Maudsley 2021; CANMAT 2018; IPS 2017; Stahl 2021). The neurobiology of mood and the wider guideline-anchored management PLAN belong to the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes; the perinatal frame and acute emergency management belong to the Perinatal/women's mental health and emergency psychiatry notes.

22.1 Mechanism: GABA potentiation, sodium-channel block and more

The molecular target. Valproate is a simple branched-chain fatty acid whose mechanism is multiple and incompletely understood (Maudsley 2021; Stahl 2021). The best-taught actions are

potentiation of GABA: it inhibits the catabolism of gamma-aminobutyric acid (by inhibiting GABA-transaminase) and probably increases GABA synthesis, raising inhibitory tone; and a phenytoin-like, use-dependent blockade of voltage-gated sodium channels that dampens high-frequency neuronal firing (Maudsley 2021; Stahl 2021).

The downstream and neuroplastic actions. Beyond GABA and sodium channels, valproate weakly attenuates calcium T-currents, reduces the turnover of arachidonic acid, depletes inositol, activates the ERK pathway and promotes brain-derived neurotrophic factor expression while reducing protein kinase C, and it acts as a histone deacetylase inhibitor altering gene transcription (Maudsley 2021; Stahl 2021). These signalling and epigenetic effects are the presumed substrate of its mood-stabilising and neuroplastic actions.

22.2 The forms: sodium valproate, valproic acid and divalproex

Three interchangeable forms of one active moiety. Valproate is dispensed in three forms, all metabolised to **valproic acid**, which is the pharmacologically active species (Maudsley 2021). Distinguish them by name because the examiner will: **sodium valproate** and valproic acid (classically licensed for epilepsy), and **divalproex** (semi-sodium valproate, the 1:1 coordination compound of valproic acid and sodium valproate, classically licensed for acute mania) (Maudsley 2021). There are no important efficacy differences between the forms; divalproex may have marginally better gastric tolerability.

Sodium valproate

The sodium salt; the controlled-release form can be given once daily, other forms at least twice daily (Maudsley 2021).

Valproic acid

The free acid and the active moiety to which all forms are metabolised (Maudsley 2021).

Divalproex (semi-sodium valproate)

A 1:1 compound of valproic acid and sodium valproate; the form used in most mania trials, slower-absorbed, possibly better tolerated (Maudsley 2021).

> **INDIA**
>
> Lead with the Indian brand, then the generic. Sodium valproate is marketed in India as **Valprol-CR**, **Encorate** or Valparin Chrono (sodium valproate); divalproex as **Valance** or Divaa (divalproex) (KDT 2019). All three chemical forms convert to valproic acid, so brand choice is driven by formulation (once-daily controlled-release versus twice-daily) and tolerability, not by a difference in the active drug.

22.3 Indications: acute mania and maintenance, not bipolar depression alone

Where it works. The core **indications**: **acute mania** (a first-line antimanic agent, response rate around 50 percent, number needed to treat 2 to 4) and **bipolar maintenance** or prophylaxis, best supported when it was the agent that worked in the acute manic episode (Maudsley 2021; CANMAT 2018; IPS 2017). CANMAT lists divalproex as a first-line monotherapy for acute mania and among first-line maintenance monotherapies for bipolar I disorder (CANMAT 2018). The Indian Psychiatric Society names valproate as a first-line monotherapy for acute mania and,

with lithium, as a best-evidenced maintenance agent, and the IPS guidelines quote an acute-mania serum target of 50 to 125 mcg/mL (IPS 2017).

Where it is not first choice. Valproate is **not for bipolar depression as monotherapy**: the evidence in bipolar depression is at best a small-to-medium effect and it is not a first-line agent for the depressive pole (Maudsley 2021; CANMAT 2018). It has limited utility in rapid-cycling illness. A hard practice point: NICE recommends against starting valproate for bipolar disorder in primary care, and both NICE and the Indian Psychiatric Society bar its use to treat bipolar illness in women of childbearing age (NICE 2014; IPS 2017).

RULE **Valproate is an anti-manic and maintenance agent, not a bipolar-depression monotherapy.** Reach for it in mania and for relapse prevention, not to lift the depressive pole on its own.

22.4 Initiation, dosing and the serum range

Starting and titrating. Titrate the dose upward against response and adverse effects; loading-dose regimens are generally well tolerated and give a faster antimanic response (Maudsley 2021). A common adult approach starts around 500 mg twice daily (or a weight-based load of roughly 20 to 30 mg/kg/day) and increases every few days. Controlled-release sodium valproate can be given once daily; other formulations require at least twice-daily dosing (Maudsley 2021).

The serum level, held more loosely than lithium. Plasma level monitoring is of more limited use than with lithium, but there is a linear relationship in acute mania: levels below **55 mg/L** are no more effective than placebo, and levels above **94 mg/L** give the most robust response (Maudsley 2021). The practical acute-mania target is a serum valproate of about **50 to 100 mg/L** (CANMAT: 350 to 700 micromol/L; IPS quotes 50 to 125 mcg/mL), taken as a trough immediately before the next dose (CANMAT 2018; IPS 2017; Maudsley 2021). Adverse effects and toxicity rise sharply once the level exceeds 100 mg/L.

PARAMETER	VALUE	SOURCE
Acute-mania serum target	**50 to 100 (levels below 55 no better than placebo; above 94 most robust)**	Maudsley 2021
CANMAT acute-mania target	**350 to 700 micromol/L (50 to 100 microg/mL)**	CANMAT 2018
IPS acute-mania target	50 to 125 mcg/mL	IPS 2017
Sample timing	trough, immediately before the next dose	Maudsley 2021
Adverse effects escalate above	100	Maudsley 2021

Valproate serum monitoring, in mg/L (equivalently microg/mL or mcg/mL) unless stated. Used more loosely than the lithium level; the number that matters most is the acute-mania trough (Maudsley 2021; CANMAT 2018; IPS 2017).

50 to 100
ACUTE-MANIA SERUM VALPROATE (MG/L)

below 55
SERUM NO BETTER THAN PLACEBO (MG/L)

above 100
ADVERSE EFFECTS ESCALATE (MG/L)

22.5 Adverse effects: the common set and the dangerous ones

The everyday set. The common, adherence-limiting adverse effects: **weight gain** (can be marked, worse when combined with clozapine or olanzapine), a dose-related **tremor** (intention or postural, in up to a quarter of patients), **hair loss** with curly regrowth, **sedation** and lethargy (especially at starting doses above 750 mg/day), gastric irritation and nausea (Maudsley 2021). Peripheral oedema also occurs.

The haematological and metabolic dangers. Valproate can cause **thrombocytopenia** (also leucopenia and red-cell hypoplasia), and **hyperammonaemia**, which can produce nausea and, when marked, an encephalopathy even with normal liver enzymes (Maudsley 2021). Two organ-threatening reactions dominate the safety picture: **hepatotoxicity**, ranging from the common early asymptomatic transaminase rise to rare fulminant hepatic failure (young children on multiple anticonvulsants are at greatest risk), and **pancreatitis** (Maudsley 2021; KDT 2019). Any patient with rising liver enzymes should be evaluated clinically, with albumin and clotting checked.

ADVERSE EFFECT	NOTE
Weight gain	Can be significant; worse with clozapine or olanzapine (Maudsley 2021)
Tremor	Dose-related, in up to a quarter; intention or postural (Maudsley 2021)
Hair loss	With characteristic curly regrowth (Maudsley 2021)
Sedation / lethargy	Especially at starting doses above 750 mg/day (Maudsley 2021)
Thrombocytopenia	Also leucopenia, red-cell hypoplasia; drives the FBC monitoring (Maudsley 2021)
Hyperammonaemia	Nausea, and an encephalopathy that can occur with normal LFTs (Maudsley 2021)
Hepatotoxicity	Common early transaminase rise; rare fulminant hepatic failure, highest in young children on polytherapy (Maudsley 2021)
Pancreatitis	Rare but serious; drives the low threshold to investigate abdominal pain (Maudsley 2021)

The valproate adverse-effect set. The four highlighted rows are the ones that drive baseline and periodic FBC and LFTs (Maudsley 2021).

MNEMONIC

VALPROATE

Weight gain, Ammonia (hyperammonaemia), Liver toxicity (hepatotoxicity), Pancreatitis, Reduced platelets (thrombocytopenia), Oedema, Alopecia (curly regrowth), Tremor, teratogen: a memory hook for the adverse-effect and reproductive-risk set to hold cold.

22.6 Monitoring: baseline and periodic LFTs and FBC

The pre-treatment work-up. Because the organ dangers are hepatic and haematological, the baseline screen is a **full blood count** and **liver function tests**, with a baseline weight or BMI (Maudsley 2021; NICE 2014). Take a menstrual history and a pregnancy test with contraceptive counselling in any woman of childbearing potential before the first tablet.

On-treatment monitoring. NICE recommends repeating the **FBC and LFTs** at 6 months and monitoring BMI; the product characteristics advise more frequent LFTs in the first 6 months, with albumin and clotting if enzymes are abnormal (Maudsley 2021; NICE 2014). CANMAT frames it as menstrual history, haematology and liver function at 3-to-6-month intervals in the first year on maintenance divalproex, then yearly, alongside serum valproate levels (CANMAT 2018).

TRAP **Starting valproate without baseline FBC and LFTs.** You lose the safety baseline for the two organ-threatening reactions, hepatotoxicity and thrombocytopenia, and cannot later attribute a change to the drug.

22.7 Teratogenicity: the highest-risk mood stabiliser

The malformation risk. Valproate is an established major human teratogen and the single worst mood stabiliser in pregnancy. It has a clear causal link with **neural tube** defects including spina bifida, and the overall major-malformation rate is around **10 percent**, higher than carbamazepine (Maudsley 2021). It is also linked to atrial septal defects, cleft palate, hypospadias, polydactyly, craniosynostosis and reduced neonatal head circumference (Maudsley 2021). Folate does not reliably prevent anticonvulsant-induced neural-tube defects once pregnancy is established because the tube closes within about twenty-eight days, in the fourth week, so folate must be given before conception.

The neurodevelopmental risk, and its dose-dependence. Beyond structural malformation there is a clear causal association with **neurodevelopmental** harm: a European Medicines Agency review found that up to **40 percent** of pre-school children exposed in utero had some developmental delay (delayed walking and talking, memory, speech and language problems, lower intellectual ability), with lower IQ and an increased rate of autism-spectrum diagnosis, and the processing, working-memory and learning deficits are dose-related (Maudsley 2021). This IQ and autism signal, dose-related and lasting, is the fact the examiner most wants verified.

~10%	up to 40%	5 mg/day
MAJOR MALFORMATION RATE (MAUDSLEY)	PRE-SCHOOL DEVELOPMENTAL DELAY AFTER IN-UTERO EXPOSURE	HIGH-DOSE PRE-CONCEPTION FOLIC ACID

The prescribing rule that follows. Because of this, valproate is contraindicated in women of childbearing potential unless a formal pregnancy-prevention programme is in place (Maudsley 2021; NICE 2014; IPS 2017). If a woman planning pregnancy is already on it, withdraw it gradually (over at least 4 weeks, or 2 to 4 weeks per the perinatal guidance) while she uses effective contraception, adding high-dose folic acid **5 mg/day** continued through the first trimester (Maudsley 2021; CANMAT 2018; BAP 2016). If she becomes pregnant on valproate it

should generally be stopped. In the UK it may not be initiated in patients under 55 or continued in a woman of childbearing potential unless two specialists agree no other treatment is effective or tolerated (Maudsley 2021).

RULE **Do not use valproate in a woman who could become pregnant without a pregnancy-prevention programme.** The neural-tube and dose-related IQ and autism risk makes it the mood stabiliser to avoid in childbearing-potential women.

TRAP **Prescribing valproate to a young woman for bipolar disorder without counselling the teratogenicity.** It is the classic marked error: no discussion of neural-tube defects, the IQ and autism risk, contraception or pre-conception folate.

INDIA

The childbearing-potential rule applies squarely in Indian practice: valproate (Valprol-CR, Encorate; divalproex Valance) is common and cheap, but in a woman who could conceive it should not be started for bipolar disorder without a documented pregnancy-prevention plan and explicit counselling on neural-tube and neurodevelopmental risk (IPS 2017; NICE 2014). The Indian Psychiatric Society explicitly advises avoiding valproate in pregnancy for its high teratogenicity, neural-tube defects and neurodevelopmental harm (IPS 2017).

22.8 PCOS, menstrual disturbance and other reproductive effects

The endocrine effect in women. Separate from teratogenicity, valproate causes hyperandrogenism in women and is linked to **pcos** (polycystic ovary syndrome) with menstrual disturbance, weight gain and metabolic features, though the strength of the association is debated (Maudsley 2021). This is a further reason to take and monitor a menstrual history in women on valproate, and to prefer an alternative in a young woman where reproductive and metabolic concerns weigh heavily (CANMAT 2018).

PEARL

Two distinct reproductive harms travel together for valproate: the in-utero **teratogenicity** (neural-tube and neurodevelopmental), which threatens a future fetus, and **pcos** with menstrual disturbance, which affects the woman herself. Both push toward avoiding valproate in young women of childbearing potential.

22.9 Interactions: protein binding, enzyme inhibition and glucuronidation

The key interactions. Valproate is highly protein-bound and can be displaced by other protein-bound drugs such as aspirin, raising free levels toward toxicity; aspirin also inhibits its metabolism (Maudsley 2021). Conversely valproate can displace warfarin, raising the free anticoagulant level. As an enzyme inhibitor of glucuronidation it raises the levels of several drugs, most importantly lamotrigine (valproate roughly doubles lamotrigine exposure, hence the halved lamotrigine titration and the raised rash risk), and also tricyclics such as clomipramine, quetiapine and phenobarbital (Maudsley 2021). Drugs that inhibit CYP enzymes (erythromycin, fluoxetine, cimetidine) can raise valproate levels in turn.

INTERACTING DRUG	EFFECT
Lamotrigine	Valproate inhibits its glucuronidation, roughly doubling levels; halve the lamotrigine dose and titrate slowly (raised rash risk) (Maudsley 2021)
Aspirin	Displaces protein-bound valproate and inhibits its metabolism, raising free valproate toward toxicity (Maudsley 2021)
Warfarin	Displaced by valproate, raising free anticoagulant level (Maudsley 2021)
Erythromycin, fluoxetine, cimetidine	CYP inhibition raises valproate levels (Maudsley 2021)
Carbapenems	Sharply lower valproate levels (a well-known interaction to avoid) (KDT 2019)

The high-yield valproate interactions. The lamotrigine interaction is the one most often examined, because it dictates the halved lamotrigine titration (Maudsley 2021).

HOLD THIS

Valproate is an effective anti-manic and maintenance mood stabiliser, but with the worst reproductive profile of the class: a roughly 10 percent major-malformation rate with neural-tube defects and a dose-related fall in IQ with an autism signal, so it is contraindicated in women of childbearing potential without a pregnancy-prevention programme.

GOOD TO REMEMBER

- **Mechanism:** GABA potentiation (inhibits GABA-transaminase) plus use-dependent sodium-channel blockade, with histone-deacetylase and neuroplastic effects (Maudsley 2021; Stahl 2021).
- **Indications:** anti-manic and maintenance mood stabiliser (first-line acute mania, first-line maintenance), NOT bipolar depression as monotherapy (CANMAT 2018; IPS 2017).
- **Forms and Indian brands:** sodium valproate (Valprol-CR, Encorate), valproic acid, divalproex/semi-sodium valproate (Valance); all become valproic acid (KDT 2019; Maudsley 2021).
- **Serum target:** acute-mania trough around 50 to 100 mg/L (CANMAT 350 to 700 micromol/L; IPS 50 to 125 mcg/mL), held more loosely than the lithium level (Maudsley 2021; CANMAT 2018; IPS 2017).
- **Signature adverse effects:** weight gain, tremor, hair loss, sedation, thrombocytopenia, hyperammonaemia, and the organ-threatening hepatotoxicity and pancreatitis (Maudsley 2021).
- **Monitoring:** baseline and periodic FBC and LFTs, plus weight or BMI (Maudsley 2021; NICE 2014).
- **Teratogenicity:** the highest-risk mood stabiliser, around 10 percent major malformations with neural-tube defects and up to 40 percent developmental delay, dose-related IQ loss and autism risk; contraindicated in women of childbearing potential without a pregnancy-prevention programme, with pre-conception folic acid 5 mg/day (Maudsley 2021; NICE 2014; IPS 2017).
- **PCOS:** hyperandrogenism, polycystic ovary syndrome and menstrual disturbance in women (Maudsley 2021).
- **Key interaction:** inhibits glucuronidation of lamotrigine, roughly doubling its level, so halve and slow the lamotrigine titration (Maudsley 2021).

23 · Carbamazepine and oxcarbazepine

Carbamazepine is the interaction-heavy mood stabiliser: an anticonvulsant that works but is a second-line anti-manic and a third-line prophylactic agent, chosen after lithium and valproate have failed or are unsuitable. Examiners rarely ask you to reach for it; they ask you to survive it. The whole topic is really three keyed facts: it blocks sodium channels (the mechanism it shares with phenytoin and lamotrigine), it is a potent CYP3A4 inducer that **induces its own metabolism** so the level falls over the first few weeks, and it carries a distinctive safety set of hyponatraemia, blood dyscrasias and the HLA-B*1502 Stevens-Johnson association. Get those three right and the question is yours.

This note teaches **carbamazepine** and its better-tolerated analogue **oxcarbazepine** as mood stabilisers: the mechanism, the dose and plasma level, the pharmacokinetic headache of enzyme induction, the adverse-effect set with its monitoring, and where each sits in the guideline algorithm. Verify every level and interaction; a swapped direction or a forgotten contraceptive failure is a critical error. For where mood stabilisers sit in the acute-mania and maintenance algorithm see the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes; the CYP background sits in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

23.1 What it is and where it sits

A second-line stabiliser. Carbamazepine (Tegretol or Mazetol) is an iminostilbene anticonvulsant, structurally related to the tricyclics, licensed for bipolar illness in patients who do not respond to lithium (Maudsley 2021). Two placebo-controlled trials of the extended-release formulation confirm efficacy in acute mania, with roughly double the placebo response, but it is not well tolerated and NICE does not recommend it first-line for mania (Maudsley 2021, NICE 2014). CANMAT places carbamazepine as a second-line monotherapy for acute mania and as a recommended (not first-line) maintenance agent (CANMAT 2018). It is thus the agent you reach for when lithium and valproate have failed, not the agent you start with.

RULE **Second line, not first.** Carbamazepine is a second-line anti-manic and a later-line maintenance stabiliser, used after lithium and valproate, not instead of them.

23.2 Mechanism: sodium-channel blockade

Use-dependent sodium-channel blockade. The core action is blockade of voltage-dependent (voltage-gated) sodium channels, stabilising the inactivated state and dampening high-frequency repetitive firing (Stahl 2021). This is the same molecular target as phenytoin and lamotrigine, and it is thought to underlie both the anticonvulsant and the mood-stabilising effect. Oxcarbazepine (Oxetol), a structural derivative of carbamazepine, blocks the same voltage-dependent sodium channels but in addition increases potassium conductance and modulates high-voltage-activated calcium channels (Maudsley 2021). Its active moiety is the monohydroxy metabolite (licarbazepine), which is why oxcarbazepine avoids the epoxide metabolite responsible for much of carbamazepine's toxicity and much of its enzyme induction.

23.3 Dose and plasma level

Titrate low and slow, monitor the trough. Start at **100 to 200 mg** twice daily and titrate against response and tolerability towards **400 mg** twice daily, higher in some patients; controlled clinical trials of efficacy in bipolar disorder use **800 to 1200 mg/day** (Maudsley 2021). The modified-release preparation (Tegretol Retard) gives smoother levels and is better tolerated. The therapeutic plasma range used as an anticonvulsant is **4 to 12 mg/L** (evidence in affective illness is weaker; a level of at least 7 mg/L may be needed), sampled as a trough immediately before the first dose of the day (Maudsley 2021). Levels above 12 mg/L carry a higher side-effect burden. Carbamazepine cannot be loaded, and rapid titration provokes sedation and ataxia (Goodman and Gilman 2018).

PARAMETER	CARBAMAZEPINE	NOTE
Starting dose (mg twice daily)	**100 to 200**	Titrate slowly; cannot be loaded
Usual target (mg twice daily)	400	Trial doses often 800 to 1200 mg/day total
Therapeutic plasma level (mg/L)	**4 to 12**	Trough, before the morning dose; anticonvulsant range
When to recheck the level	**2 to 4 weeks after a dose change**	Because autoinduction moves the level

Carbamazepine dosing and plasma monitoring: start low, target a trough of 4 to 12 mg/L, and recheck after autoinduction settles.

23.4 The pharmacokinetic headache: enzyme induction and autoinduction

A potent CYP3A4 inducer that induces its own metabolism. This is the single most examined fact. Carbamazepine is a hepatic **enzyme induction** agent, a potent inducer of CYP3A4 (and P-glycoprotein), and it induces the very enzymes that metabolise itself. An initial plasma half-life of around **30 hours** falls to around **12 hours** on chronic dosing, so the level a resident measures in week one drifts downward over the first few weeks even on a fixed dose (Maudsley 2021, K&S 2024). This is why the level must be re-checked **2 to 4 weeks** after any dose increase: the target may no longer be met once autoinduction is complete. Because CYP3A4 handles a large fraction of drugs, carbamazepine lowers the plasma level of many co-prescribed agents, making it one of the most interaction-heavy drugs in psychiatry.

RULE **Carbamazepine induces CYP3A4, including its own metabolism and the pill.** The level falls over the first weeks, and the level of many co-drugs (oral contraceptives, other psychotropics) falls with it; watch the level and the interactions.

23.5 The interactions that matter: the oral contraceptive and the psychotropics

Induction lowers other drug levels. As a CYP3A4 inducer, carbamazepine accelerates the metabolism of oral contraceptives, reducing their plasma concentration and causing contraceptive failure and unplanned pregnancy; adequate non-hormonal or higher-oestrogen contraception must be ensured, and prophylactic folate given, if it cannot be avoided in a woman of childbearing potential (Maudsley 2021). It similarly lowers the levels of many psychotropics

metabolised by CYP3A4, including some antipsychotics and other anticonvulsants (for example it lowers plasma lamotrigine and, by inducing UGT and CYP, valproate). Pharmacodynamically, its anticonvulsant effect is opposed by seizure-threshold-lowering drugs, its marrow-suppressing potential is amplified by clozapine, and its hyponatraemic tendency is worsened by sodium-depleting diuretics; rare neurotoxicity is reported when combined with lithium (Maudsley 2021).

CO-DRUG	EFFECT OF CARBAMAZEPINE	CONSEQUENCE
Oral contraceptive	**Level LOWERED (CYP3A4 induction)**	Contraceptive failure, unplanned pregnancy
Lamotrigine	Level LOWERED	Loss of stabiliser cover; lamotrigine dose may need raising
Some antipsychotics (CYP3A4 substrates)	Level LOWERED	Reduced efficacy; monitor clinically
Clozapine	**Additive marrow suppression**	Avoid combination; agranulocytosis risk
Diuretics	Additive sodium depletion	Worse hyponatraemia
Lithium	Pharmacodynamic	Rare neurotoxicity reported

Carbamazepine as an enzyme inducer: it lowers the level of the pill and CYP3A4-handled psychotropics, and stacks marrow-suppression and hyponatraemia risks.

TRAP **Forgetting that carbamazepine makes the oral contraceptive fail.** A woman started on carbamazepine, still on the combined pill, is now unprotected; the classic missed interaction is contraceptive failure and pregnancy on a teratogenic drug.

23.6 Hyponatraemia (SIADH)

A common, sometimes dangerous, electrolyte effect. Carbamazepine has vasopressin-like (antidiuretic) effects, promoting water resorption and producing dilutional hyponatraemia, an SIADH-like picture (K&S 2024). Older adults, women and higher doses are the vulnerability factors, and co-prescribed sodium-depleting diuretics worsen it. Severe hyponatraemia can present as confusion or delirium. Baseline and on-treatment urea and electrolytes are checked, at least annually and whenever clinically suspected (CANMAT 2018, NICE 2014). This is the one area where oxcarbazepine is worse: it causes hyponatraemia more often, in roughly **3 to 5 percent** of patients (K&S 2024).

23.7 Blood dyscrasias and FBC monitoring

Benign leucopenia is common; aplastic anaemia and agranulocytosis are rare but fatal. Carbamazepine commonly causes a chronic, usually clinically insignificant fall in the white cell count (benign leucopenia), through inhibition of colony-stimulating factor, and lithium can reverse it (K&S 2024). The dangerous events are idiosyncratic: aplastic anaemia, agranulocytosis and pancytopenia occur in roughly **1 in 25,000 to 100,000** patients (K&S 2024; the Maudsley cites about 1 in 20,000 for agranulocytosis and/or aplastic anaemia). Because routine full blood count (FBC) monitoring poorly predicts these rare events, the practical rule is a baseline FBC plus firm counselling that fever, sore throat, rash, bruising or bleeding demand an immediate FBC and

medical review (Maudsley 2021, K&S 2024). Baseline and periodic FBC and liver function tests are standard; a raised GGT or a GGT two to three times normal is rarely a concern.

WORKED EXAMPLE

A man three weeks into carbamazepine for treatment-resistant mania develops fever, mouth ulcers and a sore throat. This is not a viral illness to be observed; it is a potential agranulocytosis until proven otherwise. Stop the drug, take an urgent FBC, and manage the neutropenia. The counselling given at the outset (report fever or sore throat at once) is what makes this catch possible.

23.8 Rash and the HLA-B*1502 Stevens-Johnson association

Screen at-risk ancestry before prescribing. About 3 percent of patients develop a benign erythematous rash, but carbamazepine can rarely progress to Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). The vulnerability is genetically determined: the HLA-B*1502 allele is strongly associated with carbamazepine-induced SJS/TEN, and it is prevalent in Han Chinese, Thai and some other Southeast Asian populations (Maudsley 2021, K&S 2024, Goodman and Gilman 2018). Genetic testing of people of Han Chinese or Thai origin is recommended before carbamazepine is started, and the drug is avoided if the patient is HLA-B*1502 positive. Because any carbamazepine rash may be the early phase of a serious reaction, most clinicians stop the drug even on a benign-looking rash; oxcarbazepine, which cross-reacts less, is a common switch (roughly two-thirds do not re-rash) (K&S 2024).

TRAP **Skipping the HLA-B*1502 screen in an at-risk patient.** In a Han Chinese or Thai patient, prescribing carbamazepine without genotyping risks a preventable Stevens-Johnson syndrome; the allele must be checked first.

23.9 Teratogenicity and the monitoring headline

An established human teratogen. Carbamazepine is a known human teratogen, associated with neural tube defects (spina bifida, of the order of 1 percent) and craniofacial abnormalities; folate pretreatment is advised and the combination with valproate is especially avoided (K&S 2024, CANMAT 2018). CANMAT and NICE advise avoiding it in pregnancy where possible; if used in a woman of childbearing potential the contraceptive interaction makes reliable non-hormonal contraception essential. The maintenance monitoring headline that CANMAT specifies: before and during carbamazepine, genotype at-risk Asian ancestry for HLA-B*1502, educate about rash and SJS, and check serum sodium at least annually, alongside baseline and periodic FBC and LFTs (CANMAT 2018).

4 to 12	30 to 12	2 to 4
THERAPEUTIC LEVEL (MG/L, TROUGH)	HALF-LIFE FALL ON AUTOINDUCTION (HOURS)	RECHECK LEVEL AFTER DOSE CHANGE (WEEKS)

23.10 Oxcarbazepine: the better-tolerated analogue

Less induction, more hyponatraemia, weaker evidence. Oxcarbazepine (Oxetol) shares the sodium-channel mechanism but is metabolised to licarbazepine without the toxic epoxide, so the

toxic effects due to the epoxide metabolite are avoided; separately it is a much weaker enzyme inducer and better tolerated: less rash, no routine benign WBC suppression, and no elevated serious blood-dyscrasia rate (K&S 2024). The two trade-offs are that it causes hyponatraemia more often (about 3 to 5 percent) and that the trial evidence in bipolar disorder is thin: a Cochrane review found insufficient adequate-quality trials to judge its efficacy or acceptability in acute bipolar episodes, and only small studies support adjunctive prophylactic use (Maudsley 2021). It is therefore a tolerability-driven alternative rather than a stronger drug. Typical tablet strengths in India are 150, 300 and 600 mg (KDT 2019).

FEATURE	CARBAMAZEPINE	OXCARBAZEPINE
Mechanism	Na-channel blockade	Na-channel blockade plus K conductance / Ca modulation
Enzyme induction	**Potent CYP3A4 inducer, autoinducing**	Much weaker inducer
Hyponatraemia	Common	**More common (about 3 to 5 percent)**
Blood dyscrasias	**Benign leucopenia; rare aplastic anaemia / agranulocytosis**	No routine WBC suppression; serious dyscrasia not elevated
Rash / SJS	HLA-B*1502 associated SJS/TEN	Lower rash frequency; many carbamazepine-rash patients tolerate it
Bipolar evidence	Second-line, RCT-supported for mania	**Insufficient adequate-quality trials (Cochrane)**

Carbamazepine versus oxcarbazepine: oxcarbazepine trades away potent induction and most of the blood and skin risk, at the cost of more hyponatraemia and weaker bipolar evidence.

HOLD THIS

Carbamazepine is a second-line stabiliser that blocks sodium channels, is a potent autoinducing CYP3A4 inducer (its own level and the pill both fall), and carries hyponatraemia, benign leucopenia with rare aplastic anaemia / agranulocytosis, and HLA-B*1502-linked Stevens-Johnson syndrome; oxcarbazepine is the better-tolerated analogue with less induction but more hyponatraemia.

INDIA

Carbamazepine is marketed in India as Tegretol (Novartis) and Mazetol, and oxcarbazepine as Oxetol; the generic stays primary in prescribing. The HLA-B*1502 point is not only a Han Chinese or Thai concern: the allele is present across parts of South and Southeast Asia, so ancestry-informed caution and a low threshold to stop on any rash are practical rules in Indian practice.

MNEMONIC

CBZ: Cuts Blood, Zaps sodium and the pill

Cuts **B**lood counts (leucopenia, rare aplastic anaemia and agranulocytosis), **Z**aps sodium (hyponatraemia) and the pill (CYP3A4 induction, contraceptive failure); plus HLA-B*1502 Stevens-Johnson syndrome. Autoinducing, so the level falls.

GOOD TO REMEMBER

- **Carbamazepine:** voltage-dependent sodium-channel blocker; potent autoinducing CYP3A4 inducer whose signature harm is the enzyme induction that fails the oral contraceptive; second-line for mania, trough level 4 to 12 mg/L.
- **Enzyme induction:** half-life falls from about 30 to 12 hours over the first weeks, so recheck the level 2 to 4 weeks after any dose change; it lowers oral contraceptive and many psychotropic levels.
- **Hyponatraemia (SIADH):** common, SIADH-like, worse with diuretics and in older women; check serum sodium at least annually.
- **Blood dyscrasias:** benign leucopenia is common; aplastic anaemia and agranulocytosis are rare (about 1 in 25,000 to 100,000) but fatal, so do a baseline FBC and counsel to report fever, sore throat or bruising at once.
- **HLA-B*1502:** allele linked to Stevens-Johnson syndrome and toxic epidermal necrolysis; screen at-risk Han Chinese, Thai and some Asian ancestry before prescribing and avoid if positive.
- **Teratogenicity:** established human teratogen (neural tube defects, craniofacial); avoid in pregnancy where possible, give folate, and never rely on a hormonal contraceptive it induces.
- **Oxcarbazepine (Oxetol):** same sodium-channel mechanism, much weaker inducer, better tolerated with no routine WBC suppression; the one drug where hyponatraemia (about 3 to 5 percent) is more frequent, and bipolar evidence is thin.

24 . Lamotrigine

lamotrigine (Lamitor, Lametec) is the mood stabiliser the board most wants tied to one clinical fact: it is the agent with the best evidence for **bipolar depression** and for maintenance, especially the prevention of depressive relapse, yet it is weak against acute mania. That split personality, strong on the depressive pole and prophylaxis but not a drug you reach for to break a manic episode, is the whole examinable point and the reason it is never used as monotherapy for acute mania (Stahl 2021). Every other high-yield fact about the drug flows from a single pharmacokinetic vulnerability: it must be introduced by **slow titration** to avoid a serious rash, and that titration is halved by valproate and roughly doubled by an enzyme inducer.

This is a pharmacology topic, so the marks are in the mechanism, the titration schedule, the interaction with valproate, and the **rash** stop-rule. The doses, the halving with valproate, the enzyme-inducer doubling and the benign-versus-serious rash distinction below are verified against Stahl's Prescriber's Guide, the Maudsley Prescribing Guidelines, the CANMAT guideline, the Indian Psychiatric Society clinical practice guideline (Stahl 2021; Maudsley 2021; Yatham 2018; Shah 2017). The guideline-anchored place of lamotrigine within the full bipolar management PLAN is set out in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes; the CYP and metabolism background sits in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

Week	Standard mg/day	With valproate mg/day, halved	With an enzyme inducer mg/day (e.g. carbamazepine)
Weeks 1 to 2	25 once daily	25 on alternate days	50 once daily
Weeks 3 to 4	50 once daily	25 once daily	100 (in divided doses)
Week 5	100 once daily	50 once daily	increase by 100 each week
Week 6	200 once daily	100 once daily	up toward 400 (divided)
Usual target	100 to 200	100	400

Stevens-Johnson stop-rule
STOP at any confluent, purpuric or tender rash, any mucosal involvement (eyes, lips, mouth), or a rash with fever or malaise. The slow titration, and halving it with valproate, are what keep the serious-rash risk low.

Fig 12.12 Lamotrigine titration and the Stevens-Johnson risk. Lamotrigine must be titrated slowly over about six weeks; the schedule is halved when combined with valproate (which raises the lamotrigine level) and roughly doubled with an enzyme inducer such as carbamazepine. The rash risk is highest with fast titration and with valproate co-therapy, so a confluent, purpuric, tender or mucosal rash, or a rash with fever, is a stop signal.

24.1 The place: best for bipolar depression and maintenance, weak for mania

Strong on the depressive pole, weak on mania. Lamotrigine has FDA and guideline standing for the **maintenance** of bipolar I disorder, where its particular strength is preventing the depressive relapse rather than the manic one (Stahl 2021; Yatham 2018). It is a first-line option (monotherapy or adjunctive) for acute **bipolar depression**, and both CANMAT and the Indian Psychiatric Society name lithium or lamotrigine among the first-line agents for that indication, particularly where antipsychotic burden is undesirable (Yatham 2018; Shah 2017). What it does **not** do is treat acute mania: onset is far too slow for a manic emergency and the evidence is weak, so it is at best adjunctive and second-line there and never a mania monotherapy (Stahl 2021).

Guideline anchoring. CANMAT lists lamotrigine (monotherapy or adjunctive) for acute bipolar I depression, targeting a minimum of 200 mg/day with slow titration from 25 mg, and lists it among first-line maintenance monotherapies for bipolar I disorder; the Indian Psychiatric Society places lamotrigine as a first-line alternative for acute bipolar depression and as a maintenance agent that is better for depressive-recurrence prevention (Yatham 2018; Shah 2017). The mirror-image caution belongs here: an antidepressant given alone in a bipolar depression risks a switch, whereas lamotrigine treats the depressive pole without that manic-switch liability.

RULE **Reach for lamotrigine for the depressive pole and for maintenance, not for acute mania.** Best evidence is in bipolar depression and depressive-relapse prevention; it is weak and slow against mania.

TRAP **Starting lamotrigine to control an acute manic episode.** It is too slow and too weak for mania; use an antimanic (lithium, valproate, or an antipsychotic) and reserve lamotrigine for the depressive pole and maintenance.

24.2 Mechanism: sodium-channel blockade and glutamate modulation

A use-dependent sodium-channel blocker that damps glutamate. In the Neuroscience-based Nomenclature lamotrigine is a glutamate voltage-gated sodium channel blocker (Glu-CB) (Stahl 2021). It acts as a **use-dependent blocker of voltage-sensitive sodium channels**, binding the open-channel conformation at the alpha pore-forming subunit; by stabilising the inactivated state of the channel it reduces the presynaptic release of the excitatory neurotransmitters glutamate and aspartate (Stahl 2021). This glutamate-modulating action is the proposed basis of its mood-stabilising, and specifically its antidepressant-in-bipolar, effect, and distinguishes its profile from the antimanic anticonvulsants.

PEARL

The mechanism explains the clinical split. Sodium-channel blockade with downstream reduction of glutamate release maps onto relapse prevention and the depressive pole rather than onto the rapid dopaminergic damping needed to abort mania, which is why lamotrigine prevents and treats bipolar depression but is a poor antimanic.

24.3 The slow titration: why it takes weeks

Titrate over weeks, not days. Lamotrigine must be introduced by **slow titration** over several weeks: the incidence of serious rash rises steeply with a fast start and with high initial doses, so the standard monotherapy schedule creeps up from 25 mg/day to a target of 200 mg/day over about six weeks (Stahl 2021; Maudsley 2021). The dose should never be escalated faster than recommended, because the excess risk is not of a trivial side effect but of Stevens-Johnson syndrome. If the patient stops the drug for 5 days or more, the titration is restarted from the beginning, as rashes have been reported on re-exposure (Stahl 2021).

Two modifiers rewrite the schedule. Valproate roughly doubles the lamotrigine level, so the schedule is **halved** when the two are combined; an enzyme inducer such as carbamazepine lowers the level, so the schedule is roughly **doubled** (higher steps, higher target) (Stahl 2021). The monotherapy, with-valproate and with-inducer schedules are set out in the table below.

PHASE	MONOTHERAPY (MG/DAY)	WITH VALPROATE, HALVED (MG/DAY)	WITH ENZYME INDUCER, DOUBLED (MG/DAY)
Weeks 1 to 2	25 daily	**25 on alternate days**	50 daily
Weeks 3 to 4	50 daily	**25 daily**	100 daily (divided)
Week 5	100 daily	50 daily	increase by 100 each week
Week 6	200 daily	100 daily	up towards 400 (divided)
Usual target	**100 to 200**	**100**	**400**

Lamotrigine bipolar titration: the monotherapy schedule creeps 25 to 200 over about 6 weeks; valproate halves every step and the target (start at 25 on alternate days, target 100); an enzyme inducer such as carbamazepine roughly doubles the schedule (start 50, target 400) (Stahl 2021; Maudsley 2021). Highlighted cells are the board-critical numbers.

25	100 to 200	6
MONOTHERAPY STARTING DOSE (MG/DAY)	MONOTHERAPY BIPOLAR TARGET (MG/DAY)	TITRATION LENGTH (WEEKS)

RULE **Titrate lamotrigine slowly and halve the schedule with valproate.** Creep 25 to 200 over about six weeks; with valproate start at 25 on alternate days and target 100.

24.4 The valproate interaction: halve the dose

Valproate can double the lamotrigine level. This is the single most examined interaction of the drug. Valproate inhibits the glucuronidation that clears lamotrigine, so it roughly **doubles** the lamotrigine plasma level; the titration rate and the ultimate dose must therefore be **reduced by 50%** to hold down the rash risk (Stahl 2021). Concretely, in the presence of valproate the start is 25 mg on alternate days (not 25 mg daily), the steps are half-sized, and the usual target falls to about 100 mg/day (Stahl 2021; Maudsley 2021). The mirror rule matters too: if valproate is later stopped once lamotrigine is stabilised, the lamotrigine dose is cautiously doubled over at least two weeks to keep it therapeutic (Stahl 2021).

The enzyme-inducer direction. Carbamazepine and the other enzyme-inducing antiepileptics (phenytoin, phenobarbital, primidone) do the opposite, lowering the lamotrigine level, so the schedule and target are roughly doubled (start 50 mg/day, target up to 400 mg/day in divided doses) (Stahl 2021). Oral contraceptives and pregnancy also lower lamotrigine levels, so the maintenance dose needs review around starting or stopping the pill and around delivery (Stahl 2021).

WORKED EXAMPLE

A woman on maintenance divalproex for bipolar I has a breakthrough depression and lamotrigine is added. Because valproate doubles the lamotrigine level, you do not use the standard 25 mg daily start: you begin lamotrigine at 25 mg on alternate days, increase in half-sized steps, and aim for about 100 mg/day rather than 200 mg/day, watching closely for rash. Using the monotherapy schedule here would roughly double the true lamotrigine exposure and sharply raise the Stevens-Johnson risk.

24.5 Stevens-Johnson syndrome and the serious rash: the stop-rule

The dangerous adverse effect is the rash. Lamotrigine can cause a **rash** in roughly 10% of patients, and the great majority of these are benign; the fear is the small minority that are a serious cutaneous reaction, namely stevens-johnson syndrome or toxic epidermal necrolysis, sometimes with multi-organ hypersensitivity (Stahl 2021). The risk of a serious rash is highest with a fast titration, with high starting doses, in children, and with valproate co-therapy, which is precisely why the schedule is slow and is halved with valproate (Stahl 2021). Most serious rashes appear early, within the first 8 weeks or so of treatment, which is the window the slow titration is designed to cover.

Tell the benign rash from the serious one. A **benign** rash peaks within days, settles in about 10 to 14 days, is spotty, non-confluent, non-tender, has no systemic features and normal bloods; here

you may reduce the dose or hold the increase, warn the patient, and monitor. A **serious** rash is confluent and widespread, or purpuric or tender, involves the neck or upper trunk, or involves the eyes, lips or mouth (mucosal involvement), or carries fever, malaise, pharyngitis, anorexia or lymphadenopathy, or abnormal blood counts or liver function (Stahl 2021). The stop-rule follows: at any sign of a serious or mucosal rash, **stop lamotrigine at once** (and stop concomitant valproate), investigate for organ involvement and admit if needed (Stahl 2021).

COMMON TRAP

A patient a fortnight into lamotrigine develops a rash with sores at the lips and mouth and a low-grade fever. Treating this as the common benign rash and merely holding the dose is the error: mucosal involvement plus systemic features is a serious rash, and the correct action is to stop lamotrigine (and valproate) immediately and investigate, not to wait and watch.

TRAP **Titrating lamotrigine too fast, or ignoring the valproate interaction, and precipitating Stevens-Johnson syndrome.** A fast start or a full monotherapy schedule on top of valproate drives the serious-rash risk; go slow and halve with valproate.

FEATURE	BENIGN RASH	SERIOUS RASH (STOP THE DRUG)
Time course	peaks in days, settles 10 to 14 days	confluent, widespread, progressive
Appearance	spotty, non-confluent, non-tender	**confluent, purpuric or tender**
Site	trunk and limbs, no mucosa	**neck / upper trunk; eyes, lips, mouth (mucosal)**
Systemic features	none	**fever, malaise, pharyngitis, anorexia, lymphadenopathy**
Bloods	normal	abnormal FBC, LFTs, urea/creatinine
Action	reduce dose / hold increase, monitor	**stop lamotrigine (and valproate); investigate; admit if needed**

Benign-versus-serious rash on lamotrigine: any mucosal involvement, systemic features or abnormal bloods marks a serious rash and mandates immediate cessation (Stahl 2021). The wider acute management of a serious drug reaction is in the Perinatal/women's mental health and emergency psychiatry notes.

INDIA

Lamotrigine is widely available in India as the generic and under brands such as Lamitor and Lametec; the tablet strengths (25, 50, 100, 200 mg) suit the six-week creep, and a 25 mg tablet on alternate days is the practical with-valproate start. The same two examinable points hold for Indian practice: lamotrigine is particularly effective for bipolar depression, and the skin-rash risk is higher with faster dose escalation and with valproate co-prescription, so titrate very gradually as per the summary of product characteristics. Note that carbamazepine-linked Stevens-Johnson syndrome is separately tied to the HLA-B*1502 allele common in Asian ancestry; the lamotrigine rash is not gene-tested that way, but the slow-titration discipline is the safeguard.

MNEMONIC

SLOW

What lamotrigine turns on: **S**tevens-Johnson risk is the danger (go slow to avoid it), **L**ow and slow titration (25 to 200 over about six weeks), **O**ne interaction to halve for (valproate doubles the level, so halve the schedule), **W**eak against mania but best for the depressive pole and maintenance.

GOOD TO REMEMBER

- **Lamotrigine (Lamitor, Lametec):** use-dependent voltage-gated sodium-channel blocker that reduces glutamate release; best evidence in bipolar depression and maintenance (depressive-relapse prevention), weak for acute mania.
- **Slow titration:** monotherapy 25 mg/day creeping to a target of 100 to 200 mg/day over about six weeks; never faster than recommended.
- **Valproate interaction:** valproate roughly doubles the lamotrigine level, so halve the titration and the target (start 25 mg on alternate days, target about 100 mg/day).
- **Enzyme inducer (carbamazepine):** lowers the level, so roughly double the schedule and target (start 50 mg/day, up to 400 mg/day).
- **Serious rash / Stevens-Johnson syndrome and toxic epidermal necrolysis:** highest risk with fast titration and valproate co-therapy; stop the drug at any serious or mucosal rash.
- **Monitoring:** no routine serum-level or blood monitoring is required; the safeguard is the slow titration and rash vigilance.

HOLD THIS

Lamotrigine is the mood stabiliser for bipolar depression and maintenance but weak for mania: titrate it slowly from 25 to 200 mg/day over about six weeks, halve the schedule and target with valproate (which doubles the level) and double it with an enzyme inducer, and stop the drug at any sign of a serious or mucosal rash because of Stevens-Johnson syndrome.

25 . Antipsychotics as mood stabilisers

The **atypical** second-generation antipsychotics are no longer bit-players in bipolar disorder: several are guideline first-line agents across one or more phases, and the whole modern algorithm for mania and bipolar depression is built on them (CANMAT 2018; Maudsley 2021). The examiner treats **antipsychotics as mood stabilisers** as a phase-matching problem. You are expected to know which atypical is first-line for mania, which for bipolar depression, which for

maintenance, why they work (a fast anti-manic effect plus, for some, a genuine antidepressant and relapse-prevention effect), and the price you pay for them (the metabolic, extrapyramidal and prolactin burden).

Organise the topic around one idea: **match the atypical to the phase, then monitor the metabolic cost for as long as the drug is used.** Every phase indication, dose and monitoring interval below is verified against the CANMAT and Indian Psychiatric Society rows, the Maudsley and Stahl (CANMAT 2018; IPS 2017; Maudsley 2021; Stahl 2021). The deep receptor pharmacology, the full adverse-effect detail and the metabolic-monitoring schedule are the property of the Schizophrenia: management, antipsychotics and adverse effects notes; this fragment carries only what is load-bearing for mood, and cross-refers the rest there. The neurobiology of mood and the wider guideline-anchored management PLAN belong to the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes.

25.1 Why antipsychotics stabilise mood: the mechanism and the trade-off

What they do at the synapse. Antipsychotics are not merely anti-psychotic: individual agents variously possess sedative, anxiolytic, anti-manic, mood-stabilising and antidepressant properties, and a few (quetiapine and olanzapine) show all of these (Stahl 2021). The shared anti-manic action is **dopamine D2 blockade or partial agonism** in the mesolimbic pathway, which rapidly damps the elevated dopaminergic drive of mania (Stahl 2021; Maudsley 2021). The antidepressant and mood-lifting actions of the broader agents come from additional targets: 5-HT2A antagonism, 5-HT7 antagonism, 5-HT1A partial agonism, alpha-2 blockade and, for quetiapine, potent noradrenaline-reuptake inhibition via its norquetiapine metabolite (Stahl 2021). The full receptor map is developed in the Schizophrenia: management, antipsychotics and adverse effects notes.

Why we reach for them, and what it costs. They are used because the anti-manic effect is fast (useful in an agitated, sleepless, high-risk manic patient) and because, unlike a pure antimanic anticonvulsant, several have real efficacy in bipolar depression and in maintenance (Maudsley 2021; CANMAT 2018). The trade-off is the class burden: **metabolic** harm (weight gain, dyslipidaemia, hyperglycaemia, worst with olanzapine), **extrapyramidal** effects and akathisia, sedation, and prolactin elevation (marked with risperidone and paliperidone) (Stahl 2021; Maudsley 2021). Because bipolar treatment is long-term, that burden is carried for years, which is exactly why the metabolic monitoring is non-negotiable.

RULE **Match the atypical to the phase.** Quetiapine is the broad one (mania, bipolar depression, maintenance); lurasidone and cariprazine are the bipolar-depression agents; aripiprazole and risperidone/paliperidone are mania and maintenance workhorses.

25.2 The FDA phase map: which atypical is licensed for which pole

The set-piece table. The cleanest way to hold this is the FDA-indication-by-phase map (Stahl 2021; Maudsley 2021). Aripiprazole covers mania, mixed episodes and maintenance; asenapine mania and mixed states; olanzapine mania, mixed episodes and maintenance, and (as the olanzapine-fluoxetine combination) bipolar depression; quetiapine spans mania, maintenance

and bipolar depression; risperidone mania and mixed episodes (and, as risperidone LAI, maintenance); cariprazine and lurasidone are the bipolar-depression agents (cariprazine also covers mania); ziprasidone mania and maintenance (Stahl 2021).

ATYPICAL (GENERIC)	MANIA / MIXED	BIPOLAR DEPRESSION	MAINTENANCE	SIGNATURE TRADE-OFF
Quetiapine (Qutipin)	**Yes**	**Yes (300 mg/day)**	**Yes**	Sedation, weight gain, moderate metabolic
Olanzapine (Oleanz)	Yes	Yes (with fluoxetine)	Yes	**Highest metabolic burden**
Aripiprazole	Yes	No (as monotherapy)	Yes (manic relapse)	Akathisia; weight-neutral
Risperidone (Sizodon)	Yes	No	Yes (as LAI)	**Prolactin elevation**
Paliperidone	Yes	No	LAI option	**Prolactin elevation**
Cariprazine	Yes	**Yes**	-	Akathisia; low metabolic
Lurasidone	No	**Yes**	-	Akathisia, nausea; low metabolic; take with food
Asenapine	Yes (incl. mixed)	No	-	Sublingual; oral hypoaesthesia

Atypical antipsychotics by bipolar phase (FDA-indication map, Stahl 2021; Maudsley 2021). The highlighted cells are the phase-defining facts to hold: quetiapine across all three poles, olanzapine's metabolic cost, the depression pair (cariprazine, lurasidone), and the prolactin pair (risperidone, paliperidone).

25.3 Quetiapine: the broadest, works across all phases

Why it is the broad one. Quetiapine (Qutipin, quetiapine) is the single atypical effective across all three bipolar phases: acute mania, acute bipolar I depression and maintenance (Stahl 2021; CANMAT 2018). Its breadth is mechanistic: D2 and 5-HT2A antagonism for the anti-manic and antipsychotic effect, and an active metabolite (norquetiapine) that is a potent noradrenaline-reuptake inhibitor and 5-HT2C antagonist, underpinning a genuine antidepressant action (Stahl 2021). CANMAT names quetiapine as a first-line monotherapy for acute mania, a first-line monotherapy for acute bipolar I depression at a target of **300 mg/day**, and a first-line maintenance monotherapy for bipolar I disorder (CANMAT 2018).

The dose and the cost. Mania and maintenance use higher divided doses (commonly around 400 to 800 mg/day); bipolar depression is treated at the lower **300 mg/day** (CANMAT 2018; Maudsley 2021). It carries moderate metabolic risk and is sedating, so it is often dosed at night (Stahl 2021). In India it is marketed as Qutipin (quetiapine), available as 25, 50, 100, 200 and 400 mg tablets (KDT 2019).

GOOD TO REMEMBER

- **Quetiapine (Qutipin):** D2/5-HT2A antagonist whose norquetiapine metabolite is a noradrenaline-reuptake inhibitor; signature cost is sedation and weight gain; the one to hold is that it is first-line across all three phases and bipolar depression is treated at 300 mg/day (CANMAT 2018; Stahl 2021).

25.4 Olanzapine: mania and maintenance, and the OFC for bipolar depression

Its place. Olanzapine (Oleanz, olanzapine) is effective in acute mania, mixed episodes and maintenance, and the **olanzapine-fluoxetine combination** (OFC) is a recognised treatment for bipolar I depression (Stahl 2021; CANMAT 2018). CANMAT places olanzapine as a first-line option for acute mania but downgrades it in maintenance and lists the OFC as a second-line option for acute bipolar I depression, both because of its metabolic profile (CANMAT 2018). It is a D2 and 5-HT2A antagonist; the fluoxetine partner adds the serotonergic antidepressant drive that olanzapine alone lacks.

The catch. Olanzapine carries the **highest metabolic** burden of the atypicals used in mood disorder, alongside clozapine: substantial weight gain, dyslipidaemia and hyperglycaemia (Stahl 2021). This is why guidelines that rank it first-line for the manic pole still demote it for long-term use. Indian brand: Oleanz (olanzapine), 2.5 to 20 mg tablets (KDT 2019).

TRAP **Ignoring the metabolic monitoring when an atypical is used long-term for mood.** Olanzapine on maintenance without weight, glucose and lipid tracking is the classic error; the drug that controlled the mania quietly builds the metabolic syndrome.

GOOD TO REMEMBER

- **Olanzapine (Oleanz):** D2/5-HT2A antagonist; signature cost is the highest metabolic burden of the mood atypicals; the one to hold is that it covers mania and maintenance, and bipolar depression only as the olanzapine-fluoxetine combination (CANMAT 2018; Stahl 2021).

25.5 Aripiprazole: mania and maintenance, weight-neutral

The mechanism that sets it apart. Aripiprazole (aripiprazole) is a **D2 partial agonist** (and 5-HT1A partial agonist, 5-HT2A antagonist), which gives it a fast anti-manic effect with a low metabolic and prolactin profile (Stahl 2021; KDT 2019). CANMAT lists it as a first-line agent for acute mania and, importantly, as a first-line maintenance monotherapy, available oral or as a once-monthly long-acting injectable, with the caveat that it prevents manic but not depressive episodes (CANMAT 2018). It is not a bipolar-depression monotherapy.

Dose and tolerability. The usual bipolar dose range is roughly **15 to 30 mg/day** (Indian dosing 5 to 30 mg/day; KDT 2019). It is essentially **weight-neutral** and carries low metabolic risk, but akathisia is its characteristic and often dose-limiting adverse effect (Stahl 2021).

GOOD TO REMEMBER

- **Aripiprazole:** D2 partial agonist; signature cost is akathisia (but weight-neutral and low prolactin); the one to hold is that it is first-line for mania and for maintenance (oral or once-monthly LAI) but prevents only the manic pole, not the depressive one (CANMAT 2018; Stahl 2021).

25.6 Risperidone and paliperidone: mania and the LAI option, at a prolactin cost

What they cover. Risperidone (Sizodon, risperidone) is a potent D2 and 5-HT2A antagonist, first-line for acute mania and mixed episodes; paliperidone (paliperidone), its active 9-hydroxy metabolite, is likewise used in mania (Stahl 2021; CANMAT 2018). Their standout maintenance role is as the **long-acting injectable** option: CANMAT recommends a long-acting injectable antipsychotic (risperidone LAI every two weeks or aripiprazole once-monthly) for the non-adherent bipolar patient to prevent relapse (CANMAT 2018).

The cost. Both are the class leaders for **prolactin elevation** (galactorrhoea, menstrual disturbance, sexual dysfunction) and carry moderate metabolic risk, more than the partial agonists (Stahl 2021). Risperidone is dosed around 1 to 6 mg/day in mania; Indian brands include Sizodon and Respidon (risperidone), 1 to 4 mg tablets (KDT 2019).

GOOD TO REMEMBER

- **Risperidone (Sizodon) and paliperidone:** potent D2/5-HT2A antagonists (paliperidone is risperidone's 9-OH metabolite); signature cost is prolactin elevation; the one to hold is mania first-line, and the long-acting injectable (risperidone LAI two-weekly) as the maintenance option for non-adherence (CANMAT 2018; Stahl 2021).

25.7 Cariprazine: mania and bipolar depression, the D3-preferring partial agonist

Why it reaches the depressive pole. Cariprazine (cariprazine) is a D2 and D3 partial agonist that is unique in being the **most potent available agent at the D3 receptor**, more potent than dopamine itself, together with 5-HT1A partial agonism (Stahl 2021). This D3-preferring profile is the presumed basis of its efficacy across both poles. CANMAT names cariprazine among the first-line options for acute mania, and lists cariprazine (with the olanzapine-fluoxetine combination) as a second-line option for acute bipolar I depression when a rapid response is desirable (CANMAT 2018).

Tolerability. It sits in the low-metabolic-risk tier (with lurasidone and aripiprazole) but, like the other partial agonists, akathisia is its characteristic adverse effect (Stahl 2021). Its long half-life and active metabolites mean effects and adverse effects accumulate over weeks.

GOOD TO REMEMBER

- **Cariprazine:** D3-preferring D2/D3 partial agonist (the most potent D3 agent available); signature cost is akathisia (low metabolic); the one to hold is that it works in both mania and bipolar depression, unusual for an anti-manic atypical (CANMAT 2018; Stahl 2021).

25.8 Lurasidone: the bipolar-depression agent

Its niche. Lurasidone (lurasidone) is a potent antagonist at 5-HT2A, D2 and 5-HT7 receptors and a 5-HT1A partial agonist (Kaplan and Sadock 2024; Stahl 2021). Its distinctive place is

bipolar depression: CANMAT lists it as a first-line treatment for acute bipolar I depression, as monotherapy or adjunctive to lithium or divalproex (CANMAT 2018). It is not licensed for acute mania. It sits with cariprazine and aripiprazole in the low-metabolic-risk tier (Stahl 2021).

The practical points. Its commonest adverse effects are sedation, akathisia and nausea, and it has a firm pharmacokinetic quirk: it must be **taken with food** (at least 350 kcal) to be adequately absorbed, and it is a CYP3A4 substrate, so it is contraindicated with strong CYP3A4 inhibitors and inducers (Kaplan and Sadock 2024; Stahl 2021). The receptor and interaction detail is developed in the Schizophrenia: management, antipsychotics and adverse effects notes.

RULE **Lurasidone and cariprazine for bipolar depression.** When the pole to treat is the depressive one, these two (plus quetiapine and the olanzapine-fluoxetine combination) are the atypicals with the evidence, not the pure anti-manic agents.

GOOD TO REMEMBER

- **Lurasidone:** 5-HT2A/D2/5-HT7 antagonist and 5-HT1A partial agonist; signature cost is akathisia and nausea (low metabolic) plus the take-with-food requirement; the one to hold is that it is first-line for bipolar depression and has no mania licence (CANMAT 2018; Kaplan and Sadock 2024).

25.9 Asenapine: mania, including mixed features

Its place. Asenapine (asenapine) is a high-affinity 5-HT2A and D2 antagonist (with broad serotonergic, dopaminergic and adrenergic actions) licensed for acute **mania and mixed states**, and it is one of the agents named first-line for acute mania by CANMAT (Kaplan and Sadock 2024; CANMAT 2018). Its usefulness in **mixed features** is the fact worth holding.

The formulation quirk. Asenapine is given **sublingually** because oral bioavailability is negligible; the patient must avoid food and drink for 10 minutes afterwards, and it commonly causes oral hypoaesthesia (Kaplan and Sadock 2024). It carries moderate metabolic risk (Stahl 2021).

GOOD TO REMEMBER

- **Asenapine:** high-affinity 5-HT2A/D2 antagonist given sublingually; signature cost is oral hypoaesthesia (and no food or drink for 10 minutes); the one to hold is mania first-line, particularly useful for mixed features (CANMAT 2018; Kaplan and Sadock 2024).

25.10 Phase-matching and the metabolic monitoring: pulling it together

The selection logic, previewing the choosing topic. The whole class resolves into a phase-matching decision (CANMAT 2018; Stahl 2021). For **acute mania**, CANMAT offers quetiapine, aripiprazole, risperidone, paliperidone, cariprazine or asenapine (alone or combined with lithium or divalproex), with an atypical-plus-mood-stabiliser combination first-line in severe presentations. For **acute bipolar I depression**, the atypical options are quetiapine, lurasidone (monotherapy or adjunctive to lithium or divalproex), the olanzapine-fluoxetine combination and cariprazine. For **maintenance**, quetiapine, aripiprazole and asenapine are first-line monotherapies, with olanzapine and paliperidone (and risperidone LAI) as second-line,

olanzapine downgraded for its metabolic risk. The **Indian Psychiatric Society** position aligns: the IPS guidelines name quetiapine, aripiprazole, risperidone, asenapine or cariprazine (with lithium or divalproex) among first-line monotherapies for acute mania and place olanzapine and ziprasidone second-line, name the olanzapine-fluoxetine combination, quetiapine, lurasidone or cariprazine as first-line for acute bipolar depression, and quetiapine and lamotrigine alongside lithium and divalproex as first-line maintenance agents, with olanzapine, carbamazepine, ziprasidone and risperidone second-line (IPS 2025). NICE recommends offering an antipsychotic (asenapine, aripiprazole, olanzapine, quetiapine or risperidone) where lithium is unsuitable for maintenance (NICE 2014). The full agent-versus-agent selection is developed in the choosing topic.

The monitoring headline. Whenever an atypical is used long-term for mood, the metabolic monitoring runs for as long as the drug does: CANMAT advises weight monthly for the first three months then every three months, with blood pressure, fasting glucose and a fasting lipid profile at 3 and 6 months then yearly, on top of the baseline metabolic and prolactin screen (CANMAT 2018). The receptor-level basis and the full adverse-effect and monitoring schedule are the property of the Schizophrenia: management, antipsychotics and adverse effects notes.

300	3	3 and 6
QUETIAPINE BIPOLAR DEPRESSION (MG/DAY)	WEIGHT CHECK FOR FIRST MONTHS (MONTHLY, THEN 3-MONTHLY)	GLUCOSE AND LIPIDS THEN YEARLY (MONTHS)

PEARL

The two atypicals that reach the depressive pole in bipolar I as first-line (lurasidone and, with quetiapine, cariprazine second-line) are exactly the ones in the low-metabolic-risk tier: the drugs you most want to keep a patient on long-term for the harder-to-treat depressive phase happen to be the metabolically kindest, which is a rare alignment of efficacy and tolerability (Stahl 2021; CANMAT 2018).

INDIA

Lead with the Indian brand where one is confirmed: quetiapine as **Qutipin** (25 to 400 mg), olanzapine as **Oleanz** (2.5 to 20 mg), risperidone as **Sizodon** or Respidon (1 to 4 mg) (KDT 2019). Aripiprazole, paliperidone, cariprazine, lurasidone and asenapine are all marketed in India but a specific brand could not be confirmed from the parsed library, so the generic is given for those (flagged under gaps). All of these are widely available and used as mood stabilisers in Indian bipolar practice.

GOOD TO REMEMBER

- **Mania (first-line atypicals):** quetiapine, aripiprazole, risperidone, paliperidone, cariprazine, asenapine, alone or with lithium/divalproex (CANMAT 2018).
- **Bipolar depression:** quetiapine and lurasidone are first-line; cariprazine and the olanzapine-fluoxetine combination are second-line (CANMAT 2018).
- **Maintenance:** quetiapine, aripiprazole, asenapine first-line; aripiprazole prevents manic (not depressive) relapse; risperidone LAI or aripiprazole once-monthly for non-adherence (CANMAT 2018).
- **The trade-off:** the metabolic burden (worst with olanzapine), extrapyramidal effects/akathisia (the partial agonists) and prolactin (risperidone, paliperidone) must be monitored for as long as the drug is used (Stahl 2021; CANMAT 2018).

HOLD THIS

Quetiapine works across all three phases; lurasidone and cariprazine are the bipolar-depression agents; and any atypical used long-term for mood earns lifelong metabolic monitoring.

26 . Choosing a mood stabiliser: the algorithms

Choosing a mood stabiliser is not a single decision, it is a decision that is remade at every phase of bipolar disorder: the agent that is first-line for **acute mania** is not the same agent that is first-line for the depressive pole, and the **maintenance algorithm** is anchored by yet another logic. This is the mood-block closer and a reliable theory question: the examiner rewards the guideline-anchored **phase-then-polarity** spine and the exact serum-level targets, not a recitation of side effects. The deep pharmacology, dosing, monitoring and teratogenicity of each agent are owned by the dedicated lithium, valproate, carbamazepine and lamotrigine topics in these notes; this topic carries the **selection algorithm**.

Lead the guideline answer with CANMAT, specifically the CANMAT and ISBD 2018 bipolar guidelines (Yatham 2018), then give the Indian Psychiatric Society (IPS 2025, Menon et al.), NICE (NICE 2014) and BAP (BAP 2016, Goodwin) positions. Across all four the organising principle the exam tests is one instruction: **pick the stabiliser by phase and by predominant polarity, with lithium anchoring maintenance and lamotrigine covering the depressive pole.**

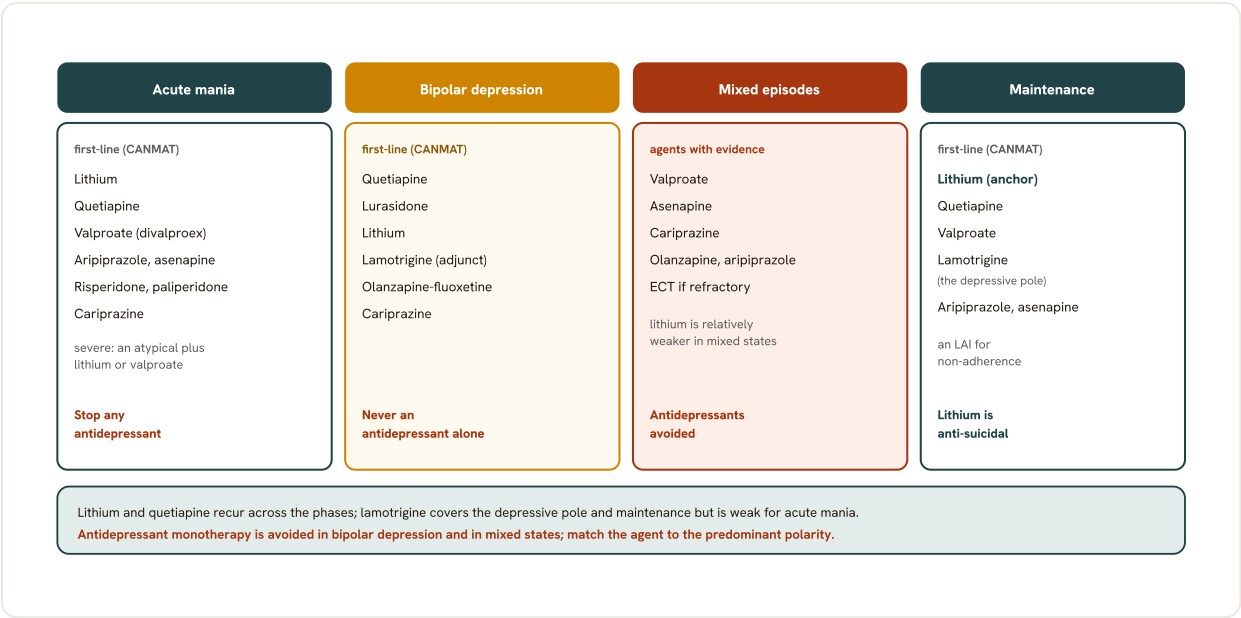


Fig 12.13 Choosing a mood stabiliser by phase, led by the CANMAT recommendations. Lithium, quetiapine and valproate anchor acute mania; quetiapine, lurasidone, lithium and lamotrigine cover bipolar depression; valproate and the atypicals (asenapine, cariprazine) with ECT cover mixed episodes; and lithium anchors maintenance with lamotrigine for the depressive pole. Antidepressant monotherapy is avoided in bipolar depression and mixed states, and any antidepressant is stopped in acute mania.

26.1 The selection logic: phase first, then predominant polarity

Phase before drug. The single most examinable idea is that you choose the agent by the phase you are treating, not by a generic label of "mood stabiliser". A drug that is genuinely first-line for mania (for example an antipsychotic or valproate) may be weak or useless for the depressive pole, and a drug that covers the depressive pole (lamotrigine) is weak for acute mania. Layered on top of phase is **predominant polarity**: a patient whose recurrences are mostly depressive is steered toward agents with depressive-pole efficacy (lamotrigine, quetiapine, lithium), whereas a mostly-manic course is steered toward lithium and the antimanic antipsychotics. The receptor-level pharmacology that underlies these differences is cross-referred to the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

RULE **Pick the stabiliser by phase and predominant polarity.** Lithium anchors maintenance; lamotrigine covers the depressive pole; the antimanic antipsychotics and valproate cover mania.

26.2 ACUTE MANIA: the CANMAT first-line monotherapies

For **acute mania**, CANMAT offers a defined first-line monotherapy list (Yatham 2018): lithium (Licab or Intalith), quetiapine (Qutipin), divalproex (Valance or Valprol), asenapine, aripiprazole, paliperidone, risperidone and cariprazine, given alone or in combination. Note what is *not* on this list: lamotrigine, carbamazepine and the antidepressants. The choice among the first-line agents is individualised on prior response, tolerability, comorbidity and the need for sedation. The IPS names essentially the same set, listing lithium, divalproex, risperidone, quetiapine, aripiprazole, asenapine or cariprazine monotherapy as first-line for acute mania, with carbamazepine, olanzapine, ziprasidone and haloperidol second-line on grounds of a less favourable safety profile (IPS 2025). NICE, for a person not already on treatment, offers haloperidol, olanzapine, quetiapine or risperidone (NICE 2014).

RULE **Acute mania first-line = lithium, an antimanic atypical (quetiapine, asenapine, aripiprazole, paliperidone, risperidone, cariprazine) or divalproex.** Individualise on tolerability and comorbidity (CANMAT 2018).

26.3 ACUTE MANIA: the first-line combination and the antidepressant rule

For severe mania, CANMAT's **first-line combination** is an atypical antipsychotic (quetiapine, aripiprazole, risperidone or asenapine) plus lithium or divalproex, preferred in severe presentations over monotherapy (Yatham 2018). The IPS agrees: combine a mood stabiliser with a second-generation antipsychotic for severe mania (IPS 2017). Two selection rules sit alongside this. First, **discontinue any antidepressant** in a patient presenting with mania, and reassess the diagnosis before starting antimanic agents in a first-episode presentation (CANMAT 2018; IPS 2017). Second, if response to an optimally dosed first-line agent is inadequate after 2 weeks, optimise the dose and address non-adherence and substance use before switching to or adding another first-line agent (CANMAT 2018). The serum-level target for lithium in acute mania is **0.8 to 1.2 mEq/L** (Yatham 2018).

TRAP **Leaving an antidepressant running in acute mania.** Antidepressants are discontinued when a patient presents in mania; continuing one is a selection error.

WORKED EXAMPLE

A 27-year-old man presents with a first severe manic episode with psychotic features while taking sertraline for a presumed depression. The sertraline is discontinued. Because the mania is severe, he is started not on monotherapy but on the first-line combination: an atypical antipsychotic, risperidone (Sizodon or Risdone), plus a mood stabiliser, lithium (Licab or Intalith), titrated to an acute-phase serum lithium of 0.8 to 1.2 mEq/L. He is reviewed at 2 weeks; because the response is only partial, the dose is optimised and adherence checked before any switch. The diagnosis is reassessed as bipolar I disorder once the episode settles, which sets up the maintenance decision.

26.4 BIPOLAR DEPRESSION: a different first-line list

The depressive pole has its own first-line set, and it is the reason lamotrigine exists in this algorithm. For acute bipolar I depression, CANMAT's first-line options are quetiapine (Qutipin), lurasidone (as monotherapy or added to lithium or divalproex), lithium, and lamotrigine (Lamitor or Lametec) as monotherapy or adjunct (Yatham 2018). Lamotrigine is titrated slowly from **25 mg** to a minimum target of **200 mg/day** to limit the rash risk; the full titration schedule and the Stevens-Johnson syndrome caution are owned by the lamotrigine topic in these notes. The IPS names the olanzapine-fluoxetine combination, quetiapine, lurasidone and cariprazine as first-line for acute bipolar depression, and is explicit that lithium is not approved as a first-line treatment here and that lamotrigine is usually not preferred for the acute phase because of its prolonged titration (IPS 2025). NICE offers fluoxetine combined with olanzapine, quetiapine alone, olanzapine alone, or lamotrigine alone (NICE 2014). A hard rule governs the whole pole: **do not use an antidepressant as monotherapy in bipolar depression**; if one is used it is only on a background mood stabiliser, paroxetine is avoided, and bupropion is preferred (IPS 2017). The management of each bipolar phase in full is owned by the dedicated bipolar-management topics.

TRAP **An antidepressant alone in a bipolar patient.** Antidepressant monotherapy is not used in bipolar depression; cover it with a mood stabiliser, and never use lamotrigine to treat acute mania (it is weak there).

26.5 MAINTENANCE ALGORITHM: lithium leads, lamotrigine for the depressive pole

The **maintenance algorithm** is where lithium is the anchor. CANMAT's first-line maintenance monotherapies for bipolar I are lithium, quetiapine, divalproex, lamotrigine, asenapine and aripiprazole, alone or in combination (Yatham 2018). Two polarity facts drive the choice: **lamotrigine is the maintenance agent for the depressive pole** and is weak against manic recurrence, whereas **aripiprazole prevents manic but not depressive episodes**. Lithium is the broadest, preventing both poles, and carries specific anti-suicide evidence (IPS 2017). A rational default is to continue into maintenance the agent that worked in the acute phase (BAP 2016; IPS 2017). The maintenance serum-level target for lithium is **0.6 to 1.0 mEq/L** (Yatham 2018); NICE and BAP frame a slightly narrower **0.6 to 0.8 mmol/L** range (NICE 2014; BAP 2016). NICE is explicit that lithium is the first-line long-term treatment, with an antipsychotic (asenapine, aripiprazole, olanzapine, quetiapine or risperidone) if lithium is unsuitable (NICE 2014). The IPS guidelines name lithium and valproate as the best-evidenced maintenance agents (IPS 2017).

RULE **Lithium leads maintenance and prevents both poles; lamotrigine covers the depressive pole; aripiprazole covers the manic pole only.** Continue what worked acutely (CANMAT 2018; NICE 2014).

26.6 MAINTENANCE: the LAI option for non-adherence

Non-adherence is the commonest cause of maintenance failure, and the algorithm has a defined answer. In a non-adherent patient, CANMAT offers a **long-acting injectable** antipsychotic as first-line to prevent relapse, specifically risperidone LAI every 2 weeks or aripiprazole once-monthly (Yatham 2018). BAP frames the same option as depot antipsychotics for prophylaxis against manic recurrence when oral adherence is erratic or injection is preferred (BAP 2016). This is a selection rule the exam likes because it links a clinical problem (non-adherence) to a specific pharmacological form; the deep antipsychotic pharmacology behind these agents is cross-referred to the Schizophrenia: management, antipsychotics and adverse effects notes.

RULE **Non-adherence in maintenance = a long-acting injectable.** Risperidone LAI two-weekly or aripiprazole once-monthly is first-line for the non-adherent patient (CANMAT 2018).

26.7 The stabiliser-selection algorithm assembled by phase

The phases and their first-line agents assemble into one table. Learn the highlighted cell in each row: it is the first-line fact the examiner tests. Each phase links to the dedicated bipolar-management topics for the full plan.

0.8 to 1.2 ACUTE-MANIA LITHIUM (MEQ/L)	**0.6 to 1.0** MAINTENANCE LITHIUM (MEQ/L)	**200** LAMOTRIGINE MINIMUM TARGET (MG/DAY)	**2 wk** REASSESS BEFORE SWITCHING IN MANIA

PHASE	CANMAT FIRST-LINE (LEAD)	FIRST-LINE COMBINATION / NEXT STEP	IPS / NICE / BAP HEADLINE
Acute mania	**Lithium, quetiapine, divalproex, asenapine, aripiprazole, paliperidone, risperidone, cariprazine (monotherapy) (CANMAT 2018)**	Atypical (quetiapine, aripiprazole, risperidone, asenapine) plus lithium or divalproex for severe mania; discontinue any antidepressant; lithium 0.8 to 1.2 mEq/L	IPS: lithium, divalproex, risperidone, quetiapine, aripiprazole, asenapine, cariprazine first-line, with olanzapine, ziprasidone and haloperidol second-line; NICE: haloperidol, olanzapine, quetiapine, risperidone (IPS 2025; NICE 2014)
Bipolar depression	**Quetiapine, lurasidone (plus lithium or divalproex), lithium, lamotrigine (CANMAT 2018)**	Lamotrigine titrated 25 to 200 mg/day; no antidepressant monotherapy; olanzapine-fluoxetine an option	IPS: olanzapine-fluoxetine, quetiapine, lurasidone or cariprazine first-line, lithium not first-line here; NICE: fluoxetine plus olanzapine, or quetiapine, or lamotrigine (IPS 2025; NICE 2014)
Mixed features	**Antimanic agents; antidepressants avoided (treat the manic pole) (CANMAT 2018)**	Lithium, valproate or an antimanic atypical; do not use an antidepressant in a mixed state (IPS 2017)	IPS: no antidepressant monotherapy in mixed episodes; consider ECT if severe (IPS 2017)
Maintenance	**Lithium, quetiapine, divalproex, lamotrigine, asenapine, aripiprazole (CANMAT 2018)**	Lamotrigine for the depressive pole; aripiprazole for the manic pole only; LAI (risperidone two-weekly or aripiprazole monthly) for nonadherence; lithium 0.6 to 1.0 mEq/L	NICE: lithium first-line long-term; IPS/BAP: lithium and valproate best-evidenced, continue what worked acutely (NICE 2014; IPS 2017; BAP 2016)

The mood-stabiliser selection algorithm by phase; first-line agents verified against CANMAT and ISBD 2018 (Yatham 2018), IPS 2017, NICE 2014 and BAP 2016. Each phase is owned in full by the dedicated bipolar-management topics.

INDIA

The Indian Psychiatric Society Clinical Practice Guidelines for bipolar disorder (IPS 2025, Menon et al.) are the guideline most likely to be named in Indian postgraduate examinations, and they map cleanly onto the phases: lithium, divalproex or a first-line antipsychotic (risperidone, quetiapine, aripiprazole, asenapine, cariprazine) for acute mania, with olanzapine, ziprasidone and haloperidol second-line; the olanzapine-fluoxetine combination, quetiapine, lurasidone or cariprazine first-line for bipolar depression; lithium and valproate as the best-evidenced maintenance agents with lithium first-line for preventing recurrence at both poles and specific anti-suicide evidence. Every agent named here is available as an inexpensive Indian brand: lithium carbonate (Licab or Intalith), sodium valproate (Valprol or Encorate), divalproex (Valance or Divaa), quetiapine (Qutipin), olanzapine (Oleanz), lamotrigine (Lamitor or Lametec) and carbamazepine (Tegretol or Mazetol). The IPS avoids antidepressant monotherapy in bipolar depression, prefers bupropion if an antidepressant is unavoidable, and avoids paroxetine.

GOOD TO REMEMBER

- **Lithium (Licab or Intalith):** broad-spectrum anchor; prevents both poles and has anti-suicide evidence; acute-mania target **0.8 to 1.2 mEq/L**, maintenance **0.6 to 1.0 mEq/L** (CANMAT 2018).
- **Quetiapine (Qutipin):** the one atypical that is first-line across mania, bipolar depression and maintenance; signature adverse effect is metabolic and sedation.
- **Divalproex / valproate (Valprol or Encorate):** first-line for acute mania and maintenance; teratogenic, so avoided in women of childbearing potential; not first-line for bipolar depression.
- **Lamotrigine (Lamitor or Lametec):** the depressive-pole agent for bipolar depression and maintenance; weak for acute mania; titrate slowly from 25 mg to a minimum of **200 mg/day** for rash risk.
- **Aripiprazole:** first-line for mania and maintenance but prevents the manic pole only, not the depressive; available as a once-monthly LAI for non-adherence.
- **The antidepressant rule:** discontinue an antidepressant in acute mania, and never use antidepressant monotherapy in bipolar depression (CANMAT 2018; IPS 2017).

PEARL

Read the algorithm as three lists that overlap but are not identical. Only a handful of agents (lithium, quetiapine, divalproex, aripiprazole, asenapine) appear on both the mania and the maintenance first-line lists; lamotrigine appears on the depression and maintenance lists but never on the mania list; lurasidone appears on the depression list. The overlap is why lithium is the safest single answer when a question does not specify the phase.

HOLD THIS

Choose the mood stabiliser by phase and predominant polarity: for acute mania give lithium, an antimanic atypical or divalproex and stop any antidepressant; for bipolar depression reach for quetiapine, lurasidone, lithium or lamotrigine and never an antidepressant alone; for maintenance lithium leads and prevents both poles while lamotrigine covers the depressive pole, with CANMAT 2018 as the lead guideline.

Treatment resistance, augmentation and special populations

27 . Treatment-resistant depression

Some depressions do not lift on the first, or even the second, well-chosen antidepressant. **Treatment-resistant depression** is the label for that clinical situation, and it is one of the highest-yield theory topics in the mood block because the examiner is testing a discipline, not a drug list: before you escalate treatment, you must prove the depression is genuinely resistant and not merely under-treated. This topic teaches the **definition** of treatment-resistant depression, how to **staging** the degree of resistance, and the evaluation that must precede the label. The augmentation ladder that follows a confirmed diagnosis (which agent, which line) is the next topic; this topic carries the definition, the staging and the pre-escalation work-up.

The single organising idea is that resistance is a matter of *degree*, not a binary switch, and that it is over-diagnosed. Most apparent resistance is **pseudoresistance**, an inadequate dose, an inadequate duration, poor adherence or the wrong diagnosis, and every guideline (CANMAT 2016; BAP 2015; IPS 2017) opens the treatment-resistant depression pathway with a mandatory review of adequacy and diagnosis before any escalation.

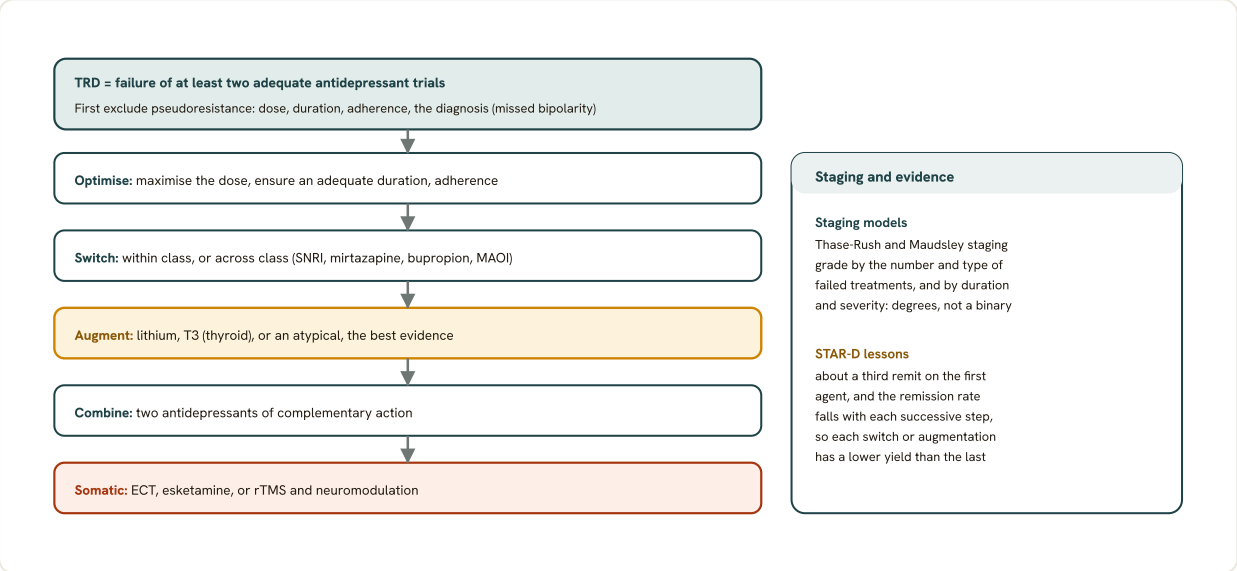


Fig 12.14 Treatment-resistant depression: staging and the augmentation ladder. Resistance means at least two failed adequate antidepressant trials, but pseudoresistance (inadequate dose or duration, non-adherence, missed bipolarity) is excluded first. The sequence then runs optimise, switch, augment (lithium, T3 or an atypical carry the best evidence), combine, and finally the somatic treatments. The STAR-D trial showed remission rates fall with each successive step.

27.1 The definition: two adequate failed trials in the current episode

The working definition. **Treatment-resistant depression** (**trd**) is conventionally defined as a failure to respond to at least **two** adequate antidepressant trials, each at an adequate dose for an adequate duration, in the current depressive episode (Tasman 2015; Maudsley 2021). Failure of a single trial is so common that it does not qualify as resistance; true resistance is better defined as failure to reach remission after two treatments given at adequate dosage and duration (Tasman 2015).

The definition is not settled. There is no universally accepted operational definition of treatment-resistant depression, which is precisely why comparisons across the literature are so difficult (Tasman 2015). Definitions vary in three ways: the *number* of failed trials required (some demand two, some more), the *outcome* threshold that counts as failure (non-response, usually less than a 50 percent symptom reduction, versus failure to reach full remission), and whether the failed trials must be of different pharmacological classes. Remission, not response, is the modern target, because response without remission carries a high relapse risk (Tasman 2015).

RULE **Two adequate antidepressant trials must fail in the current episode before the depression is called resistant.** Each trial must have been at an adequate dose for an adequate duration.

27.2 What "adequate" means: dose and duration

Adequacy is dose plus duration. A trial only counts toward resistance if it was truly adequate, meaning a therapeutic dose sustained for long enough to work. The BAP directs that before declaring a drug to have failed you must increase to a recommended therapeutic dose, and for a tricyclic aim for a dose-equivalence of at least **125 mg** if tolerated (BAP 2015). On duration, the guidelines assess response at **4 weeks** of adequate treatment and again at **6 to 8 weeks**; a marginal or low dose, or a trial cut short before this window, has not adequately tested the drug (BAP 2015; CANMAT 2016).

Optimise before you escalate. The first step in the treatment-resistant depression pathway is therefore not a new drug but optimisation: check the adequacy of the current treatment, and raise a low or marginal dose to a recommended therapeutic dose first (BAP 2015). Only a trial that was adequate in both dose and duration can be counted as a genuine failure.

2	4 to 8	50
ADEQUATE FAILED TRIALS TO DEFINE TRD	WEEKS TO JUDGE ONE ADEQUATE TRIAL	PERCENT SYMPTOM DROP DEFINING RESPONSE

27.3 Staging: resistance is a degree, not a binary

Why stage. Because resistance is a continuum, several **staging** systems quantify *how* resistant a depression is, which predicts outcome and guides how aggressively to treat (Tasman 2015). The two the board tests are the **thase-rush** five-stage model and the **maudsley staging** method; the Massachusetts General Hospital (MGH) staging method is a third. Each grades resistance by the number and type of failed treatments and, for the newer methods, the duration and severity of illness.

The clinical point of any staging system. All of them exist to make one point: neither doctor nor patient should be discouraged by a single failed trial, and good treatment demands persistence through multiple adequate trials (Tasman 2015). Staging turns "resistant or not" into a graded score that tracks the odds of remission.

27.4 The Thase-Rush five-stage model

Staged by class of drug failed. The Thase-Rush five-stage model grades resistance purely by non-response to sequential trials of antidepressants with differing mechanisms, culminating in

electroconvulsive therapy (Tasman 2015). It is the classic, examinable ladder.

STAGE	DEFINITION (CUMULATIVE)
Stage I	Failure of an adequate trial of one antidepressant
Stage II	**Stage I plus failure of a trial of an antidepressant of a different class**
Stage III	Stage II plus failure of a tricyclic antidepressant
Stage IV	Stage III plus failure of a monoamine oxidase inhibitor
Stage V	Stage IV plus failure of a course of electroconvulsive therapy

The Thase-Rush five-stage model, graded by non-response to antidepressants of progressively different mechanism and finally to ECT (Tasman 2015). Its weakness: it assumes a fixed hierarchy of drug classes and does not weigh dose, duration, augmentation or combination.

Its limitation. The Thase-Rush model presumes that a monoamine oxidase inhibitor is intrinsically superior to a tricyclic, and it cannot grade a trial by its dose or duration, nor does it credit augmentation or combination strategies (Tasman 2015). This is why the later staging methods were developed.

27.5 The Maudsley staging method

Multidimensional scoring. The Maudsley staging method (Fekadu et al. 2009) scores resistance across three separate dimensions rather than a single ladder: the *prior treatment* (number of failed antidepressants, plus augmentation and ECT), the *current symptom severity*, and the *duration* of the illness (Tasman 2015; Maudsley 2021). The points sum to a total that places the patient on a mild-to-severe resistance gradient.

Why it is preferred. By incorporating severity and chronicity, and by crediting augmentation and combination, the **maudsley staging** method predicts continuing treatment resistance and longer-term outcome better than the Thase-Rush ladder in inpatient samples (Fekadu et al. 2009; Tasman 2015). The MGH method, for comparison, assigns one point per adequate monotherapy trial of at least 6 weeks, adds 0.5 points for optimising, augmenting or combining, and adds 3 points for ECT (Petersen et al. 2005).

GOOD TO REMEMBER

- **Thase-Rush five-stage model:** grades resistance by failed drug *class* in sequence, ending at ECT (Stage V); ignores dose, duration and augmentation.
- **Maudsley staging method:** scores three dimensions, prior treatment, current symptom severity and duration of illness (Fekadu et al. 2009); better predicts persistence and outcome.
- **MGH staging method:** 1 point per adequate 6-week monotherapy trial, 0.5 for optimise/augment/combine, 3 for ECT (Petersen et al. 2005).
- **The shared message:** resistance is a degree, not a binary; do not be discouraged by one failed trial.

27.6 Before you label it resistant: reconsider the diagnosis

Resistance is often a wrong diagnosis. The first evaluation before calling any depression resistant is to reconsider the diagnosis. The BAP directs a formal diagnostic review, including the possibility of comorbid medical or psychiatric conditions and unrecognised bipolarity, psychosis or atypical features, using screening tools where helpful (BAP 2015). The commonest missed diagnoses are a missed bipolar disorder (the depression is a bipolar depression that will not respond to, and may be worsened by, an antidepressant alone), a missed psychotic depression (which needs an antipsychotic added), and a missed organic or substance cause (hypothyroidism, anaemia, alcohol or substance use) (Tasman 2015; IPS 2017).

And a comorbidity that sustains the depression. A coexisting personality disorder, a chronic medical illness, or an untreated anxiety or substance use disorder can hold a depression down and masquerade as pharmacological resistance. The Indian Psychiatric Society Clinical Practice Guidelines (Gautam et al.) make this explicit: the IPS treatment-resistant depression pathway reassesses the diagnosis to rule out bipolar disorder, substance use and medical contributors before escalating (IPS 2017). Where a finer IPS-specific staging or threshold cannot be confirmed against the guideline rows, it is flagged under gaps rather than invented.

TRAP **Calling a bipolar depression "treatment-resistant" and stacking on antidepressants.** An unrecognised bipolar depression will not respond to an antidepressant alone and can be destabilised by it; screen for bipolarity first.

27.7 Pseudoresistance: adherence, dose and duration

Confirm adherence. Once the diagnosis holds, confirm the patient actually took the drug. Non-adherence, whether from side effects, cost, or belief, is a leading cause of apparent non-response, and a depression that was never adequately dosed in the patient's body cannot be called resistant; the **ips guidelines** and the BAP both make confirming adherence a step before escalation (BAP 2015; IPS 2017). This is the essence of **pseudoresistance**: an apparent treatment resistance that is really an artefact of inadequate treatment.

The three checks that unmask pseudoresistance. Was the *dose* therapeutic? Was the *duration* long enough (at least 4 to 8 weeks at that dose)? Was *adherence* intact? If any answer is no, the depression is not resistant, it is under-treated, and the correct action is to optimise, not to escalate (BAP 2015; CANMAT 2016). A subtherapeutic or non-adherent trial simply does not count toward the two-trial definition.

RULE **Before labelling depression resistant, confirm the dose, the duration, adherence and the diagnosis.** Only then does a failed trial count.

INDIA

Pseudoresistance is disproportionately common in Indian outpatient practice, where largely out-of-pocket payment drives early self-discontinuation once the patient feels a little better or once side effects appear, and where a subtherapeutic dose may have been given to limit cost. Before any escalation, verify that a cheap generic SSRI such as escitalopram (Nexito or S-Citadep) or sertraline (Serta or Daxid) was actually taken at a therapeutic dose for an adequate duration; the commonest "resistant" case is a half-dose, half-taken first trial.

27.8 The STAR-D lessons: remission falls with each step

The landmark effectiveness trial. The STAR-D trial (the Sequenced Treatment Alternatives to Relieve Depression programme, Rush et al. 2006), a large NIH-funded practical trial highly applicable to real-world practice, gave the best available data on what happens across sequential steps (Tasman 2015). Patients who did not remit on the initial citalopram progressed through sequential, randomised steps of switching and augmentation.

Two lessons the examiner rewards. First, about a *third* of patients remit on the first agent: STAR-D reported first-step remission of roughly 28 percent by the Hamilton scale and 33 percent by the QIDS-SR, so lack of remission to a first antidepressant is common rather than exceptional (Tasman 2015). Second, remission rates *decline* with each successive step: the cumulative remission was about 37 percent after one trial, rising to 49 percent after two, but only to 50 percent after three and 51 percent after four (Tasman 2015). The small gains at steps three and four show how an increasingly resistant episode becomes progressively harder to treat.

STAR-D TREATMENT STEP	CUMULATIVE REMISSION (PERCENT)
After step 1 (citalopram)	**37**
After step 2	49
After step 3	50
After step 4	51

STAR-D cumulative remission by treatment step (Rush et al. 2006; Tasman 2015): about a third remit on the first agent, and each further step yields diminishing returns. Patients who need more steps to remit also relapse at a higher rate.

What STAR-D informs. These figures underpin the whole switch-versus-augment logic: because a first agent so often fails, a planned sequence of next steps is essential, and because returns diminish, staging and diagnostic review matter more with each failed step. STAR-D also showed that switching within class was no different in outcome from switching to another class (CANMAT 2016), and that patients needing more steps to remit relapse at a higher rate (Tasman 2015). The augmentation ladder that operationalises these next steps is the next topic.

TRAP **Reading STAR-D as evidence that antidepressants do not work.** A third remit on the first drug and roughly half by the second; the lesson is diminishing returns and the need for a planned sequence, not futility.

27.9 The pre-escalation checklist and where the ladder begins

The work-up before escalation, in order. Put the topic together as the checklist the examiner wants before any next-step drug: (1) reconsider the diagnosis, screening for missed bipolarity, psychosis, an organic or substance cause, and a medical or personality comorbidity; (2) confirm adherence; (3) confirm the dose was therapeutic; (4) confirm the duration was adequate (4 to 8 weeks); and only then (5) stage the resistance and move to the next-step algorithm (BAP 2015; IPS 2017; CANMAT 2016).

Then the ladder. Once genuine resistance is confirmed, the options are to switch antidepressant, augment or combine, or move to neurostimulation. At guideline level the first-line augmentation agents are aripiprazole or brexpiprazole (CANMAT 2016), with quetiapine, aripiprazole or lithium as the BAP first-line augmentation choices (BAP 2015); lithium augmentation has the best evidence in older people (BAP 2015). Electroconvulsive therapy is reserved for those who have not responded to other treatments (BAP 2015). The detail of that ladder, and the ECT and neurostimulation technique, belong to the next topic and to the ECT and neurostimulation notes.

HOLD THIS

Treatment-resistant depression is failure of two adequate antidepressant trials in the current episode, but most apparent resistance is pseudoresistance or a missed bipolar depression, so confirm dose, duration, adherence and diagnosis before you ever escalate.

MNEMONIC

DADD before you ESCALATE

Diagnosis (reconsider, screen for bipolarity), **A**dherence (confirm it), **D**ose (therapeutic?), **D**uration (4 to 8 weeks?). Only when all four are cleared do you stage the resistance and climb the augmentation ladder.

GOOD TO REMEMBER

- **Definition:** treatment-resistant depression is failure of at least two adequate antidepressant trials (adequate dose and duration) in the current episode; no single agreed definition exists.
- **Pseudoresistance:** most apparent resistance is a subtherapeutic dose, an inadequate duration, poor adherence or a wrong diagnosis; exclude it, and exclude missed bipolarity, first.
- **Staging:** Thase-Rush grades by failed drug class to ECT; the Maudsley staging method scores prior treatment, current severity and illness duration and predicts outcome better.
- **STAR-D:** about a third remit on the first agent (28 percent HAM-D, 33 percent QIDS-SR); cumulative remission is roughly 37, 49, 50, 51 percent across steps 1 to 4, so returns diminish.

28 . Augmentation and combination strategies

When an antidepressant has been pushed to an adequate dose for an adequate duration and the depression has still not remitted, the clinician has three moves: **switch** the antidepressant, **augment** it with a second agent of a different pharmacology, or **combine** it with a second antidepressant. This topic teaches how to choose between those moves and, once augmentation is chosen, which agent to add and in what order of evidence. It follows directly from the treatment-

resistant depression topic, which carries the definition, the staging and the pre-escalation work-up; here we climb the ladder itself. It is high-yield because the board tests a discipline, not a drug list: the examiner wants to see that you **augment a partial response** and **switch a non-response**, and that you reach for a proven **augmentation** agent rather than stacking antidepressants irrationally.

The organising principle, repeated across CANMAT (2016), the BAP (2015) and NICE (2014), is that **augmentation** and **combination** are for genuine, confirmed treatment resistance in which the diagnosis, dose, duration and adherence have already been checked. Of the augmentation options, **lithium augmentation** and the atypical antipsychotics carry the strongest and most modern evidence; **thyroid** augmentation with T3 is a real but second-line option; and combining two antidepressants is reserved, evidence-selective and never started from the outset.

28.1 The decision: switch versus augment versus combine

The response guides the move. The single decision that organises the whole ladder is the degree of response to the current antidepressant. If there has been *no* response at all, or the drug is intolerable, **switch** to another agent, because there is nothing to build on and no reason to expose the patient to a second drug. If there has been a *partial* response but not remission, and the current drug is well tolerated, **augment** or combine, because you keep a partly effective treatment and add to it (BAP 2015; CANMAT 2016). The BAP states it directly: consider a second agent for augmentation when there is partial or insufficient response with good tolerability of the current antidepressant, or after an unsuccessful switch (BAP 2015).

Switching first, then building. A rational sequence after one adequate failure is to switch to another first-line agent; switching within class is no different in outcome from switching to another class (CANMAT 2016). After more than one failure within a class, move to a different class (BAP 2015). Only once a partial response emerges, or once switching has been exhausted, does augmentation become the preferred next step.

RULE **Augment a partial response; switch a non-response.** Build on a partly effective, tolerated drug; abandon one that did nothing or cannot be tolerated.

TRAP **Stacking antidepressants irrationally instead of a proven augmentation.** Two antidepressants at the outset is not supported; a proven augmenter (lithium or an atypical) has far better evidence.

28.2 The guideline map of augmentation, at a glance

What the guidelines actually recommend. The lead guideline for this note is CANMAT: for an inadequate antidepressant response, add a first-line adjunct of aripiprazole 2 to 15 mg/day, quetiapine 150 to 300 mg/day, risperidone 1 to 3 mg/day, or brexpiprazole 1 to 3 mg/day; add lithium or triiodothyronine (T3) as a second-line adjunct with drug-level or thyroid monitoring (CANMAT 2016). The BAP ranks the same agents: add quetiapine, aripiprazole or lithium as first-line augmentation, and risperidone, olanzapine, triiodothyronine or mirtazapine as second-line (BAP 2015). NICE, where a combination of medications is chosen, positions adding a

second-generation antipsychotic (aripiprazole, olanzapine, quetiapine or risperidone) or lithium to the antidepressant, in or with advice from a specialist mental health setting (NICE 2022). The Maudsley collapses this to a headline: either lithium or quetiapine is the agent of first choice for augmenting the existing antidepressant (Maudsley 2021).

The Indian position. The Indian Psychiatric Society Clinical Practice Guidelines for depression (Gautam et al.) place augmentation within the treatment-resistant pathway, listing lithium augmentation among the recognised strategies alongside atypical antipsychotic and thyroid augmentation after two adequate trials have failed (IPS 2017). Where a precise IPS-specific ordering of augmenting agents cannot be confirmed against the guideline rows, it is flagged under gaps rather than invented; the IPS guidelines endorse augmentation as a strategy but the exact agent hierarchy is stated less rigidly than in CANMAT.

AUGMENTING AGENT	LINE / EVIDENCE	DOSE (PER DAY)	SIGNATURE CAVEAT
Lithium	First-line; strong, classic evidence; anti-suicidal	to level 0.6 to 1.0 mmol/L	Narrow window; renal, thyroid, level monitoring
Aripiprazole	First-line adjunct (CANMAT); VAST-D positive	2 to 15 mg	Akathisia, some weight gain
Quetiapine	First-line adjunct; agent of first choice (Maudsley)	150 to 300 mg	Sedation, metabolic, QTc
Brexpiprazole	First-line adjunct (CANMAT)	1 to 3 mg	Akathisia, weight gain
Risperidone	First-line adjunct (CANMAT); second-line (BAP)	1 to 3 mg	Prolactin, EPS, metabolic
Olanzapine	Second-line adjunct	2.5 to 10 mg	Highest metabolic burden
Triiodothyronine (T3)	Second-line; older evidence, well tolerated	25 to 50 mcg	Rare thyrotoxic symptoms above 25 mcg; TSH monitoring
Mirtazapine / mianserin	Second-line adjunct antidepressant	30 to 60 mg	A combination, not a true augmentation
Esketamine (intranasal)	Add to SSRI/SNRI after two failed trials	per protocol	Dissociation, blood-pressure rise; supervised dosing

Augmentation agents ranked by guideline evidence for inadequate antidepressant response (CANMAT 2016; BAP 2015; NICE 2022; Maudsley 2021). Lithium and the atypical antipsychotics carry the best modern evidence; T3 is a genuine second-line option. Doses in the header, bare figures in the cells.

28.3 Lithium augmentation: the classic, with anti-suicidal value

The evidence base. **Lithium augmentation** is the oldest and one of the best-evidenced augmentation strategies. Recent meta-analyses show robust efficacy for lithium alongside

quetiapine and the D2 partial agonists, and one meta-analysis found lithium to be the most effective augmenter (Maudsley 2021). The classic evidence derives from older RCTs combining lithium with tricyclics, which is why CANMAT positions it as a second-line adjunct even though it works (CANMAT 2016). It remains widely underused in resistant depression.

Dose to a plasma level, not a milligram target. Lithium augmentation is most effective at a lithium plasma level of **0.6 to 1.0 mmol/L** (Maudsley 2021); the CANMAT adjunctive dose range is **600 to 1200 mg/day** titrated to that therapeutic serum level (CANMAT 2016). As with any lithium prescription, check renal and thyroid function before starting and monitor the level, taking the sample 12 hours post-dose. In India the common carbonate brands are Licab and Intalith; the deeper lithium mechanism, pharmacokinetics and monitoring are carried in the lithium notes of this block.

The anti-suicidal signal. The feature that distinguishes lithium from every other augmenter is its specific effect on suicide. A meta-analysis of clinical trials concluded that lithium reduced the risk of both attempted and completed suicide by about 80 percent in patients with mood disorders, both unipolar and bipolar (Cipriani et al. 2013, BMJ), and the protective effect holds in unipolar depression, though the mechanism is unknown (Maudsley 2021). Clinical predictors of a good augmentation response include more severe depression, psychomotor retardation, weight loss, a family history of major depression, or more than three prior episodes (Maudsley 2021). The full suicide risk assessment and safety planning sit in the Somatic-symptom, sexual, impulse-control disorders and suicide notes.

0.6 to 1.0	600 to 1200	80
LITHIUM AUGMENTATION LEVEL (MMOL/L)	CANMAT ADJUNCTIVE LITHIUM (MG/DAY)	PERCENT LITHIUM SUICIDE-RISK REDUCTION (BIPOLAR)

GOOD TO REMEMBER

- **Lithium augmentation:** add lithium to a partially responding antidepressant; the classic, strong-evidence augmenter, dosed to a plasma level of **0.6 to 1.0 mmol/L** (Maudsley 2021).
- **Signature value:** specific anti-suicidal effect, reducing attempted and completed suicide by about 80 percent in mood disorders, unipolar and bipolar (Cipriani et al. 2013).
- **The one to hold:** check renal and thyroid function before starting; monitor the level 12 hours post-dose. Indian brand Licab or Intalith (lithium carbonate).

28.4 Atypical augmentation: the best modern evidence

The strongest recent evidence. Atypical augmentation, adding a second-generation antipsychotic to an antidepressant, has the best modern evidence base of all the augmentation strategies and is the first-line adjunct in CANMAT (CANMAT 2016). Aripiprazole (Indian brand Arip or Asprito), quetiapine (Qutipin), brexpiprazole, risperidone (Sizodon or Risdone) and olanzapine (Oleanz) are the examinable agents; the D2 partial agonists aripiprazole and brexpiprazole are used at lower doses than in bipolar disorder or schizophrenia because their tolerability at these doses is favourable (CANMAT 2016).

The head-to-head data. Aripiprazole augmentation of an SSRI or venlafaxine is more effective than adding placebo, which won it FDA approval as an adjunct; in the 1,500-patient VAST-D trial aripiprazole augmentation achieved remission somewhat more often than switching to bupropion or augmenting with bupropion (Kaplan and Sadock 2024). Adding quetiapine **150 to 300 mg/day** to a standard antidepressant improved response in registration trials (Kaplan and Sadock 2024), and the Maudsley names quetiapine as an agent of first choice for augmentation (Maudsley 2021). The trade-off is the antipsychotic side-effect burden: akathisia and some weight gain with the partial agonists, sedation and metabolic effects with quetiapine, and the highest metabolic risk with olanzapine, which is why olanzapine is downgraded to second-line (CANMAT 2016).

WORKED EXAMPLE

A patient on escitalopram 20 mg (Nexito or S-Citadep) for eight weeks is 40 percent better but not remitted, and tolerates the drug well. This is a partial response to a tolerated drug: augment rather than switch. A reasonable first-line adjunct is aripiprazole 2 to 5 mg titrated to 10 mg, or quetiapine 150 mg titrated toward 300 mg, warning the patient about akathisia (aripiprazole) or sedation and weight (quetiapine), and monitoring metabolic parameters.

GOOD TO REMEMBER

- **Aripiprazole:** D2/5-HT1A partial agonist; first-line adjunct at **2 to 15 mg/day**; VAST-D beat switching to or augmenting with bupropion; signature effect akathisia (Kaplan and Sadock 2024). Indian brand Arip or Asprito.
- **Quetiapine:** broad antagonist with noradrenergic (norquetiapine) action; first-line adjunct at **150 to 300 mg/day**; the Maudsley agent of first choice; signature effect sedation and metabolic gain (Maudsley 2021). Indian brand Qutipin.
- **Brexpiprazole:** D2 partial agonist, chemically related to aripiprazole; first-line adjunct at **1 to 3 mg/day** (CANMAT 2016; NICE 2014); signature effect akathisia and weight gain.
- **Risperidone / olanzapine:** risperidone **1 to 3 mg/day** (prolactin, EPS); olanzapine **2.5 to 10 mg/day** is second-line, downgraded for the highest metabolic burden. Indian brands Sizodon/Risdone and Oleanz.

28.5 Thyroid augmentation with T3 (liothyronine)

The strategy. **Thyroid** augmentation adds triiodothyronine (T3), the synthetic form liothyronine, to an antidepressant in a nonresponder. It is the most widely studied thyroid strategy for depression; T4 (levothyroxine) has far fewer supporting data in refractory depression and is chiefly reserved as a mood-stabiliser adjunct in rapid-cycling bipolar disorder (Kaplan and Sadock 2024). CANMAT and the BAP both list T3 as a second-line adjunct with thyroid-level monitoring (CANMAT 2016; BAP 2015).

Evidence and dose. Open and controlled studies show that roughly 50 to 60 percent of tricyclic nonresponders respond within 2 to 3 weeks of adding T3, and patients augmented with T3 were about twice as likely to respond as controls (Kaplan and Sadock 2024). In the STAR*D trial, T3 augmentation had remission rates comparable to other augmentation options with a more favourable adverse-event and dropout profile (Kaplan and Sadock 2024). T3 is given as a single

morning dose of **25 to 50 mcg** to avoid insomnia; 25 mcg/day is below the replacement dose so thyrotoxic symptoms are rare, but 50 mcg/day approaches the daily production range and can cause thyroid excess, so doses above 25 mcg are used with caution and TSH is monitored. In responders, taper and stop by 12 weeks; avoid in pregnancy (Kaplan and Sadock 2024).

INDIA

Triiodothyronine (liothyronine) is not freely available in India and is used only occasionally (KDT 2019), so T3 augmentation is a more theoretical than practical option on the ground here; levothyroxine is the freely available thyroid preparation. Know T3 as an examinable second-line augmenter but recognise the supply constraint in Indian practice.

GOOD TO REMEMBER

- **Thyroid (T3, liothyronine):** thyroid hormone receptor agonist added as a second-line augmenter; single morning dose **25 to 50 mcg/day**; about 50 to 60 percent of tricyclic nonresponders respond within 2 to 3 weeks (Kaplan and Sadock 2024).
- **Signature caveat:** 25 mcg is subreplacement and safe; above 25 mcg can cause thyrotoxic symptoms, so monitor TSH and cap short courses; taper and stop by 12 weeks; avoid in pregnancy.
- **India:** liothyronine is not freely available in India; levothyroxine is. T3 is the option to name, not usually the one to reach for locally.

28.6 Combination antidepressant strategies and the polypharmacy caution

What a combination is. A **combination** strategy adds a second antidepressant with a complementary mechanism to the first, most classically an SSRI or SNRI plus mirtazapine (Indian brand Mirtaz), or plus bupropion (Bupron). CANMAT rates adding mirtazapine or mianserin 30 to 60 mg/day as a second-line adjunct and notes this combination is superior to other antidepressant combinations (CANMAT 2016). The rationale is pharmacological: mirtazapine's alpha-2 and 5-HT2/5-HT3 antagonism complements the reuptake block of an SSRI or SNRI, and bupropion's noradrenaline-dopamine action adds a different mechanism.

The evidence is modest and never from the outset. The discipline the board tests is that two antidepressants are never combined at the initiation of treatment (CANMAT 2016). The CO-MED trial found no benefit from starting escitalopram plus bupropion, or venlafaxine plus mirtazapine, over monotherapy from the outset (Kaplan and Sadock 2024). Even as a later strategy the yields are small: in STAR*D the venlafaxine plus mirtazapine combination achieved remission in only about 10 percent, no better statistically than the MAOI tranylcypromine though far better tolerated, and bupropion or buspirone augmentation of citalopram each remitted about 30 percent (Kaplan and Sadock 2024). This is the case against irrational polypharmacy: stacking antidepressants adds interaction and adverse-effect risk for a small, evidence-thin gain, whereas a proven augmenter does better.

COMMON TRAP

Adding a second, then a third antidepressant from different classes and calling it a "combination" when there was never a partial response to build on. This is irrational polypharmacy, not augmentation: it multiplies serotonergic load (raising serotonin syndrome risk, especially near an MAOI, covered in the Perinatal/women's mental health and emergency psychiatry notes) for a remission gain of around 10 percent (Kaplan and Sadock 2024). Use a proven augmenter instead.

GOOD TO REMEMBER

- **Mirtazapine combination:** alpha-2 and 5-HT2/5-HT3 antagonist added to an SSRI/SNRI at **30 to 60 mg/day**; superior to other antidepressant combinations (CANMAT 2016); STAR*D venlafaxine plus mirtazapine remitted only about 10 percent. Indian brand Mirtaz.
- **Bupropion combination:** noradrenaline-dopamine reuptake inhibitor added for a complementary mechanism; STAR*D bupropion augmentation of citalopram remitted about 30 percent (Kaplan and Sadock 2024). Indian brand Bupron.
- **The hold:** never combine two antidepressants at the outset (CO-MED negative); combination is a later, evidence-selective move, weaker than lithium or atypical augmentation.

28.7 When to move to esketamine or ECT

Esketamine and ketamine. For depression that has failed at least two adequate antidepressant trials, intranasal esketamine (Indian brand Spravato) is added to an ongoing SSRI or SNRI, monitoring blood pressure and for dissociative effects (CANMAT 2023). Intravenous racemic ketamine is a second-line adjunct for a rapid antidepressant effect, including rapid reduction of suicidal ideation, again with blood-pressure and dissociation monitoring; both act at the NMDA receptor and work within hours rather than weeks, which is their signature advantage over conventional augmenters. Non-esketamine racemic ketamine given orally, intramuscularly or intranasally is third-line given variable protocols (CANMAT 2023). The deeper esketamine and ketamine pharmacology is carried in its own fragment; here it is the escalation pointer.

ECT. When augmentation and combination have not delivered remission, or where the depression is severe, psychotic, or carries acute suicide risk, electroconvulsive therapy is the next step and remains the most effective acute treatment for severe depression (BAP 2015); the technique sits in the ECT and neurostimulation notes. The escalation logic is that the ladder runs optimise, switch, augment or combine, then esketamine or ECT, matched to the severity, the degree of resistance and the urgency.

PEARL

Two features push you past the augmentation ladder straight toward esketamine or ECT: *urgency* (acute suicide risk, food and fluid refusal, psychotic or catatonic depression) and *rapidity of effect needed*. Conventional augmenters take 2 to 6 weeks; ECT and ketamine/esketamine act far faster, which is precisely why they earn their place when time is the constraint.

GOOD TO REMEMBER

- **Esketamine (intranasal):** NMDA-receptor antagonist added to an SSRI/SNRI after at least two failed antidepressant trials; monitor blood pressure and dissociation (CANMAT 2023). Indian brand Spravato.
- **Ketamine (IV racemic):** second-line adjunct for rapid effect and rapid reduction of suicidal ideation; acts within hours; monitor blood pressure and dissociation.
- **ECT:** the step when augmentation and combination fail or when severity or suicide risk demands the fastest, most effective acute treatment (BAP 2015); technique in the ECT and neurostimulation notes.

HOLD THIS

Augment a partial response and switch a non-response: lithium (to a level of 0.6 to 1.0 mmol/L, and anti-suicidal) and the atypical antipsychotics have the best augmentation evidence, T3 is a second-line option, and two antidepressants are never combined from the outset.

29 . Depression in the elderly

Depression in later life is a high-frequency examinable topic because it looks different from depression in the young, it is dangerous (older men carry the highest completed-suicide rate of any group), and it is under-treated precisely when it is most treatable. **Depression in the elderly** (depression in the elderly, also termed geriatric depression) is tested as a triad: recognise the atypical presentation, exclude the organic mimic, and prescribe with geriatric caution. This fragment teaches the presentation and the assessment, then the pharmacology caveats that make prescribing in the old a different discipline from prescribing in the young (Kaplan & Sadock 2024; Maudsley 2021).

The organising phrase to hold is **start low and go slow**, but the trap it breeds is under-dosing to remission-failure, so the counter-phrase is equally examinable: reach an adequate dose despite starting low. Every dose, serum figure and monitoring interval below is verified against the CANMAT guideline rows, the Maudsley and the parsed textbooks; the wider frailty and cognitive workup cross-refers to the Consultation-liaison, geriatric and transcultural psychiatry notes (CANMAT 2016; Maudsley 2021).

29.1 The presentation: somatic and cognitive, not classically sad

More somatic and cognitive complaints. The older depressed patient frequently does not say they are sad. **Geriatric depression** presents disproportionately with somatic and cognitive complaints: bodily preoccupation, pain, fatigue, weight loss, sleep disturbance, agitation, and a subjective sense of memory failure, often with the affective core masked or denied (Kaplan & Sadock 2024; Shorter Oxford 2018). Anhedonia, psychomotor retardation and loss of drive are common, guilt is often absent, and the picture can be dominated by anxiety or by hypochondriacal fixation rather than low mood.

Why this matters. Because the mood complaint is muted and the somatic and cognitive complaints are loud, **late-life** depression is repeatedly misattributed to physical illness, to normal ageing, or to early dementia, and left untreated. Screening therefore has to be active, not reactive.

RULE **In the old, look for depression behind somatic and cognitive complaints, not behind a complaint of sadness.** The affective core is often masked or denied.

29.2 Pseudodementia: the depression-related cognitive impairment

The cognitive syndrome that mimics dementia. Depression in the old can produce cognitive impairment severe enough that the patient is misclassified as demented, historically termed pseudodementia (depressive pseudodementia), better called depression-related cognitive impairment. This is the most common potentially reversible cause of an apparent dementia, and missing it is catastrophic because a treatable, potentially fatal illness is passed off as an untreatable one (Companion 2010; Tasman 2015).

Discriminating it from true dementia. The examinable discriminators favour depression: a relatively abrupt, datable onset with the patient complaining loudly of memory loss, giving "don't know" answers, showing poor effort but preserved cued recall and orientation, and a personal or family history of mood disorder. True degenerative dementia is insidious, the patient conceals or is unaware of deficits, confabulates or near-misses rather than saying "don't know", and cued recall does not rescue performance (Companion 2010; Kaplan & Sadock 2024).

FEATURE	DEPRESSIVE PSEUDODEMENTIA	DEGENERATIVE DEMENTIA
Onset	**Relatively abrupt, datable**	Insidious, undatable
Complaint of memory loss	**Emphasised by patient**	Concealed or unaware
Typical answer	"Don't know", gives up	Near-miss or confabulation
Cued recall	Improves with cueing	Does not improve
Effort	Poor effort, distressed	Effortful, unconcerned
Mood history	Personal or family mood disorder	Usually absent

The classic discriminators between depression-related cognitive impairment and a degenerative dementia (Companion 2010; Kaplan & Sadock 2024). The picture can overlap, and depression can coexist with or herald a true dementia, so a therapeutic antidepressant trial and follow-up cognition are part of the workup.

TRAP **Writing off a reversible depressive pseudodementia as an untreatable dementia.** It is the commonest reversible cause of apparent dementia; treat the depression and reassess cognition.

29.3 The vascular depression concept

Cerebrovascular disease drives some late-onset depression. The vascular depression hypothesis (Alexopoulos 1997) holds that cerebrovascular disease predisposes to, precipitates or perpetuates some **late-life** depressive syndromes. It rests on the high comorbidity of depression with vascular risk factors, the excess of depression after stroke, and the burden of deep white-matter hyperintensities on MRI in late-onset depression (Kaplan & Sadock 2024).

The recognisable phenotype. Vascular depression tends to present with psychomotor retardation, anhedonia, prominent executive dysfunction, poor insight into the illness and disability, and relatively less guilt, on a background of hypertension and other vascular risk.

White-matter and microstructural disconnection of frontostriatal circuits predicts a poorer and slower response to antidepressants, which is one reason late-life depression is given a longer time to respond (Kaplan & Sadock 2024; Maudsley 2021).

PEARL

Late-onset first-ever depression in an older patient with vascular risk factors, executive slowing and white-matter change on imaging is the vascular-depression picture: expect a slower antidepressant response, treat the vascular risk factors alongside the mood, and do not mistake the executive slowing for early dementia.

29.4 The higher suicide risk in older men

The lethal edge of the topic. Completed suicide rates rise with age and are highest in older men, who use more lethal methods, give fewer warnings, are more often socially isolated and bereaved, and whose depression is more likely to be missed. An older man presenting with depression, physical illness, recent loss and alcohol use is a high-lethality combination that mandates explicit risk assessment at the first contact (Kaplan & Sadock 2024). The full structured suicide risk assessment and safety planning belong to the Somatic-symptom, sexual, impulse-control disorders and suicide notes.

RULE **Ask every depressed older patient, and especially every older man, directly about suicide.** Older men have the highest completed-suicide rate and give the fewest warnings.

29.5 Assessment: screen, exclude an organic cause and drugs, test cognition

Screen. Use a structured instrument because the presentation is atypical: the Geriatric Depression Scale (self-report, yes or no, tolerated by the frail elderly) is the standard screen, with the PHQ-9 or a HAM-D also acceptable; whatever is chosen, repeat it to track response (measurement-based care).

Exclude an organic cause and drugs. Before attributing the picture to primary depression, exclude the medical and iatrogenic mimics that are common in the old. Screen and treat comorbid hypothyroidism and B12 or folate deficiency, look for occult malignancy, anaemia, renal or hepatic failure, Parkinson's disease, and covert cerebrovascular or neurodegenerative disease. Review the drug chart for depressogenic agents (corticosteroids, beta-blockers, some centrally acting antihypertensives, opioids, interferon) and for the anticholinergic and sedative burden that itself impairs cognition and mood.

Test cognition. Perform bedside cognitive testing (for example the MMSE or MoCA) to characterise the deficit, to establish a baseline before starting a drug, and to separate depression-related impairment from an evolving dementia over follow-up. The wider frailty, functional, falls-risk and comprehensive geriatric assessment frame is the Consultation-liaison, geriatric and transcultural psychiatry notes.

29.6 The drug caveats: start low and go slow, prefer an SSRI

The prescribing frame. Ageing changes pharmacokinetics (reduced renal and hepatic clearance, altered volume of distribution, longer half-lives) and pharmacodynamics (greater receptor sensitivity), and the old are on more concurrent drugs, so the **drug caveats** in the elderly all follow from one principle: **start low** and go slow (Maudsley 2021; CANMAT 2016). Begin at about half the usual adult starting dose (for example escitalopram **5 mg/day**, sertraline **25 mg/day**) and titrate slowly, watching tolerability at each step.

Prefer an SSRI. The first-line agent in the old is a well-tolerated SSRI, and the two workhorses are sertraline (Serta or Daxid) and escitalopram (Nexito or S-Citadep), chosen for a clean interaction profile, low anticholinergic load and cardiac safety (CANMAT 2016; Maudsley 2021). The specific geriatric hazards to manage are hyponatraemia, falls, the anticholinergic burden, drug interactions and the citalopram and escitalopram QTc cap.

CAVEAT IN THE ELDERLY	WHAT TO DO	WHY
Start low, go slow	Half the adult start (escitalopram 5, sertraline 25), titrate slowly	Reduced clearance, greater sensitivity, polypharmacy
Prefer an SSRI	Sertraline or escitalopram first-line	Clean interactions, low anticholinergic load, cardiac safety
Hyponatraemia (SIADH)	Check sodium at baseline and 2 to 4 weeks; recheck if drowsy, confused or falling	SSRIs cause SIADH; risk highest in the old, in women, on diuretics
Falls	Review at each visit; minimise sedatives and orthostatic-load drugs	Antidepressants raise fall and fracture risk in the old
Anticholinergic burden	Prefer low-anticholinergic agents; avoid the TCAs	Cumulative anticholinergic load worsens cognition and delirium
Drug interactions	Prefer escitalopram or sertraline over fluoxetine, paroxetine, fluvoxamine	The clean SSRIs are weak CYP inhibitors; the others are potent
Citalopram and escitalopram QTc cap	Citalopram maximum 20, escitalopram maximum 10, in the elderly	Dose-related QTc prolongation; caps are lower in over-65s
Avoid the TCAs	Not first-line; use only where unavoidable	Anticholinergic, orthostatic hypotension, cardiotoxic, lethal in overdose

The verified geriatric drug caveats (Maudsley 2021; CANMAT 2016). The three highlighted rows are the highest-yield: start low and go slow, watch hyponatraemia, and respect the citalopram and escitalopram QTc dose caps in the elderly.

The citalopram and escitalopram QTc cap. Citalopram and escitalopram cause a dose-related QTc prolongation and are the most cardiotoxic of the SSRIs (albeit modestly so), which is why the licensed maximum is reduced in the old: in the elderly, citalopram is capped at **20 mg/day** and escitalopram at **10 mg/day** (Maudsley 2021). Where QTc is a concern, sertraline is the cleaner cardiac choice.

TRAP **Titrating citalopram or escitalopram past the reduced elderly ceiling, or missing an SSRI-induced hyponatraemia.** Respect the QTc caps and check sodium at baseline and 2 to 4 weeks.

5	20	10
ESCITALOPRAM START IN ELDERLY (MG/DAY)	CITALOPRAM ELDERLY MAX (MG/DAY)	ESCITALOPRAM ELDERLY MAX (MG/DAY)

INDIA

In Indian practice the outpatient workhorses are the cheap generic SSRIs, led by sertraline (Serta or Daxid) and escitalopram (Nexito or S-Citadep), which suits a largely out-of-pocket, medically complex elderly population. The TCAs (amitriptyline as Tryptomer, imipramine as Depsonil) remain cheap and available and are still reached for, but their anticholinergic, orthostatic and cardiotoxic load makes them a poor first choice in the old; keep them off first line and prefer the clean SSRI.

29.7 Treatment: adequate dose despite starting low, and a longer wait

Reach an adequate dose. Starting low does not mean staying low. The commonest management error in the old is to under-dose out of caution and leave the patient at a homeopathic, sub-therapeutic dose that never reaches remission. Titrate up to a full adequate antidepressant dose as tolerated (for example sertraline toward **50 to 200 mg/day**, escitalopram toward the elderly ceiling of **10 mg/day**), and judge the trial only once an adequate dose has been given for an adequate time (CANMAT 2016; BAP 2015).

Allow a longer time to respond. In older people the antidepressant response may take longer, so allow more time before declaring failure, and continue treatment after remission because continued antidepressant treatment roughly halves the relapse rate (BAP 2015). For treatment resistance in the old, lithium augmentation has the best evidence, with about half of patients responding to a switch or augmentation (BAP 2015); the deep next-step ladder is the treatment-resistance topic.

The guideline position. At guideline level, CANMAT and the SSRI-first frame apply to the old as to the young, individualised to the patient with a lower start, and the **Indian Psychiatric Society** Clinical Practice Guidelines likewise place the SSRIs first-line for late-life depression with a reduced starting dose and slow titration (CANMAT 2016; IPS 2018). Beyond this SSRI-first-with-caution position, a finer elderly-specific IPS dose could not be confirmed from the parsed source and is flagged rather than invented.

RULE **Start low and go slow, but still reach an adequate dose in the elderly.** Judge the trial only at a full dose given for an adequate (and, in the old, longer) time.

29.8 ECT: a good response in severe or psychotic late-life depression

ECT works well in the old. Severe, psychotic, food-and-fluid-refusing or actively suicidal late-life depression responds well to electroconvulsive therapy, and age is not a contraindication; the elderly, particularly those with psychotic depression, are among the best responders to ECT

(Kaplan & Sadock 2024). It is the treatment of choice where a rapid, definitive response is needed, where the patient is not eating or drinking, or where drug options are exhausted or poorly tolerated. The technique, the anaesthetic considerations and the cognitive-side-effect management belong to the ECT and neurostimulation notes.

GOOD TO REMEMBER

- **Presentation:** somatic and cognitive complaints with the affective core masked; screen actively.
- **Pseudodementia:** depression-related cognitive impairment is the commonest reversible cause of apparent dementia; abrupt onset, "don't know" answers, cued recall improves; treat and reassess.
- **Vascular depression:** late-onset, executive slowing, vascular risk, white-matter change; slower antidepressant response.
- **Suicide:** highest completed-suicide rate is in older men; ask directly at first contact.
- **Sertraline (Serta or Daxid):** SSRI, clean and cardiac-safe, first-line in the old; start **25 mg/day**, target **50 to 200 mg/day**.
- **Escitalopram (Nexito or S-Citadep):** SSRI, clean, dose-related QTc; start **5 mg/day**, elderly maximum **10 mg/day**.
- **Citalopram:** SSRI, dose-related QTc; elderly maximum **20 mg/day**.
- **Drug caveats:** start low and go slow, prefer an SSRI, watch hyponatraemia and falls, mind the anticholinergic burden and interactions, respect the QTc caps, avoid the TCAs.
- **ECT:** a good response in severe or psychotic late-life depression; age is not a contraindication.

MNEMONIC

SAD-SAFE

The elderly prescribing caveats: **S**tart low, **A**dequate dose still reached, **D**rug interactions minimised; **S**odium (hyponatraemia) watched, **A**nticholinergic burden avoided (no TCAs), **F**alls guarded against, **E**CG-aware QTc caps on citalopram and escitalopram.

HOLD THIS

In late-life depression, start low and go slow with a clean SSRI (sertraline or escitalopram) but still reach an adequate dose over a longer trial, watching hyponatraemia, falls, anticholinergic burden and the elderly QTc caps of citalopram 20 mg and escitalopram 10 mg, and remember ECT works well in severe or psychotic late-life depression.

30 . Suicide risk in mood disorders: the pharmacological angle

Why this closes the mood block. Mood disorders carry the highest **suicide risk** in psychiatry, and the drugs a resident chooses either lower that risk, do nothing, or add a lethal means to a suicidal patient's cupboard. This note teaches only the **mood-specific** risk picture and the **pharmacological** angle: which agent has genuine anti-suicidal evidence, which drug not to hand over in bulk, and what to counsel and monitor at the start of treatment. The full clinical **suicide risk** assessment, the stratification interview and the safety-planning method are taught separately in the Somatic-symptom, sexual, impulse-control disorders and suicide notes; the acute serotonin-syndrome and NMS frame sits in the Perinatal/women's mental health and emergency psychiatry notes.

Exam framing is blunt: examiners want the one psychotropic with the strongest mortality evidence (lithium), the psychotic-overlap agent (clozapine), the early-treatment activation caveat, and the overdose-safety principle (never a large tricyclic antidepressant supply to a suicidal patient). Get those four and you have the topic.

30.1 The burden: where the risk concentrates

Highest risk in psychiatry. Lifetime suicide in bipolar disorder is estimated at around 15 percent, among the highest of any psychiatric condition (Maudsley 2021). The risk is not spread evenly across the illness course: it clusters in **severe depression**, in **mixed states**, in the **depressive phase** of bipolar illness, in the **early bipolar illness** (the first years after diagnosis, the first decade), and in the **early recovery phase** as psychomotor retardation lifts before mood and hopelessness do. Recurrent unipolar depression carries a substantial risk too. The mood-specific message: a mixed, agitated or early-course presentation is a higher-risk presentation.

~15	mixed / depressive	first years
LIFETIME SUICIDE IN BIPOLAR (PERCENT)	HIGHEST-RISK MOOD PHASES	EARLY ILLNESS, HIGHEST RISK WINDOW

RULE **Phase drives risk.** Severe depression, mixed states, early bipolar illness and the early recovery phase are the danger windows, screen and act hardest there.

30.2 Lithium: the anti-suicidal drug

The strongest evidence of any psychotropic. The **lithium anti-suicidal** effect is the single most important pharmacological fact in this topic. A meta-analysis of randomised trials concluded that lithium reduced the risk of both attempted and completed suicide by roughly 80 percent in patients with mood disorders, and lithium-treated patients are less likely to complete suicide than patients on other mood stabilisers (Cipriani 2005, Maudsley 2021). This is an effect on suicide and on **all-cause mortality**, not merely on mood-episode counts, and it holds in bipolar illness and appears to protect in unipolar depression too (mechanism unknown). Even naturally occurring lithium in drinking water is inversely related to population suicide rates. No antidepressant, anticonvulsant or antipsychotic has evidence of this strength for reducing suicide in mood disorders.

The clinical consequence. The anti-suicidal effect is a positive reason to weigh lithium in a high-risk bipolar or recurrent depressive patient, over an anticonvulsant stabiliser that lacks the mortality evidence. It runs partly independent of mood-episode prevention, so a patient at high suicide risk gains from lithium even where another agent might control episodes. Note the plasma targets from the mood-stabiliser topic: minimum effective prophylaxis around **0.4 mmol/L**, optimal prophylaxis **0.6 to 0.8 mmol/L**, and the CANMAT maintenance range **0.6 to 1.0 mEq/L** (Maudsley 2021, CANMAT 2018). Full initiation, monitoring and toxicity are taught in the lithium notes; here the point is the anti-suicidal indication.

~80	0.6 to 0.8	0.6 to 1.0
SUICIDE RISK REDUCTION ON LITHIUM (PERCENT)	OPTIMAL PROPHYLAXIS LITHIUM (MMOL/L)	CANMAT MAINTENANCE LITHIUM (MEQ/L)

RULE **Lithium reduces suicide.** In a high-risk bipolar or recurrent depressive patient, weigh lithium specifically for its anti-suicidal and all-cause mortality benefit.

PEARL

The anti-suicidal benefit is why an examiner asks "what would you add for a bipolar patient with repeated attempts" and expects lithium, not a switch to valproate. The evidence base is Cipriani 2005: attempted and completed suicide both cut by about 80 percent.

30.3 Clozapine: the psychotic-overlap anti-suicidal agent

The second drug with real anti-suicidal evidence. Where a mood disorder overlaps with a psychotic illness, or in schizophrenia and schizoaffective disorder, clozapine has a specific anti-suicidal effect. Roughly 5 to 10 percent of patients with schizophrenia eventually complete suicide, and clozapine treatment markedly reduces the suicide rate, demonstrated in the international suicide prevention trial (InterSePT, Meltzer 2003). Clozapine is therefore the antipsychotic to consider for suicidality in the psychotic overlap, remembering its haematological and cardiac monitoring burden (the deep antipsychotic pharmacology sits in the Schizophrenia: management, antipsychotics and adverse effects notes). Lithium remains the answer for the pure mood disorder; clozapine is the answer where a chronic psychotic illness drives the risk.

GOOD TO REMEMBER

- **Lithium:** the strongest anti-suicidal and all-cause mortality evidence of any psychotropic in mood disorders, roughly 80 percent risk reduction (Cipriani 2005); weigh it in high-risk bipolar or recurrent depression, prophylaxis target 0.6 to 0.8 mmol/L.
- **Clozapine:** specific anti-suicidal effect in schizophrenia and the psychotic overlap (InterSePT, Meltzer 2003); the antipsychotic to consider when a chronic psychotic illness drives suicidality, with its neutropenia and cardiac monitoring.

30.4 Early antidepressant activation and the paediatric suicidality signal

Counsel and monitor at the start. Antidepressant treatment has been associated with an increased risk of suicidal thoughts and acts in the early weeks, particularly in children, adolescents and young adults, the basis of the regulatory black-box warning (Maudsley 2021). Two mood-specific mechanisms matter: early **activation** or agitation before mood lifts, and the recovery-phase energising of a still-hopeless patient. The relative risk is raised above placebo in the young, but the **absolute risk stays very small**, and the most effective way to prevent suicide in depression is to treat the depression effectively. The practical rule is to warn the patient (and family for a young person) about early activation, tell them how to seek help, and review early. NICE advises review within 1 week if the person is aged 18 to 25 or there is particular concern about suicide risk, and within 2 weeks otherwise (NICE 2022). Rates also rise when antidepressants are stopped, so apply the same care on discontinuation.

The paediatric point. In children and adolescents the small antidepressant suicidality signal is why guidelines restrict prescribing largely to SSRIs, and why fluoxetine is the best-evidenced first

choice in this age group (BAP 2015). The signal is a reason to counsel and monitor, not a reason to withhold treatment from a depressed adolescent who needs it.

1 week	first weeks
REVIEW IF AGE 18 TO 25 OR HIGH SUICIDE CONCERN	PEAK ACTIVATION / SUICIDALITY WINDOW

TRAP **Starting and walking away.** Not counselling about early activation and not reviewing a young patient within a week or two of starting an antidepressant, when the suicidality signal peaks.

WORKED EXAMPLE

A 19-year-old with moderate depression is started on fluoxetine. You counsel him and a parent that the first two weeks can bring restlessness or worsened thoughts before improvement, agree a help-seeking plan, and book review at one week because he is under 25. This is the correct application of the early-activation and paediatric-signal rules: treat, but counsel and monitor early.

GOOD TO REMEMBER

- **Early antidepressant activation:** raised suicidality signal in the first weeks in the young (black-box), absolute risk small; the discriminator is treat-but-counsel, warn on activation and review within 1 week if aged 18 to 25 or high concern (NICE 2022).
- **Paediatric first choice:** restrict to SSRIs, fluoxetine best evidenced; the first management step is family counselling plus early review, not withholding treatment (BAP 2015).

30.5 Overdose safety: never a large TCA supply

The drug is the means. A suicidal mood-disorder patient may take a deliberate overdose of whatever you prescribe, so overdose lethality is a prescribing decision, not an afterthought. Guidelines advise choosing antidepressants that are **better tolerated and safer in overdose**: SSRIs and other newer antidepressants are first-line, partly for this reason (BAP 2015). The tricyclic antidepressant class is the danger. A tricyclic overdose of about 10 times the daily dose can be fatal, death is usually from **cardiac toxicity** (type I antiarrhythmic membrane effect, QRS widening, arrhythmia), and TCA mortality per ingestion runs roughly 25-fold higher than SSRIs (Kaplan and Sadock 2024). Amitriptyline (Tryptomer) is among the leading single-drug causes of death by overdose. Therefore **avoid a large TCA supply** in a suicidal or high-risk patient: if a TCA is genuinely needed, dispense small quantities, and prefer the safer-in-overdose SSRI wherever the choice is open. A pre-existing QTc of 450 ms or more is a contraindication to TCA treatment (Kaplan and Sadock 2024).

AGENT / CLASS	OVERDOSE PROFILE	SUICIDAL-PATIENT IMPLICATION
SSRIs, newer antidepressants	**relatively safe in overdose**	first-line choice on safety grounds (BAP 2015)
Tricyclic antidepressants (amitriptyline, Tryptomer)	**fatal at ~10x daily dose; cardiotoxic; ~25x SSRI mortality**	avoid a large supply; dispense small quantities; QTc >=450 ms contraindicates
Lithium (Licab, Intalith)	narrow therapeutic index, toxic > 1.5 mEq/L	anti-suicidal, but a means in overdose: dispense with care and monitor levels

Overdose lethality as a prescribing lens for the suicidal mood-disorder patient.

TRAP **Handing over a cardiotoxic overdose.** Giving a suicidal patient a large quantity of a cardiotoxic tricyclic when a safer-in-overdose SSRI would do.

INDIA

Amitriptyline (Tryptomer) and imipramine (Depsonil) are cheap, ubiquitous and often the default in general and non-psychiatric Indian practice for depression and pain. That very availability is the hazard in a suicidal patient: lead with an SSRI (escitalopram, Nexito or S-Citadep; sertraline, Serta or Daxid; fluoxetine, Fludac) and, if a TCA is unavoidable, dispense small quantities and enlist family means-restriction. Lithium carbonate (Licab, Intalith) is inexpensive and widely available, so the anti-suicidal option is realistic in Indian practice.

GOOD TO REMEMBER

- **Tricyclic antidepressants (amitriptyline, Tryptomer):** cardiotoxic membrane effect, fatal at roughly 10x the daily dose, about 25-fold the SSRI overdose mortality; never a large supply to a suicidal patient, QTc >=450 ms contraindicates (Kaplan and Sadock 2024).
- **Safer-in-overdose choice:** SSRIs and newer antidepressants are first-line partly because they are safer in overdose (BAP 2015); prefer them wherever the clinical choice is open.

MNEMONIC

LiCK the risk: Lithium, Clozapine, Keep TCAs small

The three pharmacological moves against suicide in mood disorders: Lithium (strongest anti-suicidal, weigh it in high-risk mood disorder), Clozapine (anti-suicidal in the psychotic overlap), and Keep TCA supply small (safer-in-overdose SSRI first, small quantities if a TCA is used).

GOOD TO REMEMBER

- **Where the risk sits:** highest in severe depression, mixed states, early bipolar illness and the early recovery phase; lifetime bipolar suicide around 15 percent.
- **Lithium is anti-suicidal:** the strongest evidence of any psychotropic (roughly 80 percent risk reduction, plus all-cause mortality); weigh it in high-risk bipolar or recurrent depression.
- **Clozapine:** anti-suicidal in the psychotic overlap (InterSePT).
- **Avoid a large TCA supply, counsel early-activation:** lead with a safer-in-overdose SSRI, dispense TCAs in small quantities, warn about early antidepressant activation and review the young patient early.

HOLD THIS

Of every psychotropic, lithium has the strongest evidence for reducing suicide and all-cause mortality in mood disorders, so weigh it in a high-risk patient; and never hand a suicidal patient a large supply of a cardiotoxic tricyclic when a safer-in-overdose SSRI will do.

31 · ECT in mood disorders: indications and place

Why this matters. This topic is about the **place in algorithm**, not the technique. Electroconvulsive therapy (ECT) is the single most effective and most rapid antidepressant treatment available, and the examiner wants to know exactly where it sits: which mood presentations make it a first-line emergency option, where it otherwise slots in behind the drugs, and the one selection trade-off (a powerful, fast response against a transient memory cost). The engineering of the seizure, the electrode placement, the electrical dosing and the anaesthetic all belong to the ECT and neurostimulation notes; what is held here is the selection logic in mood disorder.

Exam framing. The high-yield answer is the list of **indications for ect** in mood disorder and its **place in algorithm**. ECT is a first-line option in the mood emergencies (a life-threatening or immediately dangerous depression or mania) and otherwise sits after adequate pharmacological trials as a treatment for drug-refractory illness. The syndromal criteria and the guideline-anchored drug plan are in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes; the full suicide-risk assessment is in the Somatic-symptom, sexual, impulse-control disorders and suicide notes; the acute-emergency and perinatal framing is in the Perinatal/women's mental health and emergency psychiatry notes.

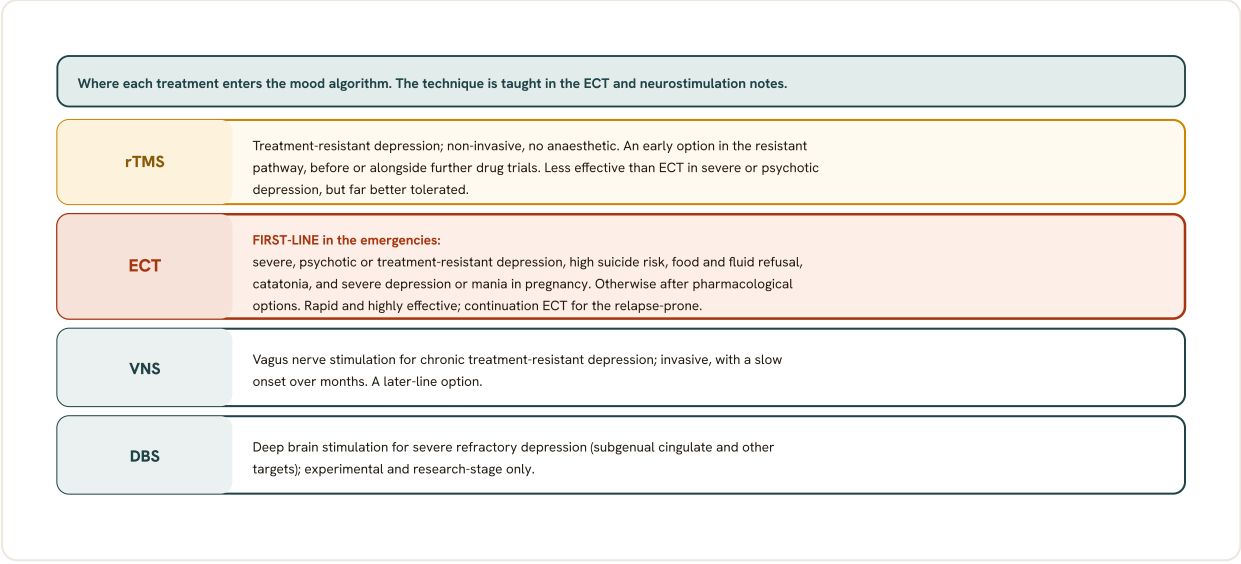


Fig 12.15 Where ECT and neuromodulation enter the mood-disorder algorithm. ECT is first-line in the emergencies (severe, psychotic or treatment-resistant depression, high suicide risk, food refusal, catatonia, pregnancy) and highly effective; rTMS is an early, non-invasive option in the treatment-resistant pathway; VNS is a slow, invasive later-line option; and DBS remains experimental. The technique of each is taught in the ECT and neurostimulation notes.

31.1 ect in mood disorders: strong efficacy and rapid onset

The property that drives every indication is that ECT is both highly effective and fast. In severe depressive illness the response rate is on the order of **70%** for real ECT against roughly **40%** for simulated (sham) treatment, giving a number-needed-to-treat of about **3 to 4** (UK ECT Review Group 2003; Shorter Oxford 2018), and under naturalistic conditions the response rate approaches **80%** (Companion 2010). In head-to-head comparisons ECT is at least as effective as, and works faster than, tricyclic antidepressants and MAOIs in severely depressed inpatients (UK ECT Review Group 2003; Shorter Oxford 2018). This combination of high response and rapid onset is precisely why ECT is reached for early whenever bringing about improvement quickly is essential rather than optional.

RULE **Use ECT mainly when it is essential to improve the patient quickly.** The strongest indications are an immediate high suicide risk, depressive stupor, and danger to physical health from food and fluid refusal (Shorter Oxford 2018).

31.2 The indications for ECT in mood disorder

The examiner wants the indication list held as a set. Combining the standard textbook indications (Shorter Oxford 2018) with the NICE and Royal College criteria, ECT in mood disorder is indicated for:

Severe depression needing a rapid response

severe depressive illness where quick improvement is essential, or when other treatments have failed (NICE 2009)

Psychotic depression

severe depression with mood-congruent delusions or hallucinations, one of the classic and best-responding ECT indications (Maudsley 2021)

Treatment-resistant depression

depression that has not responded to adequate trials of antidepressant drugs, with or without psychotic features (Shorter Oxford 2018)

High suicide risk or food-and-fluid refusal
an immediate high risk of suicide, or life-threatening refusal of food and fluids on the basis of extreme retardation or nihilism (RCPsych 2005)

Catatonia
severe non-organic catatonia, particularly with stupor and poor oral intake or drug non-response (NICE 2003)

Severe or treatment-resistant mania
a prolonged or severe manic episode, or mania unresponsive to pharmacotherapy or with life-threatening exhaustion (NICE 2003; IPS 2017)

Pregnancy where drugs are undesirable
severe depression or mania in pregnancy where medication is undesirable or has failed (CANMAT 2016; IPS 2017)

Across these, the unifying theme is severity plus urgency: the depressive picture that carries marked weight loss, early-morning waking, retardation and delusions is the one that responds best, and delusions and retardation are the features that most distinguish patients who respond to real ECT from those who respond to placebo (UK ECT Review Group 2003; Shorter Oxford 2018). Suicidal risk is named as the first and most important indication in the Indian standard text.

INDICATION IN MOOD DISORDER	CLINICAL TRIGGER	PLACE
Severe depression, rapid response needed	Life-threatening or where speed is essential	**First-line in the emergency**
Psychotic depression	Depression with delusions or hallucinations	**Early; strong ECT indication**
High suicide risk	Immediate, active suicidality	**First-line in the emergency**
Food and fluid refusal	Stupor, retardation, nihilism, dehydration	**First-line in the emergency**
Catatonia	Stupor, mutism, poor intake, drug non-response	**First-line / early**
Treatment-resistant depression	Failed adequate drug trials	After pharmacotherapy
Severe or treatment-resistant mania	Prolonged, exhausting, or drug-refractory mania	Emergency to after-drugs
Pregnancy, drugs undesirable	Severe perinatal depression or mania	**First-line where drugs avoided**

The mood-disorder indications for ECT and where each sits (Shorter Oxford 2018; NICE 2003/2009; IPS 2017; CANMAT 2016).

31.3 Its place in algorithm: first-line in the emergency, otherwise after drugs

The **place in algorithm** has two settings. In the mood emergencies, an immediate high suicide risk, depressive stupor with food and fluid refusal, life-threatening catatonia, and severe or exhausting mania, ECT is a **first-line option** that should be brought in without waiting for drugs to work or fail (Shorter Oxford 2018; IPS 2017). Outside those emergencies, ECT sits **after pharmacological options**: NICE positions it as a treatment for severe depression that is life-threatening or where a rapid response is required, or when other treatments have failed, and it is not used routinely for moderate depression (NICE 2009). For ordinary treatment-resistant depression, BAP places ECT among the next-step options for patients who have not responded to other treatments (BAP 2015). The Indian Psychiatric Society position is explicit that **modified ECT is first-line** for severe mania with food or fluid refusal or exhaustion, psychotic mania unresponsive to pharmacotherapy, severe bipolar depression with suicidality or stupor, mixed states with active suicidality, and catatonia, and that ECT should otherwise be considered for acute mania, mixed episodes or bipolar depression that is severe, refractory, suicidal, catatonic, psychotic, or in pregnancy (IPS 2017).

TRAP **Do not delay ECT through a sequence of failed drug trials in a life-threatening depression.** In a patient who is actively suicidal, in depressive stupor, or refusing food and fluids, ECT is first-line, not a last resort after every drug has failed.

31.4 Continuation and maintenance ECT for the relapse-prone

Response to an acute ECT course is high, but relapse rates after it are also high, especially in patients refractory to drugs (Shorter Oxford 2018). The answer for relapse-prone patients is **continuation and maintenance ECT**: after the acute course brings remission, further ECT sessions are given at spacing intervals (for example weekly, then fortnightly, then monthly) to hold the gain, usually alongside continuation pharmacotherapy. In psychotic depression, one small randomised controlled trial found maintenance ECT plus nortriptyline superior to nortriptyline alone at **2 years**, and ECT may be more protective against relapse in psychotic than in non-psychotic depression (Maudsley 2021). Maintenance ECT is therefore the tool reserved for patients who respond well to acute ECT but relapse rapidly on drugs alone. The dosing and scheduling of the maintenance course itself are in the ECT and neurostimulation notes.

31.5 Practical points relevant to choice: efficacy, memory, consent

Three practical facts drive the decision to use ECT and the conversation with the patient. First, **efficacy**: ECT is the most effective and most rapid treatment for severe mood disorder, and bilateral ECT is moderately more effective than unilateral (Companion 2010). Second, the **transient cognitive adverse effect**: both anterograde and retrograde memory disturbances are common, but they are usually mild and recovery occurs within about **1 to 6 months** of treatment, and unilateral ECT causes much less memory impairment than bilateral. This memory cost is the main reason patients hesitate and the main thing to weigh against ECT's speed and power. Third, **consent or the legal pathway**: ECT is always given after informed consent from the patient, or, where the patient lacks capacity, through the relevant legal pathway and local

statutory procedure. The technique, the electrode placement, the electrical dosing and the anaesthetic detail are all cross-referred to the ECT and neurostimulation notes.

70 vs 40	3 to 4	1 to 6
RESPONSE, REAL VS SHAM ECT (%)	NUMBER-NEEDED-TO-TREAT, ECT IN DEPRESSION	MEMORY RECOVERY AFTER ECT (MONTHS)

The three numbers a resident should hold: efficacy against sham, NNT, and time to memory recovery (UK ECT Review Group 2003).

INDIA

ECT is widely available and heavily used across Indian psychiatry, and the norm in current Indian practice is **modified ECT**, that is, ECT given under general anaesthesia with a muscle relaxant (usually succinylcholine) and oxygenation. Direct (unmodified) ECT, given without anaesthesia or muscle relaxation, is no longer standard and carries a fracture and dislocation risk; the Mental Healthcare Act 2017 restricts unmodified ECT. The Indian Psychiatric Society makes modified ECT first-line for the mania and bipolar-depression emergencies listed above (IPS 2017). The anaesthetic and modified-ECT technique itself is in the ECT and neurostimulation notes.

PEARL

The single feature that best predicts a good ECT response in depression is the presence of **psychotic features (delusions)**, followed by psychomotor retardation; these are the very features that separate real-ECT responders from placebo responders (UK ECT Review Group 2003).

TRAP **Do not quote a permanent memory loss as a reason to withhold ECT from a dying patient.** The memory effect is usually mild and recovers within 1 to 6 months, and unilateral placement minimises it; in a life-threatening depression the balance clearly favours treating.

HOLD THIS

ECT is the fastest and most effective treatment in severe mood disorder and is first-line, not last resort, in the emergencies: severe/psychotic depression, high suicide risk, food and fluid refusal, catatonia, severe or refractory mania, and severe mood illness in pregnancy where drugs are undesirable.

MNEMONIC

SPRINT

Suicide risk high, **P**sychotic depression, **R**esistant (treatment-resistant), **I**ntake refused (food and fluids), **N**ot-eating catatonia, **T**oo-severe mania or pregnancy where drugs are undesirable: the mood indications where ECT is reached for early.

GOOD TO REMEMBER

- **Indications for ect (mood):** severe depression needing rapid response, psychotic depression, treatment-resistant depression, high suicide risk or food-and-fluid refusal, catatonia, severe or treatment-resistant mania, and severe depression or mania in pregnancy where drugs are undesirable.
- **Place in algorithm:** first-line in the emergencies (high suicide risk, stupor, food/fluid refusal, catatonia, exhausting mania); otherwise after adequate pharmacotherapy for drug-refractory illness (NICE 2009; IPS 2017).
- **Efficacy and onset:** the most effective and most rapid treatment for severe mood disorder; about 70% real vs 40% sham response, NNT 3 to 4, roughly 80% naturalistic response (UK ECT Review Group 2003; Companion 2010).
- **Adverse effect to hold:** transient anterograde and retrograde memory disturbance, usually mild, recovering within 1 to 6 months; unilateral placement causes less.
- **Continuation/maintenance ECT:** spaced sessions after the acute course for relapse-prone patients; maintenance ECT plus nortriptyline beat nortriptyline alone at 2 years in psychotic depression (Maudsley 2021).
- **Consent and legality:** given after informed consent or through the legal pathway; the norm in Indian practice is modified ECT under anaesthesia with a muscle relaxant. Technique is elsewhere.

32 · Neuromodulation in depression

Why this matters. This topic is about the **place in algorithm**, not the technique. The examiner wants to know where each device sits in the treatment-resistant depression pathway: which is licensed and offered early, which is invasive and held back, and which is still research only. The engineering of coils, currents and electrodes belongs to the ECT and neurostimulation notes; what is held here is the selection logic. Three devices matter, in descending order of how routinely they are used: rtms (repetitive transcranial magnetic stimulation), vns (vagus nerve stimulation) and dbs (deep brain stimulation).

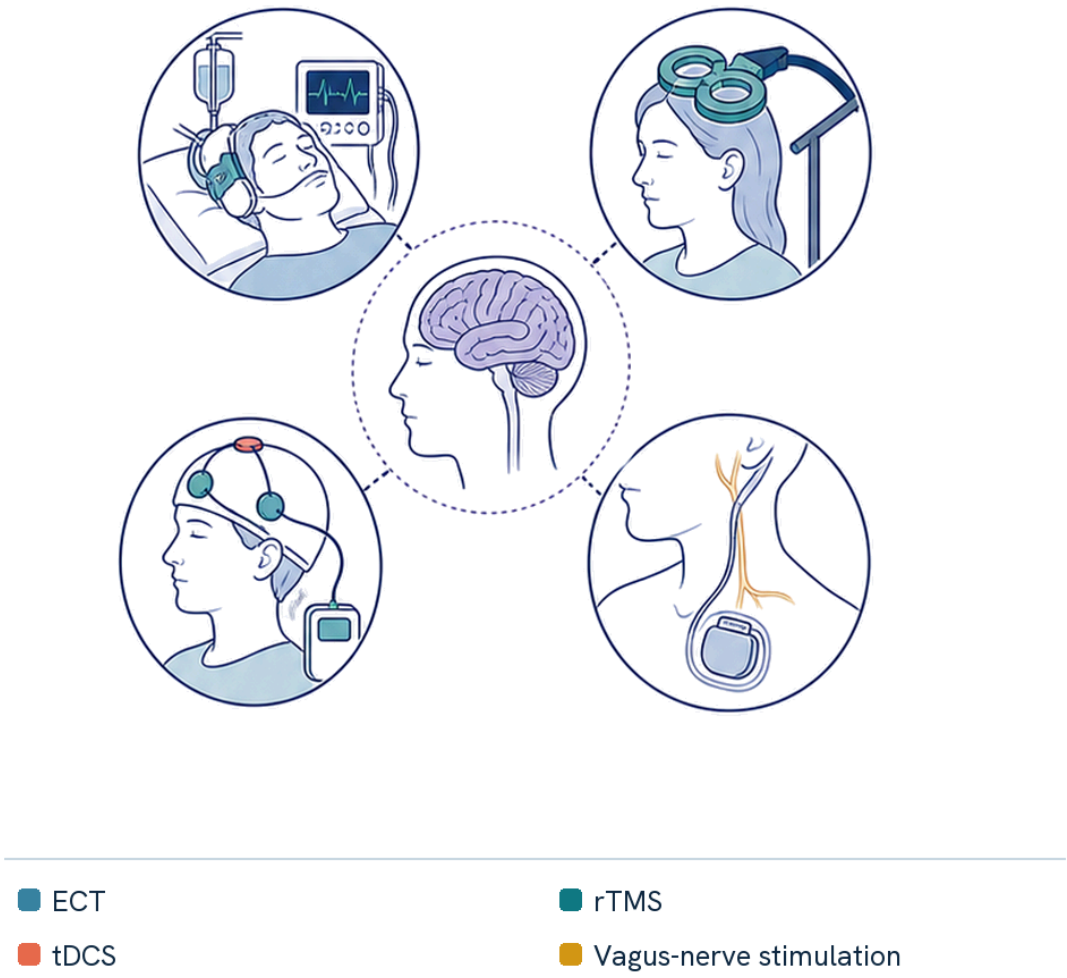


Fig 12.16 Major neuromodulation modalities differ in delivery: electroconvulsive therapy under anaesthesia, focal repetitive transcranial magnetic stimulation, transcranial direct-current stimulation and implanted vagus-nerve stimulation.

The frame is neuromodulation as a step in the pathway after antidepressants have underperformed. rTMS is a genuine guideline-supported option that can be brought in early; VNS and DBS are progressively more invasive and progressively less established, so they sit later in the ladder or outside routine practice altogether. The full technique of each device, the coil physics, the stimulation parameters and the surgery, is cross-referred to the ECT and neurostimulation notes; the wider acute-emergency and perinatal framing is in the Perinatal/women's mental health and emergency psychiatry notes.

32.1 rTMS: the licensed, non-invasive, early option in treatment-resistant depression

rtms is a non-invasive brain-stimulation technique delivered awake in an outpatient chair with no anaesthetic and no seizure induction, which is exactly why it earns an early place in the algorithm. CANMAT recommends rTMS as a **first-line** neuromodulation option for major depressive disorder that has not responded to at least one adequate antidepressant trial (CANMAT 2016), so it is a first-line-to-early option in the treatment-resistant pathway and can be offered before or

alongside further drug trials rather than being reserved for the very end. The standard protocol is high-frequency stimulation (**at least 5 Hz**) over the left dorsolateral prefrontal cortex, or low-frequency stimulation (**1 Hz or less**) over the right dorsolateral prefrontal cortex, delivered **20 to 40 min** per session, daily on 5 days a week for **4 to 6 weeks** (CANMAT 2016). It is non-invasive, well tolerated, and its commonest adverse effects are scalp discomfort and headache, with a rare seizure risk; this good tolerability, alongside the absence of anaesthetic and cognitive load, is the selling point that puts it ahead of the more invasive options.

RULE **rTMS is an evidence-based option in treatment-resistant depression, offered before or alongside further drug trials.** It is non-invasive, needs no anaesthetic, and is a first-line neuromodulation choice, not a last resort.

32.2 Theta-burst variants shorten the session

The practical evolution of rTMS is **theta-burst stimulation**. Intermittent theta-burst stimulation (iTBS) is offered as a first-line rTMS protocol that is non-inferior to conventional high-frequency rTMS but delivers the treatment in a much shorter session, on the order of **about 3 min** rather than 20 to 40 min (CANMAT 2023). Because each session is so short, accelerated protocols that pack several sessions into each day can compress a whole course into as little as **5 days** (CANMAT 2023). The theta-burst variants therefore make rTMS faster and more scalable without losing efficacy, which further supports its early place in the algorithm.

at least 5	20 to 40	about 3
HIGH-FREQUENCY RTMS, LEFT DLPFC (HZ)	STANDARD RTMS SESSION (MIN)	ITBS SESSION (MIN)

Verified rTMS parameters and the theta-burst session time (CANMAT 2023).

32.3 rTMS relative to ECT: less effective in severe or psychotic depression, better tolerated

The comparison the examiner wants is rTMS against ECT. For treatment-resistant patients the brain-stimulation alternatives to ECT, including rTMS, have **lower efficacy than traditional ECT**, so ECT remains the more powerful treatment for severe, psychotic or highly refractory depression (Kaplan & Sadock 2024). What rTMS offers instead is far better tolerability: it is non-invasive, needs no anaesthetic, and carries none of the anaesthetic and memory burden that makes many patients reluctant to accept ECT (Kaplan & Sadock 2024). The trade-off is the whole point of its place in algorithm, rTMS is the less effective but far better tolerated option, so it is preferred earlier and in less severe treatment-resistant pictures, while ECT is chosen when depth of response matters most, particularly in severe or psychotic depression. The device physics and the ECT technique itself are in the ECT and neurostimulation notes.

GOOD TO REMEMBER

- **rTMS mechanism:** non-invasive focal magnetic stimulation of the dorsolateral prefrontal cortex, awake, no anaesthetic, no induced seizure; signature adverse effects are scalp discomfort and headache with a rare seizure risk.
- **rTMS place:** CANMAT first-line neuromodulation for treatment-resistant depression; the one indication to hold is treatment-resistant depression that has failed at least one adequate antidepressant trial, offered before or alongside further drug trials.
- **rTMS vs ECT:** less effective than ECT in severe or psychotic depression, but better tolerated; the discriminator is tolerability (no anaesthetic, no memory load) traded against ECT's greater efficacy.
- **iTBS:** first-line theta-burst rTMS protocol, non-inferior to high-frequency rTMS, session about 3 min; the number to hold is that accelerated courses can be as short as 5 days.

32.4 VNS and DBS: the later-line and the experimental options

vns is an **invasive, later-line** option. It requires a surgically implanted pulse generator, with an electrode wrapped around the left cervical vagus nerve and the battery placed subcutaneously in the left chest wall (Kaplan & Sadock 2024). Its defining problem for the algorithm is a **slow onset**: only about **15%** of patients respond in the first 3 months, rising to roughly **30%** by 12 months, and response rates are lower than with ECT (Kaplan & Sadock 2024). VNS is approved as a long-term adjunctive treatment for chronic or recurrent treatment-resistant depression and is therefore worth considering only when patients have already failed less invasive treatments, so it sits late in the ladder rather than early (Kaplan & Sadock 2024).

dbs is **experimental** and research-stage for severe refractory depression. It involves surgical implantation of stimulating electrodes into a deep target, most studied at the **subgenual cingulate** cortex, with other targets under investigation (Kaplan & Sadock 2024; New Oxford 2020). The evidence base is still unsettled: small open-label and prospective studies of subgenual DBS were encouraging, but a large industry-supported controlled trial was stopped early on a futility analysis, and DBS for depression is not an approved routine treatment (Kaplan & Sadock 2024). Most of these newer neurostimulation therapies remain in an experimental phase of development (Kaplan & Sadock 2024), so DBS belongs to research protocols and last-resort refractory cases, not the routine algorithm. The neurosurgical technique and target physiology are in the ECT and neurostimulation notes.

DEVICE	INVASIVENESS	PLACE IN ALGORITHM	KEY CAVEAT
rTMS	Non-invasive, no anaesthetic	**First-line-to-early in treatment-resistant depression**	Less effective than ECT in severe/psychotic depression, better tolerated
VNS	Invasive, implanted generator	Later-line, chronic treatment-resistant depression	**Slow onset (about 15% at 3 months, about 30% at 12 months)**
DBS	Invasive, deep electrodes	Experimental, research-stage only	**Subgenual cingulate and other targets; controlled trial stopped for futility**

Place in algorithm of the three neuromodulation options in depression (CANMAT 2016; Kaplan & Sadock 2024; New Oxford 2020).

TRAP **Do not offer DBS or VNS as routine options.** DBS is experimental and research-stage; VNS is an invasive, slow-onset, later-line adjunct, not a mainstream step, and neither substitutes for rTMS or ECT in the ordinary pathway.

Guideline level. CANMAT names rTMS a first-line neuromodulation treatment for treatment-resistant depression and offers iTBS as a first-line rTMS protocol, with ECT reserved for severe, psychotic or refractory illness (CANMAT 2023). NICE similarly supports rTMS for depression as a recognised non-invasive option while positioning ECT for severe or life-threatening depression (NICE 2014). The Indian Psychiatric Society (IPS guidelines, Gautam et al. depression CPG) endorses ECT for severe and treatment-resistant depression, but a specific IPS position on rTMS, VNS and DBS in depression could not be confirmed against the parsed library and is flagged rather than invented; the IPS stance is named here and left as could-not-be-confirmed.

HOLD THIS

rTMS is a first-line, non-invasive, no-anaesthetic option in treatment-resistant depression (less effective than ECT but better tolerated); VNS is invasive, later-line and slow; DBS is experimental only.

GOOD TO REMEMBER

- **rtms:** non-invasive, no anaesthetic, first-line neuromodulation for treatment-resistant depression; hold high-frequency left DLPFC or low-frequency right DLPFC, 20 to 40 min per session, iTBS about 3 min.
- **vns:** invasive implanted generator on the left vagus nerve, later-line adjunct for chronic treatment-resistant depression; signature caveat is slow onset (about 15% respond at 3 months, about 30% at 12 months).
- **dbs:** invasive deep electrodes, experimental and research-stage for severe refractory depression; the target to hold is the subgenual cingulate, and a large controlled trial was stopped for futility.

33 . Psychotherapies for depression: the place

In a drug-focused chapter the drug is not the whole answer, and the board rewards the resident who knows exactly where a talking treatment sits in the depression algorithm. **Psychotherapy for depression** is not a soft alternative offered when medication fails; for mild-to-moderate illness a structured **first-line psychological** treatment is a genuine first-line option in its own right, and for moderate-to-severe illness combined treatment (medication plus psychotherapy) outperforms either alone (CANMAT 2016; Shorter Oxford 2018). This topic teaches the evidence-based *place* of psychotherapy for depression, the guideline-anchored algorithm; the *technique* of each therapy is cross-referred to the Psychotherapies, clinical assessment, MSE and nosology notes.

Ground the place in the guidelines. Lead with **CANMAT**: the Canadian Network for Mood and Anxiety Treatments names cognitive behavioural therapy, interpersonal therapy and behavioural activation as first-line psychological treatments for acute major depression, and directs that where feasible a psychological treatment (CBT or IPT) be combined with an antidepressant

because combined treatment is superior to either alone (CANMAT 2016). The place is then confirmed by the Indian Psychiatric Society, NICE and the BAP. Every first-line status below is verified against the CANMAT guideline rows and the Shorter Oxford (CANMAT 2016; Shorter Oxford 2018).

33.1 The three first-line psychological therapies

CBT, IPT and behavioural activation. The examinable list of **first-line psychological** treatments for acute major depression is three structured, time-limited, evidence-based therapies (CANMAT 2016). **cbt** (cognitive behaviour therapy) targets the depressive cognitive triad and maladaptive behaviour; **ipt** (interpersonal therapy) works on grief, role transitions, role disputes and interpersonal deficits; and **behavioural activation** uses scheduled activity and operant principles to re-engage the patient with rewarding behaviour. Head-to-head, none of the three is convincingly superior to the others, and each is as effective as pharmacotherapy in moderately depressed outpatients (Shorter Oxford 2018).

Each is first-line, alone, in mild-to-moderate depression. For a mild-to-moderate depressive episode, any one of CBT, IPT or behavioural activation may be offered as a stand-alone first-line treatment without medication (CANMAT 2016; Shorter Oxford 2018). Specific psychotherapies are more effective than treatment-as-usual in mild-to-moderate depression, particularly in primary care, and perform as well as drug treatment in the moderately depressed (Shorter Oxford 2018).

CBT

Cognitive behaviour therapy: restructures the depressive cognitive triad and reactivates behaviour; first-line for acute depression.

IPT

Interpersonal therapy: targets grief, role transitions, role disputes and interpersonal deficits; first-line for acute depression.

Behavioural activation

Scheduled, reward-linked activity using operant principles; first-line for acute depression and simple to train.

RULE **Offer an evidence-based psychotherapy first-line in mild-to-moderate depression, and combine it with medication in severe depression.** CBT, IPT and behavioural activation are all first-line for acute major depression.

TRAP **Treating every depression with medication alone when a psychological therapy is indicated.** In mild-to-moderate illness a structured psychotherapy alone is first-line; in severe illness the correct move is to add it, not to omit it.

33.2 The place in the algorithm: alone, combined, or for relapse prevention

Alone in mild-to-moderate; combined in moderate-to-severe. The place is a two-step rule. In a mild-to-moderate episode, offer a first-line psychological therapy (CBT, IPT or behavioural activation) as a first-line option alone, matching the efficacy of an antidepressant (CANMAT

2016; Shorter Oxford 2018). In more severe or recurrent illness, add the psychotherapy to medication rather than relying on either alone, because combined treatment is superior to pharmacotherapy alone for many patients (CANMAT 2016; Shorter Oxford 2018).

And for relapse prevention. After the acute phase, psychotherapy has a maintenance place: CANMAT names CBT and mindfulness-based cognitive therapy (MBCT) as first-line psychological treatments to prevent relapse (CANMAT 2016). Mindfulness-based cognitive therapy is the paradigm example, delivered in remission to patients with recurrent depression to reduce the relapse rate. Add adjunctive CBT to ongoing antidepressant treatment as a recognised next-step option in the patient who has not fully responded (BAP 2015).

ILLNESS SEVERITY / PHASE	THE PLACE OF PSYCHOTHERAPY	EVIDENCE-BASED OPTION
Mild-to-moderate, acute	**First-line, alone (no medication needed)**	CBT or IPT or behavioural activation
Moderate-to-severe, acute	**Add to medication (combined is superior)**	Antidepressant plus CBT or IPT
Partial response to an antidepressant	Add as a next-step to ongoing medication	Adjunctive CBT
Remission, recurrent illness	First-line for relapse prevention	CBT or mindfulness-based cognitive therapy (MBCT)

The place of psychotherapy for depression across severity and phase, verified against CANMAT (CANMAT 2016) and the BAP (BAP 2015): alone in mild-to-moderate illness, added to medication in more severe or recurrent illness, and first-line for relapse prevention.

WORKED EXAMPLE

A 30-year-old teacher presents with a first, mild-to-moderate depressive episode without suicidality, and asks to avoid tablets. Rather than defaulting to an SSRI, offer a first-line psychological therapy alone: a course of CBT, IPT or behavioural activation is a legitimate first-line treatment here and matches antidepressant efficacy in this severity band (CANMAT 2016). Contrast a 45-year-old with a severe, recurrent episode: here the correct move is combined treatment, an antidepressant plus CBT or IPT, because combined treatment is superior to medication alone, followed by CBT or MBCT in remission to prevent the next relapse.

33.3 Where the guidelines agree: CANMAT, the IPS, NICE and the BAP

CANMAT (lead). Offer CBT, interpersonal therapy or behavioural activation as first-line psychological treatments for acute major depression; where feasible combine a psychological treatment (CBT or IPT) with an antidepressant, as combined treatment is superior to either alone; and for maintenance offer CBT or MBCT first-line to prevent relapse (CANMAT 2016).

The Indian Psychiatric Society. The **indian psychiatric society** Clinical Practice Guidelines for depression (Gautam et al.) endorse structured psychotherapy, chiefly CBT and IPT, as a treatment for depression, offered alone in milder illness and combined with pharmacotherapy in moderate-to-severe illness (IPS 2017). The precise severity thresholds and the exact list of first-line psychotherapies in the current **ips guidelines** could not be confirmed from the parsed

library and are flagged under gaps rather than invented; the IPS is named and the position stated only to the level that is verified.

NICE and the BAP. NICE runs a stepped-care model: for less severe depression it prefers the least intrusive psychological options first (guided self-help, group CBT, group behavioural activation) and does not routinely start an antidepressant first-line, reserving combined psychotherapy-plus-antidepressant for more severe depression (NICE 2022). The BAP concurs that adding CBT to ongoing antidepressant treatment is a valid next-step option when response is incomplete (BAP 2015).

INDIA

In Indian practice the access barrier is real: trained CBT and IPT therapists are concentrated in cities and the private sector, so the guideline-ideal of psychotherapy alone for mild-to-moderate depression is often not deliverable, and a low-cost generic SSRI becomes the pragmatic first step. Behavioural activation is the most transportable of the three because, unlike CBT, therapist training in its techniques is claimed to be simple and quickly accomplished (Shorter Oxford 2018), which makes it well suited to task-shifted, non-specialist delivery in resource-limited settings.

33.4 The technique lives elsewhere; what to hold here

Cross-reference, do not duplicate. The actual technique of each therapy, the CBT thought record and cognitive triad, the IPT interpersonal inventory and four problem areas, and the behavioural activation activity schedule, is taught in the Psychotherapies, clinical assessment, MSE and nosology notes. For these notes, hold only the *place*: which therapies are first-line, when they stand alone, when they combine with medication, and where they prevent relapse.

The one line that answers the viva. When the examiner asks "what is the place of psychotherapy in depression?", answer with the two-step rule plus the maintenance rider: first-line alone in mild-to-moderate illness, added to medication in moderate-to-severe illness because combined treatment is superior, and CBT or MBCT for relapse prevention (CANMAT 2016).

3	Combined	MBCT
FIRST-LINE PSYCHOTHERAPIES (CBT, IPT, BA)	SUPERIOR TO MEDICATION ALONE (MODERATE-TO-SEVERE)	FIRST-LINE FOR RELAPSE PREVENTION

MNEMONIC

CIB, then M

CBT, **I**PT, **B**ehavioural activation are the three first-line psychotherapies for acute depression; **M**BCT (with CBT) is first-line for relapse prevention. Alone in mild-to-moderate, combined in severe.

GOOD TO REMEMBER

- **CBT, IPT and behavioural activation:** the three first-line psychological treatments for acute major depression; each may be offered alone in mild-to-moderate illness (CANMAT 2016).
- **Alone vs combined:** first-line alone in mild-to-moderate depression, added to medication in moderate-to-severe or recurrent illness because combined treatment is superior to either alone.
- **Relapse prevention:** CBT or mindfulness-based cognitive therapy (MBCT) is first-line to prevent relapse after remission (CANMAT 2016).
- **The technique:** the technique of each is cross-referred to the Psychotherapies, clinical assessment, MSE and nosology notes; hold only the place here.

HOLD THIS

Offer an evidence-based psychotherapy (CBT, IPT or behavioural activation) first-line and alone in mild-to-moderate depression, add it to medication in moderate-to-severe or recurrent depression because combined treatment is superior to either alone, and use CBT or mindfulness-based cognitive therapy for relapse prevention; the technique is taught elsewhere.

34 . Managing bipolar depression

The depressive pole is where most of the illness burden of bipolar disorder sits, and it is the phase the board most wants you to manage **differently** from unipolar depression. The single organising idea is a warning: the drugs that break a unipolar depression are not the drugs you reach for here, because an **antidepressant** given without anti-manic cover can flip a depressed bipolar patient into mania. This is a management topic, so the marks are in the guideline-anchored selection, the first-line agents, and the recognition and handling of a treatment-emergent switch, not in a recitation of side effects. The deep per-drug pharmacology (lithium, valproate, lamotrigine, quetiapine, the antidepressant classes) is owned by the earlier topics in these notes; this topic carries which agent, which phase, which line, and the manic-switch rule.

Lead the answer with CANMAT (Yatham 2018, the CANMAT/ISBD 2018 guideline), then give the Indian Psychiatric Society position, now carried by the 2025 IPS bipolar update (IPS 2025, Menon et al., which supersedes the 2017 Shah guideline), and the NICE and BAP positions. Every first-line agent, dose, serum level and switch fact below is verified against the CANMAT/ISBD guideline, the Indian Psychiatric Society clinical practice guideline, the Maudsley Prescribing Guidelines, Stahl and Kaplan and Sadock (Yatham 2018; Menon 2025; Shah 2017; Maudsley 2021; Stahl 2021; Kaplan and Sadock 2024). The full syndrome and the wider guideline-anchored management PLAN sit in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes; the receptor pharmacology and CYP metabolism behind agent selection sit in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

34.1 Why bipolar depression is managed differently

It is not unipolar depression with a manic history bolted on. Episodes of bipolar depression, compared with unipolar depression, tend to be more rapid in onset, more frequent, shorter, and more likely to carry reverse neurovegetative features such as hypersomnia and hyperphagia and, at times, psychotic features (Maudsley 2021). Two facts drive the whole management plan. First,

the antidepressant response is different: unopposed antidepressants are relatively less effective (perhaps not effective at all) in bipolar than in unipolar depression (Maudsley 2021). Second, and decisively, giving an antidepressant alone risks a **manic switch** and destabilisation of the illness course. So the agents of choice are anti-manic mood stabilisers and specific atypical antipsychotics, not antidepressants.

RULE **Treat bipolar depression with quetiapine, lurasidone, lamotrigine or lithium, not an antidepressant alone.** The first-line agents are anti-manic mood stabilisers and specific atypicals, chosen to cover the depressive pole without flipping the patient into mania (Yatham 2018).

34.2 CANMAT: the first-line agents for bipolar I depression

Lead with CANMAT. For acute bipolar I depression the CANMAT/ISBD guideline names the **first-line** options as: quetiapine (Qutipin) monotherapy; lurasidone monotherapy or adjunctive to lithium or divalproex; lithium (Licab, Intalith) monotherapy; lamotrigine (Lamitor, Lametec) monotherapy or adjunctive; and lurasidone or adjunctive lamotrigine (Yatham 2018). The verified target doses are quetiapine to about **300 mg/day** (the licence and practice range for bipolar depression is **300 to 600 mg/day**), lurasidone **20 to 120 mg/day**, lithium to an acute serum level of **0.8 to 1.2 mEq/L**, and lamotrigine slowly titrated from 25 mg to a minimum of **200 mg/day** (Yatham 2018; Maudsley 2021). One mechanistic pearl the board likes: the antidepressant efficacy of these antipsychotics in bipolar depression is not a dopamine-blocking effect, since aripiprazole and most pure D2 blockers do not work in acute bipolar depression (Maudsley 2021).

The second-line rapid-response pair. When a rapid response is desirable, CANMAT places cariprazine and the **olanzapine-fluoxetine combination** as second-line for acute bipolar I depression (Yatham 2018). The olanzapine-fluoxetine combination (the fixed-dose OFC, olanzapine 6 or 12 mg with fluoxetine 25 or 50 mg) is genuinely effective and is the strongest single piece of evidence for any antidepressant helping in bipolar depression, but note the antidepressant is always paired with an anti-manic partner, never given alone (Maudsley 2021).

TRAP **Naming aripiprazole as a first-line agent for bipolar depression.** Aripiprazole works for mania and manic-relapse prevention but does not have efficacy in acute bipolar depression; the depression antipsychotics are quetiapine, lurasidone, cariprazine and olanzapine (Maudsley 2021).

34.3 NICE and the Indian Psychiatric Society position

NICE. To treat bipolar depression NICE recommends fluoxetine combined with olanzapine, or quetiapine on its own; if the patient prefers, consider olanzapine without fluoxetine, or lamotrigine on its own (NICE 2014; Maudsley 2021). NICE therefore treats lamotrigine as second-line, whereas BAP has lamotrigine and lurasidone as first-line options with the caveat that a mood stabiliser or antipsychotic will still be needed to protect against mania in the longer term (Goodwin 2016).

India. The **Indian Psychiatric Society** clinical practice guideline (IPS 2017, Shah et al.) for acute bipolar depression names quetiapine (**300 to 600 mg**) or the olanzapine-plus-fluoxetine combination as first-line, with lithium and lamotrigine as alternatives, particularly where the antipsychotic burden is undesirable. Crucially the IPS guidelines state that antidepressant monotherapy is contraindicated, and that antidepressants should not be used in rapid cycling or mixed episodes; if an antidepressant is used at all, paroxetine is avoided and bupropion is preferred (Shah 2017). This maps cleanly onto CANMAT, and the indian psychiatric society (IPS) position, as set out in the ips guidelines, is the guideline most likely to be named in an Indian postgraduate examination.

INDIA

The IPS bipolar guideline has been updated: the 2025 IPS bipolar update (IPS 2025, Menon et al., Indian J Psychiatry 2026;68:8-43) supersedes the 2017 Shah guideline and now names the first-line options for acute bipolar depression as the olanzapine-fluoxetine combination (Oleanz plus Fludac), quetiapine (Qutipin), lurasidone and cariprazine, with lithium (Licab, Intalith) and lamotrigine (Lamitor, Lametec) as further options. It keeps the core rule that antidepressant monotherapy or unopposed antidepressant use is not recommended in bipolar depression; where an antidepressant is judged necessary, an SSRI or bupropion (Bupron) is preferred, always under anti-manic cover. All first-line agents are inexpensive Indian brands.

34.4 The first-line bipolar-depression agents at a glance

The first-line and rapid-response agents assemble into one table. Learn the highlighted cell in each row: it is the fact the examiner tests, and it is the line or the caveat, not the side-effect list (which is owned by the per-drug topics).

300 to 600	20 to 120	0.8 to 1.2	200
QUETIAPINE BIPOLAR DEPRESSION (MG/DAY)	LURASIDONE RANGE (MG/DAY)	ACUTE LITHIUM LEVEL (MEQ/L)	LAMOTRIGINE MINIMUM TARGET (MG/DAY)

AGENT (INDIAN BRAND)	CANMAT LINE	DOSE / TARGET	THE BOARD-CRITICAL POINT
Quetiapine (Qutipin)	First-line monotherapy	300 mg/day target (300 to 600 mg/day range)	**Broadest agent: works across mania, bipolar depression and maintenance; not associated with switching to mania (Maudsley 2021)**
Lurasidone	First-line, monotherapy or adjunctive to lithium/divalproex	20 to 120 mg/day	**Metabolically favourable (minimal weight gain); signature adverse effects are nausea and akathisia; take with food (Maudsley 2021)**

AGENT (INDIAN BRAND)	CANMAT LINE	DOSE / TARGET	THE BOARD-CRITICAL POINT
Lithium (Licab, Intalith)	First-line monotherapy	Acute serum level 0.8 to 1.2 mEq/L	**The only agent with specific anti-suicide evidence; acute-depression efficacy is modest but relapse prevention is strong (Maudsley 2021)**
Lamotrigine (Lamitor, Lametec)	First-line, monotherapy or adjunctive	Slow titration 25 to a minimum of 200 mg/day	**Best for the depressive pole and prevention, weak against acute mania; does not induce switching or rapid cycling; slow titration for rash (Yatham 2018)**
Olanzapine-fluoxetine combination (Oleanz + Fludac)	Second-line (for rapid response)	Olanzapine 6 or 12 mg with fluoxetine 25 or 50 mg/day	**Strongest evidence for an antidepressant helping in bipolar depression, but the antidepressant is always paired with olanzapine, never alone (Maudsley 2021)**
Cariprazine	Second-line (for rapid response)	Per licence	**Efficacious in bipolar depression with low weight-gain propensity; smaller effect size than lurasidone (Maudsley 2021)**

First-line and second-line agents for acute bipolar I depression, CANMAT lead (Yatham 2018) with doses verified against the Maudsley Prescribing Guidelines. Indian brands lead each row, this being the chapter where brands belong. Highlighted cells are the examinable line-or-caveat, not the side-effect profile.

WORKED EXAMPLE

A woman with bipolar I disorder, well on maintenance divalproex, presents with a breakthrough depressive episode. The correct next step is not to add an SSRI: add or switch to a first-line bipolar-depression agent, for example lurasidone adjunctive to the divalproex, or quetiapine, or add lamotrigine (titrated at half the usual rate because valproate doubles the lamotrigine level, targeting about 100 mg/day). Reaching for an antidepressant alone here risks a manic switch and rapid cycling, and the antidepressant is relatively less effective in this setting anyway (Yatham 2018; Maudsley 2021).

34.5 The antidepressant-in-bipolar question

The default is: do not. An **antidepressant in bipolar** depression is avoided as monotherapy because of two linked hazards: the risk of a **manic switch** (a flip into hypomania or mania) and the risk of destabilising the illness into rapid cycling (Yatham 2018; Kaplan and Sadock 2024).

Unopposed antidepressants (that is, without mood-stabiliser protection) are generally to be avoided in bipolar depression, especially in bipolar I disorder (Maudsley 2021). If an antidepressant is used at all it is only **with an anti-manic mood stabiliser** as cover, it is **avoided in mixed features and in rapid cycling**, and the adjunctive evidence is weak. Indeed, controlled data suggest a mood stabiliser alone is about as effective as a mood-stabiliser-plus-antidepressant combination (Maudsley 2021).

The nuances the board rewards. Not all antidepressants carry equal switch risk. Venlafaxine (an SNRI) appears more likely than an SSRI or bupropion to induce a switch to mania (Leverich 2006; Maudsley 2021). Tricyclics and MAOIs are usually best avoided. Where an antidepressant is judged necessary, an SSRI (or bupropion) under mood-stabiliser cover is preferred, and the IPS specifically prefers bupropion and avoids paroxetine (Shah 2017). Some guidelines allow a more permissive use of antidepressants in bipolar II depression, where sertraline does not appear to increase switch rates, but bipolar I depression is where the prohibition is firmest (Altshuler 2017; Maudsley 2021).

TRAP **Giving antidepressant monotherapy in a bipolar depression and precipitating a switch or rapid cycling.** An antidepressant is only ever added under anti-manic cover, is avoided in mixed features and rapid cycling, and is never the first-line agent (Yatham 2018; Shah 2017).

34.6 Treatment-emergent mania: recognise it and manage it

What it is. **Treatment-emergent mania** (the treatment-emergent mania of the guidelines) is a switch into hypomania or mania that appears on treatment, classically driven by an antidepressant, sometimes within the first weeks of exposure. In a patient being treated for what looked like a unipolar depression, a treatment-emergent affective switch on antidepressant monotherapy reclassifies the diagnosis as bipolar disorder (Shah 2017; Kaplan and Sadock 2024). Recognise it as the emergence of elevated or irritable mood, reduced need for sleep, increased energy, pressured speech, overactivity or risk-taking against a background of antidepressant use (or a dose increase).

How to manage it. The steps are, in order: **stop (or reduce) the antidepressant**; **optimise the mood stabiliser** (raise lithium or valproate towards the anti-manic range, or add or up-titrate an **atypical antipsychotic**); and reassess the diagnosis and future prophylaxis. In a first-episode manic presentation, discontinue any antidepressant and reassess the diagnosis before starting antimanic agents (Yatham 2018; Shah 2017). One safety point sits alongside this: abruptly adding a serotonergic antidepressant to an existing regimen, or the accidental co-prescription during a switch, can precipitate serotonin syndrome, whose acute management is owned by the Perinatal/women's mental health and emergency psychiatry notes.

RULE **Treatment-emergent switch: stop the antidepressant, optimise the stabiliser, add or up-titrate an atypical.** A switch on antidepressant monotherapy reclassifies the depression as bipolar (Shah 2017).

PEARL

The manic switch is not just an adverse event, it is a diagnostic event. A first manic or hypomanic episode emerging on an antidepressant given for depression converts the working diagnosis from unipolar depression to bipolar disorder and changes the whole prophylaxis plan towards a mood stabiliser, not an antidepressant (Kaplan and Sadock 2024).

MNEMONIC

QuLLL

The four verified CANMAT first-line agents for bipolar depression, in one handle: **Qu**etiapine, **L**urasidone, **L**ithium, **L**amotrigine (Yatham 2018). If you can name only four things in the exam, name these four, and add that an antidepressant is never given alone.

HOLD THIS

Bipolar depression is treated first-line with quetiapine, lurasidone, lithium or lamotrigine (and the olanzapine-fluoxetine combination or cariprazine second-line for rapid response), and never with an antidepressant alone, because unopposed antidepressants risk a manic switch and rapid cycling.

GOOD TO REMEMBER

- **Quetiapine (Qutipin):** multi-acting atypical; the broadest bipolar agent (mania, depression, maintenance); first-line monotherapy for bipolar depression at **300 to 600 mg/day**; not associated with switching (Yatham 2018; Maudsley 2021).
- **Lurasidone:** atypical, metabolically favourable; first-line for bipolar depression, monotherapy or adjunctive to lithium/divalproex, **20 to 120 mg/day**; signature adverse effects nausea and akathisia; take with food (Yatham 2018; Maudsley 2021).
- **Lithium (Licab, Intalith):** first-line monotherapy; acute-depression target serum level **0.8 to 1.2 mEq/L**; the one agent with specific anti-suicide evidence; the full monitoring and toxicity detail is owned by the lithium topics in these notes (Yatham 2018).
- **Lamotrigine (Lamitor, Lametec):** best for the depressive pole and prevention, weak against acute mania; does not induce switching or rapid cycling; slow titration 25 to a minimum of **200 mg/day** for rash; halve the schedule with valproate (Yatham 2018; Stahl 2021).
- **Olanzapine-fluoxetine combination (Oleanz + Fludac):** second-line for rapid response; olanzapine 6 or 12 mg with fluoxetine 25 or 50 mg/day; strongest evidence for an antidepressant helping in bipolar depression, but the antidepressant is always paired, never alone (Yatham 2018; Maudsley 2021).
- **Antidepressant in bipolar:** never monotherapy; only with an anti-manic stabiliser; avoided in mixed features and rapid cycling; venlafaxine carries the higher switch risk, bupropion is preferred over paroxetine (Shah 2017; Leverich 2006).
- **Treatment-emergent mania (the discriminator and first step):** a switch into hypomania or mania on treatment; a switch on antidepressant monotherapy reclassifies the diagnosis as bipolar; first step is to stop the antidepressant, then optimise the stabiliser or add an atypical (Shah 2017; Yatham 2018).

35 . Managing bipolar mixed episodes

A **mixed state** is where depressive and manic or hypomanic symptoms co-occur, and it is the presentation that most often gets the pharmacology wrong. The examiner is testing one insight: a **mixed state does not behave like either pure pole,** it carries the highest suicide risk in the bipolar course, and the drug you reach for a "mixed depression" is not an antidepressant. This is a dedicated management topic. The mixed-episode and mixed-features SYNDROME, its criteria and its neurobiology, is owned by the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes; this topic carries the guideline-anchored pharmacotherapy.

Lead the answer with CANMAT (CANMAT 2018, Yatham et al.), then give the Indian Psychiatric Society position, now carried by the 2025 IPS bipolar update (IPS 2025, Menon et al., which supersedes the 2017 Grover and Avasthi guideline and names divalproex first-line and carbamazepine second-line for acute mixed episodes), and the BAP (BAP 2016) and NICE (NICE 2014) positions. The agents with the best mixed-state evidence are the atypicals asenapine, cariprazine, olanzapine and aripiprazole, and valproate (divalproex); lithium is relatively weaker for classic mixed and dysphoric presentations; and antidepressants are avoided.

35.1 The principle: a mixed state responds differently from a pure pole

Define it first. A **mixed state** spans two things the exam wants named distinctly: a full **mixed episode** (co-occurring depressive and manic or hypomanic symptoms meeting threshold, the classic dysphoric mania and agitated mixed depression) and the milder DSM-5 **mixed features** specifier attached to a manic, hypomanic or depressive episode (Kaplan and Sadock 2024). Dysphoric mania is manic overactivity, pressured speech and reduced sleep carried on a dysphorically excited, irritable, anxious mood, often with agitation and suicidal ideation (Kaplan and Sadock 2024). **Why it matters.** The mixed state carries a **high suicide risk**, among the highest of any phase of the illness, because manic-level drive and energy sit on top of depressive despair (IPS 2017). It responds differently from a pure manic or a pure depressive episode, so it is managed as its own entity, not as "the mania" or "the depression" that happens to be present.

RULE **Treat the mixed state as its own high-suicide-risk entity.** It is not a pure pole with extra symptoms, and it does not respond like one.

35.2 Lithium is relatively weaker in classic mixed and dysphoric presentations

The single most tested selection fact: **lithium underperforms in mixed and dysphoric presentations.** Kaplan and Sadock is explicit that patients with concomitant depressive symptoms, that is dysphoric mania, respond more poorly to lithium, as do those with a high cumulative episode burden; and in subtype analyses the irritable manic subtype responded significantly better to divalproex than to lithium, while the classic euphoric manic subtype responded similarly to both (Kaplan and Sadock 2024). Lithium keeps its place as the anti-suicide agent of the illness and a first-line antimanic and maintenance drug, but it is not the drug you build a classic mixed or dysphoric-manic plan around. Its deep pharmacology, dosing and monitoring are owned by the lithium topics in these notes.

TRAP **Reaching first for lithium in a dysphoric mania.** Dysphoric and irritable presentations respond more poorly to lithium and better to divalproex or an atypical (Kaplan and Sadock 2024).

35.3 Valproate (divalproex): the mixed-state mood stabiliser of choice

Mechanism. Valproate broadens GABAergic inhibitory tone, blocks voltage-sensitive sodium channels and modulates T-type calcium currents, damping the excitatory drive that fuels the manic and agitated components of a mixed state (Stahl 2021). **Where it wins.** Valproate and divalproex have specific evidence in dysphoric mania, mixed affective episodes and rapid cycling, and outperform lithium in irritable and dysphoric presentations (Kaplan and Sadock 2024). CANMAT lists divalproex as a first-line monotherapy for acute mania (which includes mixed presentations) at a serum level of **350 to 700 micromol/L** (50 to 100 microg/mL) (CANMAT 2018). **Signature cautions.** Weight gain, tremor, hair loss, thrombocytopenia and hepatotoxicity; and the hard rule that it is **teratogenic** (neural tube defects, neurodevelopmental harm) and is not started in a woman of childbearing potential without a pregnancy-prevention programme (NICE 2014; IPS 2017). The full valproate pharmacology and teratogenicity are owned by the valproate topic in these notes.

GOOD TO REMEMBER

- **Valproate (divalproex; Valprol or Encorate, divalproex Valance or Divaa):** broadens GABA and blocks sodium channels; specific evidence in dysphoric mania, mixed and rapid-cycling states; acute-mania serum target **50 to 100 microg/mL** (CANMAT 2018). Signature: teratogenic, avoid in women of childbearing potential.

35.4 Asenapine: a first-line atypical for mixed states

Mechanism. Asenapine is a high-affinity 5-HT2A and D2 antagonist with a broad serotonergic, dopaminergic and adrenergic binding profile structurally related to mirtazapine (Stahl 2021; Kaplan and Sadock 2024). **Where it wins.** CANMAT names asenapine among the first-line agents for acute mania (alone or in combination), and it has a specific licensed indication for acute manic and mixed episodes of bipolar I disorder, making it one of the go-to atypicals when the presentation is mixed (CANMAT 2018; Stahl 2021). **Dose.** It must be given **sublingually** (about 35 percent bioavailable sublingually, under 2 percent if swallowed), typically **5 to 10 mg twice daily** (10 to 20 mg/day) for mania, with no food or drink for 10 minutes after dosing (Stahl 2021). **Signature effects.** Sublingual oral hypoaesthesia, sedation and a moderate metabolic burden.

GOOD TO REMEMBER

- **Asenapine:** sublingual 5-HT2A/D2 antagonist; first-line for acute manic and mixed episodes of bipolar I; dose **5 to 10 mg twice daily** sublingually, no food or drink for 10 minutes; signature is sublingual oral hypoaesthesia. Indian brand could not be confirmed from the library; prescribe by generic name.

35.5 Cariprazine: the atypical that spans the mixed spectrum

Mechanism. Cariprazine is a D3-preferring D2 and D3 partial agonist with 5-HT1A partial agonism; the D2 blockade in limbic areas treats mania and psychosis while D3 partial agonism in the midbrain enhances prefrontal dopamine to address the depressive and cognitive components, so it works across the bipolar mood spectrum in one agent (Stahl 2021). **Where it wins.** CANMAT names cariprazine among the first-line agents for acute mania, and it carries evidence across manic, mixed and bipolar-depressive presentations, which is exactly the coverage a mixed state needs (CANMAT 2018; Stahl 2021). **Dose.** Acute bipolar mania is **3 to 6 mg/day** once daily, titrated from 1.5 mg; Stahl notes the more manic the features, the higher the dose within range (Stahl 2021). **Signature effect.** Akathisia, which is dose-related and reduced by slower titration.

GOOD TO REMEMBER

- **Cariprazine:** D3-preferring D2/D3 partial agonist that spans the mixed spectrum in one agent; first-line acute mania at **3 to 6 mg/day**; signature is akathisia. Indian brand could not be confirmed from the library; prescribe by generic name.

35.6 Olanzapine and aripiprazole: the other evidenced atypicals

Two further atypicals round out the mixed-state toolkit. Olanzapine (Oleanz) is a first-line antimanic with evidence in mixed episodes, useful where rapid control of agitation is the priority, at the cost of the heaviest metabolic burden of the group, so weight, glucose and lipids are monitored (CANMAT 2018). Aripiprazole is a D2 and D3 partial agonist and 5-HT1A partial agonist, a first-line antimanic with a favourable metabolic profile, again with mixed-episode data (CANMAT 2018; Stahl 2021). CANMAT also endorses combination therapy, an atypical (quetiapine, aripiprazole, risperidone or asenapine) added to lithium or divalproex, as a first-line option for acute mania, especially in severe presentations, and that combination logic carries into severe mixed states (CANMAT 2018). The deep antipsychotic pharmacology and the shared adverse-effect set are owned by the Schizophrenia: management, antipsychotics and adverse effects notes.

GOOD TO REMEMBER

- **Olanzapine (Oleanz):** first-line antimanic with mixed-episode evidence; signature is the heaviest metabolic burden of the group; monitor weight, fasting glucose and lipids (CANMAT 2018).
- **Aripiprazole:** D2/D3 and 5-HT1A partial agonist; first-line antimanic, mixed-episode data, favourable metabolic profile; signature is akathisia (CANMAT 2018).

35.7 The critical caution: antidepressants are avoided in the mixed state

This is the crux of the topic. **Antidepressants are avoided** in a mixed state: they worsen the manic pole and drive the agitation, so a mixed "depression" is not treated with an antidepressant, and any antidepressant already running is discontinued (IPS 2017; CANMAT 2018). The IPS guidelines are unusually direct here: do not use antidepressants as monotherapy in bipolar depression, nor in rapid cycling disorder or mixed episodes; if an antidepressant is unavoidable, avoid paroxetine and prefer bupropion, and never as monotherapy (IPS 2017). CANMAT

reserves antidepressants for pure, non-mixed bipolar depression only, and instructs that antidepressants be discontinued in patients presenting with mania (CANMAT 2018). The mechanistic reason is simple: adding a pro-monoaminergic drug to a state that already contains manic activation pours fuel on the exact symptoms driving the risk.

RULE **Treat a mixed state with valproate or an atypical (asenapine, cariprazine) and stop antidepressants.** The mixed pole is managed from the manic side, not the depressive side.

TRAP **Treating the depressive symptoms of a mixed episode with an antidepressant.** It worsens the manic pole and the agitation and raises the suicide risk; discontinue any antidepressant instead.

35.8 ECT for severe or refractory mixed episodes

When the mixed episode is severe, treatment-refractory, or dominated by active suicidality, catatonia or psychosis, ECT is the answer. The IPS names modified ECT as first-line for mixed states with active suicidality and endorses ECT for a mixed episode that is severe, refractory, associated with suicidality, catatonia or psychosis, or occurring in pregnancy (IPS 2017). It is the fastest route to control when pharmacotherapy is too slow or has failed, and it side-steps the antidepressant problem entirely because it is not pole-specific. The ECT technique, electrode placement and cognitive monitoring are owned by the ECT and neurostimulation notes; the wider acute-emergency and perinatal frame is owned by the Perinatal/women's mental health and emergency psychiatry notes.

GOOD TO REMEMBER

- **ECT in a mixed state:** first-line for severe or refractory mixed episodes and for mixed states with active suicidality, catatonia, psychosis or in pregnancy; not pole-specific, so it avoids the antidepressant problem (IPS 2017).

35.9 The mixed-state options at a glance

The whole selection assembles into one table. Learn the highlighted cell in each row, and learn that antidepressants are the row you do not add.

50 to 100	5 to 10	3 to 6
ACUTE-MANIA VALPROATE (MICROG/ML)	ASENAPINE PER DOSE, TWICE DAILY (MG)	CARIPRAZINE ACUTE MANIA (MG/DAY)

OPTION	LINE AND ROLE	DOSE OR SERUM TARGET	SIGNATURE CAUTION
Valproate (divalproex)	**First-line mood stabiliser for dysphoric mania, mixed and rapid-cycling states; beats lithium here**	Acute-mania serum **50 to 100 microg/mL** (350 to 700 micromol/L)	Teratogenic; avoid in women of childbearing potential
Asenapine	**First-line atypical, licensed for acute manic and mixed episodes of bipolar I**	**5 to 10 mg twice daily** sublingually (10 to 20 mg/day)	Sublingual oral hypoaesthesia; no food or drink for 10 minutes

OPTION	LINE AND ROLE	DOSE OR SERUM TARGET	SIGNATURE CAUTION
Cariprazine	**First-line atypical spanning manic, mixed and depressive poles in one agent**	Acute mania **3 to 6 mg/day**, titrate from 1.5 mg	Akathisia (dose-related; slower titration reduces it)
Olanzapine	First-line antimanic with mixed-episode evidence; rapid agitation control	Standard antimanic dosing	**Heaviest metabolic burden of the group**
Aripiprazole	First-line antimanic, mixed-episode data, metabolically favourable	Standard antimanic dosing	Akathisia
Lithium	Anti-suicide agent and first-line antimanic overall, but relatively weaker for classic mixed and dysphoric presentations	Acute-mania serum 0.8 to 1.2 mEq/L	**Underperforms in dysphoric and irritable mania versus divalproex**
ECT	For severe or refractory mixed episodes, active suicidality, catatonia, psychosis or pregnancy	Acute course per protocol	Not pole-specific; avoids the antidepressant problem
Antidepressant	**Avoided: worsens the manic pole and agitation; discontinue any that is running**	Not indicated in the mixed state	Reserved only for pure, non-mixed bipolar depression, never as monotherapy

The mixed-state pharmacotherapy options, CANMAT-led, with the antidepressant row shown as the one you remove; doses and serum targets verified against CANMAT 2018, Stahl 2021 and Kaplan and Sadock 2024.

INDIA

The IPS bipolar guideline is now the 2025 update (IPS 2025, Menon et al.), which keeps divalproex first-line and carbamazepine second-line for acute mixed episodes; the earlier 2017 guideline (Grover and Avasthi et al.) still gives the sharpest examinable line for the mixed state: antidepressants are not used as monotherapy in bipolar depression, rapid cycling or mixed episodes, and if an antidepressant is unavoidable, avoid paroxetine and prefer bupropion (IPS 2017). The IPS also flags that suicide risk in bipolar disorder is among the highest of any psychiatric condition (lifetime around 15 to 20 percent) and is greatest in mixed states and the depressive phase, and names modified ECT as first-line for mixed states with active suicidality (IPS 2017). Valproate (Valprol or Encorate; divalproex Valance or Divaa) and olanzapine (Oleanz) are widely and cheaply available in India. Asenapine and cariprazine are the newer atypicals here and a confirmed Indian brand could not be verified from the library, so prescribe them by generic name.

WORKED EXAMPLE

A 29-year-old man is brought in agitated, sleepless for four nights, speaking rapidly and irritably, but voicing hopelessness and a plan to end his life; he has been on an SSRI for a presumed depression for three weeks. This is a dysphoric mania, a mixed state, and the suicide risk is high. The SSRI is **stopped**, not increased. He is started on a mixed-state agent, divalproex titrated to an acute-mania serum level of 50 to 100 microg/mL, or an atypical such as asenapine or cariprazine, with lithium a weaker choice for this dysphoric picture. If agitation, suicidality or refusal of oral medication makes control urgent, or the episode is refractory, ECT is first-line. Nobody adds an antidepressant to this presentation.

COMMON TRAP

Labelling the presentation "bipolar depression" because the mood is low and the patient is suicidal, then reaching for an antidepressant. If manic-side symptoms co-exist, agitation, racing thoughts, reduced sleep, pressured speech, irritability, it is a mixed state, and the antidepressant is the wrong drug. Manage it from the manic side with valproate or an atypical and stop any antidepressant.

PEARL

Read the drive, not just the mood. A suicidal patient who is also energised, sleepless and pressured has the lethal combination the mixed state is famous for: the despair supplies the intent and the manic activation supplies the capacity to act. That is why the mixed state is the highest-risk phase and why you treat it from the manic pole.

HOLD THIS

A mixed state is high-suicide-risk and does not respond like a pure pole: treat it with valproate or an atypical such as asenapine or cariprazine (olanzapine or aripiprazole also work, lithium is weaker for dysphoric mania), use ECT for severe or refractory cases, and stop antidepressants rather than treating the depressive symptoms with one.

36 . Maintenance and prophylaxis of bipolar disorder

Bipolar disorder is a lifelong, recurrent illness, so the acute episode is only half the task: the harder, higher-yield half is the **maintenance treatment of bipolar** disorder, the long-term relapse prevention that keeps a patient euthymic between episodes. The examiner wants a guideline-anchored answer built around one anchor drug and one organising idea: **lithium is the backbone of maintenance, and you match the agent to the patient's predominant pole.** A resident who can name the first-line maintenance agents, quote the maintenance lithium level, and justify continuing treatment long-term after multiple episodes has the marks.

This is a selection topic, so it is **guidelines**-first. The lead guideline is CANMAT (Yatham 2018); the **Indian Psychiatric Society** position (the **IPS guidelines**, Shah/Grover et al. IPS 2017), the BAP (Goodwin 2016) and NICE (NICE 2014) are corroborating. The acute-episode drug pharmacology sits in the lithium and valproate topics; the neurobiology of mood and the wider guideline-anchored management PLAN belong to the Mood disorders: classification, depressive

and bipolar syndromes, neurobiology notes; the perinatal and acute-emergency frame to the Perinatal/women's mental health and emergency psychiatry notes.

36.1 The goal of maintenance: prevent both poles, not just the last one

What maintenance is for. Maintenance (also called continuation-plus-prophylaxis) aims to prevent recurrence of both manic and depressive episodes, reduce sub-syndromal symptoms, lower suicide risk, and preserve function (Yatham 2018; Maudsley 2021). Bipolar disorder spends more time in the depressive than the manic pole, so an agent that only blocks mania leaves the commonest source of morbidity untreated.

Prophylaxis as the frame. The word **prophylaxis** captures the core intent: because relapse is the rule, treatment is preventive rather than reactive, and the default assumption is that an effective agent is continued well beyond symptomatic recovery (Maudsley 2021).

RULE **Maintenance protects both poles.** Judge a maintenance agent by whether it prevents the depressive pole as well as mania, since depression dominates the bipolar course.

36.2 CANMAT first-line maintenance: lithium the anchor

The verified first-line set. CANMAT names, as first-line maintenance monotherapy for bipolar I disorder: lithium, quetiapine, divalproex, lamotrigine, asenapine, and aripiprazole, alone or in combination (Yatham 2018). Lithium (Licab, Intalith) is the anchor: it is the single best-evidenced prophylactic agent and the only psychotropic with a dedicated anti-suicidal signal (Maudsley 2021; Yatham 2018). The target **maintenance treatment of bipolar** lithium level is **0.6 to 1.0 mEq/L** (Yatham 2018).

The anti-suicidal evidence. Lithium reduces the risk of suicide and of relapse requiring hospitalisation (relative risk about 0.34 in one analysis), and this mortality benefit is specific to the ion and not shared by valproate (Maudsley 2021). This is why lithium is preferred in a bipolar patient with any suicide-risk history; the full suicide risk assessment belongs to the Somatic-symptom, sexual, impulse-control disorders and suicide notes.

AGENT (INDIAN BRAND)	MECHANISM / CLASS	POLE IT BEST PREVENTS	KEY MAINTENANCE NUMBER	SIGNATURE CAUTION
Lithium (Licab, Intalith)	Monovalent cation; GSK3-beta and inositol effects	Both poles; best anti-manic and anti-suicidal	Level 0.6 to 1.0 mEq/L	Renal, thyroid, calcium; narrow window
Quetiapine (Qutipin)	Atypical antipsychotic; D2 and 5-HT2A, norquetiapine NET	Both poles (broad-spectrum)	Continue effective acute dose	Metabolic gain, sedation
Divalproex (Valance, Divaa)	Anticonvulsant; enhances GABA, blocks Na channels	Manic pole predominantly	Level about 50 to 100 mcg/mL	Teratogen; avoid in childbearing potential

AGENT (INDIAN BRAND)	MECHANISM / CLASS	POLE IT BEST PREVENTS	KEY MAINTENANCE NUMBER	SIGNATURE CAUTION
Lamotrigine (Lamitor, Lametec)	Anticonvulsant; blocks Na channels, cuts glutamate	Depressive pole (weak for mania)	Target about 200 mg/day; slow titration	Rash / Stevens-Johnson; titrate from 25 mg
Asenapine	Atypical antipsychotic; broad D2 and 5-HT2A	Manic pole predominantly	Sublingual; continue effective dose	Oral hypoaesthesia, sedation
Aripiprazole (oral or LAI)	D2 partial agonist	Manic pole (does not prevent depression)	Once-monthly LAI option	Akathisia; poor for depressive pole

CANMAT first-line maintenance monotherapy agents for bipolar I disorder, mapped to predominant pole and the one maintenance number to hold (Yatham 2018; Maudsley 2021). Lithium and lamotrigine highlighted as the two polarity anchors.

TRAP **Using aripiprazole or asenapine alone in a depression-predominant patient.** These prevent mania but not the depressive pole; the patient keeps relapsing into depression on apparently adequate maintenance.

36.3 The polarity index: matching the agent to the predominant pole

The concept. The **polarity index** (Popovic et al. 2012) quantifies whether a maintenance drug is more anti-manic or more anti-depressive: it is the ratio of the number-needed-to-treat to prevent depression over the NNT to prevent mania (New Oxford 2020; Tasman 2015). A polarity index above 1 marks a manic-predominant agent; below 1 marks a depressive-predominant agent. This gives the clinical **match the polarity** heuristic a number.

The values to hold. Lithium sits close to balanced at **1.39** (mildly manic-predominant but effective both ways); lamotrigine is the strongly depressive-predominant agent at **0.40**; quetiapine is near-balanced at 1.14; olanzapine 2.98 and risperidone LAI 12.09 are strongly manic-predominant (Popovic et al. 2012; Tasman 2015). So a patient whose recurrences are mostly depressive is anchored on lithium and lamotrigine; one whose recurrences are mostly manic leans to an antipsychotic or divalproex.

1.39	0.40	12.09
LITHIUM POLARITY INDEX	LAMOTRIGINE POLARITY INDEX	RISPERIDONE LAI POLARITY INDEX

PEARL

Read the polarity index as a compass: above 1 points to mania-prevention (antipsychotics, divalproex), below 1 points to depression-prevention (lamotrigine at 0.40). Lithium near 1.39 is the all-rounder you build around and then add a pole-matched partner if one pole keeps breaking through.

36.4 Lamotrigine for the depressive pole

Its niche. Lamotrigine (Lamitor, Lametec) is the maintenance agent for the depressive pole: it prevents depressive recurrence well but is weak against mania, so it is rarely used as the sole agent in a mania-predominant patient (Yatham 2018; Maudsley 2021). It is added or substituted when depression is the recurring problem.

The titration rule. Because of the risk of rash and Stevens-Johnson syndrome, lamotrigine must be titrated slowly, starting at **25 mg/day** and building over weeks to a target near **200 mg/day** (Yatham 2018; Maudsley 2021). Valproate roughly doubles lamotrigine levels and mandates a halved lamotrigine dose and even slower titration.

TRAP **Titrating lamotrigine too fast, or forgetting the valproate interaction.** Rapid escalation, or full-speed titration alongside valproate, sharply raises the Stevens-Johnson risk.

36.5 The LAI option for non-adherence

When to reach for a depot. Non-adherence is the leading modifiable driver of relapse, so in a repeatedly non-adherent patient CANMAT offers a long-acting injectable antipsychotic to prevent recurrence: risperidone LAI every 2 weeks or aripiprazole once-monthly (Yatham 2018). The BAP concurs, recommending a depot antipsychotic for prophylaxis against manic recurrence when oral adherence is erratic (Goodwin 2016). Mirror-image data show fewer admissions and bed-days after switching to an LAI of aripiprazole or paliperidone (Maudsley 2021).

The polarity caveat. LAI antipsychotics are strongly manic-predominant (risperidone LAI polarity index 12.09), so they protect against mania far more than depression; a depression-prone non-adherent patient still needs a pole-matched agent alongside (Popovic et al. 2012).

36.6 What IPS, BAP and NICE recommend

The Indian Psychiatric Society. The **IPS guidelines** (the **Indian Psychiatric Society** bipolar CPG, Shah/Grover et al. IPS 2017) keep lithium as the first-choice long-term prophylactic agent, valued for its prophylactic and anti-suicidal evidence, with valproate, carbamazepine, lamotrigine and atypical antipsychotics as alternatives, and psychoeducation as the non-pharmacological base (IPS 2017). The IPS agrees the drug that controlled the acute episode is the rational one to continue long-term. Note: the IPS bipolar CPG is not in the guideline database used for this note, so its first-line ranking is stated here as consistent with the parsed sources rather than DB-verified.

BAP. Continue the lithium or valproate that treated the acute manic episode as a rational long-term choice, and consider a depot antipsychotic where adherence is poor (Goodwin 2016).

NICE. NICE positions lithium as the first-line long-term pharmacological treatment for bipolar disorder, with valproate second-line (avoided in women of childbearing potential), and olanzapine or quetiapine as further options (NICE 2014).

INDIA

Lead with the Indian brand: lithium carbonate is Licab or Intalith, divalproex is Valance or Divaa, sodium valproate is Valprol or Encorate, lamotrigine is Lamitor or Lametec, quetiapine is Qutipin, olanzapine is Oleanz. Lithium remains cheap and widely stocked, which matters for a lifelong prophylactic; the IPS and CANMAT positions converge on lithium as the maintenance anchor.

36.7 Choice and duration: how long to continue

The duration rule. This is the **choice and duration** question the examiner presses on. Maintenance is long-term and often indefinite: after multiple episodes, or after even one severe episode (for example with high suicide risk, psychosis, or major functional damage), prophylaxis is continued for years and frequently for life (Maudsley 2021; Yatham 2018). There is no fixed stop point analogous to the 6-to-9-month continuation rule in unipolar depression; the recurrent nature of the illness means treatment is not routinely withdrawn after a good year.

Choosing the agent. Choose by (i) what worked acutely (continue it), (ii) the predominant polarity (lithium or lamotrigine for depressive-predominant; antipsychotic or divalproex for manic-predominant), (iii) suicide risk (favour lithium), and (iv) childbearing potential (avoid valproate) (Yatham 2018; Maudsley 2021).

RULE **Anchor on lithium, match the polarity, continue long-term.** After multiple or severe episodes, maintenance is indefinite, not a one-year course.

TRAP **Stopping maintenance after one good year and inviting relapse.** Withdrawing a prophylactic mood stabiliser after a single well year, especially abruptly, sharply raises recurrence risk (rebound mania is a particular hazard with abrupt lithium withdrawal).

36.8 Relapse prevention: predictors and the psychosocial base

The evidence. The **relapse prevention** evidence is strongest for lithium among pharmacological agents, and adding a structured psychosocial intervention lowers relapse further (Yatham 2018). CANMAT makes adjunctive psychoeducation a first-line relapse-prevention intervention in euthymic patients (for example the Barcelona or Life Goals programmes, at least 5 sessions) (Yatham 2018).

The predictors of relapse. The modifiable and non-modifiable predictors a resident should list: non-adherence (the single biggest modifiable driver), residual or sub-syndromal symptoms, comorbid substance use, sleep and circadian disruption, high expressed emotion in the family, and stressful life events (Yatham 2018; Maudsley 2021). The **psychoeducation** and lifestyle base (regular sleep and routine, mood monitoring, early-warning-sign action plans, substance avoidance) targets exactly these.

WORKED EXAMPLE

A 30-year-old woman with bipolar I, three lifetime episodes (two depressive, one manic) and one past suicide attempt, is euthymic on lithium (Licab) at a level of 0.7 mEq/L. Because her recurrences are depression-predominant and she has a suicide history, lithium is the correct anchor (anti-suicidal, near-balanced polarity index 1.39); lamotrigine (Lamitor) is added for the depressive pole given its polarity index of 0.40. She joins a psychoeducation group, keeps a sleep and mood chart, and treatment is planned as long-term rather than time-limited.

36.9 Flibanserin: a note at the mood-sexual interface

What it is and is not. Flibanserin is included here only to fix its place at the **sexual-interface**: it is a **flibanserin** agent for **hypoactive sexual desire** disorder (HSDD) in premenopausal women, a 5-HT1A agonist and 5-HT2A antagonist that in the prefrontal cortex lowers serotonin and raises noradrenaline and dopamine (Kaplan and Sadock 2024). It was originally trialled as an antidepressant and failed, so it is emphatically not a mood stabiliser and has no maintenance role in bipolar disorder.

The one fact to hold. Flibanserin is FDA-approved (2015), dosed at **100 mg** at night, with dizziness, sedation and fatigue as its common adverse effects and a historical caution about alcohol and hypotension (Kaplan and Sadock 2024). It matters for the exam as a discriminator: a serotonergic mood/sexual-interface drug for female HSDD, distinct from any bipolar prophylactic.

HOLD THIS

Bipolar maintenance is anchored on lithium (level 0.6 to 1.0 mEq/L, anti-suicidal), lamotrigine is added for the depressive pole, you match the agent to the predominant polarity, and you continue long-term after multiple or severe episodes.

MNEMONIC

LQ-DLAA

The six CANMAT first-line maintenance agents: Lithium, Quetiapine, Divalproex, Lamotrigine, Asenapine, Aripiprazole. Lead the list with Lithium (the anchor) and remember Lamotrigine is the one for the depressive pole.

GOOD TO REMEMBER

- **Lithium (Licab, Intalith):** monovalent cation (GSK3-beta and inositol effects); best prophylactic and only anti-suicidal mood stabiliser; maintenance level 0.6 to 1.0 mEq/L, polarity index 1.39. First-line maintenance anchor.
- **Quetiapine (Qutipin):** atypical antipsychotic (D2 and 5-HT2A, norquetiapine NET); broad-spectrum, near-balanced polarity index 1.14; metabolic gain and sedation are the signature caution. First-line maintenance.
- **Divalproex (Valance, Divaa):** anticonvulsant (GABA enhancement, Na-channel block); manic-predominant; teratogen, so avoid in women of childbearing potential. First-line maintenance.
- **Lamotrigine (Lamitor, Lametec):** Na-channel blocker cutting glutamate; the depressive-pole agent (polarity index 0.40), weak for mania; rash / Stevens-Johnson signature, titrate from 25 mg to about 200 mg/day. First-line for depression-predominant maintenance.
- **Asenapine:** sublingual atypical antipsychotic (broad D2 and 5-HT2A); manic-predominant; oral hypoaesthesia is the signature. First-line maintenance.
- **Aripiprazole (oral or once-monthly LAI):** D2 partial agonist; prevents mania but not depression; akathisia signature; the once-monthly LAI is the non-adherence option. First-line maintenance monotherapy.
- **Flibanserin:** 5-HT1A agonist / 5-HT2A antagonist for female hypoactive sexual desire disorder; 100 mg nocte; NOT a mood stabiliser, no bipolar maintenance role. The mood-sexual-interface discriminator.

Apply and consolidate

37 . Apply: four worked pharmacotherapy vignettes

The mood-block pharmacotherapy syllabus is easiest to hold when it is rehearsed as clinical decisions rather than drug lists, and the exam frequently poses exactly that: a short case, a demand for the next drug, and an implied demand for the reasoning behind it. This closing topic runs **four** short worked vignettes that each fuse a scenario, the reasoning and the resolution, so that the antidepressant-selection, lithium-initiation, emergency and treatment-resistance chapters are exercised together as they will be at the bedside.

How to read each vignette. Every vignette below is presented as a worked example: it starts with the case (each opens with the literal marker "case:"), states the reasoning against a named guideline or a verified dose, and ends with the resolution and the trade-off. The class detail behind each is developed in the parent topics; here the skill is **application**. Doses, serum levels and first-line agents are verified against the Maudsley Prescribing Guidelines, Stahl, CANMAT, the BAP and the Indian Psychiatric Society CPGs (Maudsley 2021; Stahl 2021; CANMAT 2016; Malhi 2015; Gautam 2017). Where a brand is named it leads with the Indian brand.

37.1 Vignette 1: an antidepressant choice in comorbid depression with chronic pain and prior SSRI sexual dysfunction

The decision. This vignette is a **selection** problem: two patient-specific factors, a comorbid pain syndrome and an intolerable adverse effect on the previous drug, should steer the choice off the default SSRI. The reasoning turns on matching the drug's secondary pharmacology to the comorbidity, and its adverse-effect profile to what the patient could not tolerate before. Both

candidates below are CANMAT first-line agents, so the choice is a trade-off, not a hierarchy (CANMAT 2016).

WORKED EXAMPLE

Case: a 46-year-old man with a moderate depressive episode and long-standing diabetic neuropathic pain. A prior trial of an SSRI (escitalopram) helped his mood but caused marked sexual dysfunction that he found intolerable, and he stopped it. Reasoning: the SSRI class as a whole causes sexual dysfunction through serotonin-transporter blockade, so simply swapping to another SSRI is likely to reproduce the problem; the comorbid neuropathic pain is a positive reason to choose a drug that treats both targets. The two rational off-SSRI choices are an SNRI, duloxetine (Duzela), which is CANMAT first-line for major depression at 60 mg/day and separately licensed for diabetic neuropathic pain and fibromyalgia because of its noradrenergic action on descending spinal pathways; or bupropion (Bupron), a noradrenaline-dopamine reuptake inhibitor that is CANMAT first-line at 150 to 300 mg/day and carries the lowest sexual-dysfunction rate of the common antidepressants. Resolution: duloxetine is the sharper choice here because it treats the depression and the neuropathic pain with one drug, and it does not aggravate the previous problem the way another SSRI would; the trade-off is that duloxetine, like the SSRIs, can itself cause some sexual dysfunction, whereas bupropion would spare sexual function most fully but does nothing for the pain. If the sexual adverse effect were the single dominant concern and there were no pain, bupropion would be the first pick.

The trade-off stated cleanly. Duloxetine (Duzela) 60 mg/day wins on the pain comorbidity; bupropion (Bupron) 150 to 300 mg/day wins on sexual tolerability. A third option, mirtazapine (Mirtaz) 15 to 45 mg/day, also spares sexual function and aids sleep and appetite but does not treat pain (Stahl 2021; CANMAT 2016). Both duloxetine and bupropion require the standard adequate-trial window before they can be judged: response is assessed at 4 weeks and again at 6 to 8 weeks (BAP 2015; CANMAT 2016). The SSRI-versus-SNRI class detail and the full antidepressant-selection algorithm are set out in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes.

RULE **Let the comorbidity and the prior intolerance pick the antidepressant.** Comorbid pain points to duloxetine; prior sexual dysfunction points to bupropion or mirtazapine, never to a second SSRI.

TRAP **Swapping one SSRI for another after SSRI-induced sexual dysfunction.** The adverse effect is a serotonin-transporter class effect, so a second SSRI usually reproduces it; switch class, not molecule.

37.2 Vignette 2: lithium initiation, target level, the twelve-hour trough and the no-NSAID counselling

The decision. This vignette is an **initiation and monitoring** problem: the baseline work-up, the target serum level for the phase being treated, the sampling rule, and the interaction counselling that keeps the patient out of toxicity. Every figure below is verified (Maudsley 2021; Yatham 2018; Shah 2017).

WORKED EXAMPLE

Case: a 30-year-old woman with bipolar I disorder, recovering from an acute manic episode, for whom lithium is chosen for maintenance. Reasoning: before the first tablet, establish the two organs lithium threatens and the cardiac baseline. The baseline work-up is renal function (eGFR, creatinine, urea and electrolytes), thyroid function (TSH), serum calcium, weight or BMI, an ECG where there are cardiovascular risk factors, and, because lithium is a human teratogen (Ebstein anomaly), a pregnancy test with contraception counselling in a woman of child-bearing potential (Maudsley 2021; Yatham 2018). Start lithium carbonate (Licab, or the controlled-release Intalith CR) and titrate to a maintenance target of 0.6 to 1.0 mmol/L, drawing the level as a twelve-hour trough: the blood is taken 12 hours (ideally 10 to 14 hours) after the last dose, which for a bedtime dose means the next morning before the day's tablet. Recheck the trough 5 to 7 days after each dose change, then roughly 3-monthly once stable, with renal and thyroid function about 6-monthly. Resolution: counsel the patient that anything reducing renal lithium clearance raises the level and can cause toxicity, so she must avoid NSAIDs (ibuprofen, diclofenac) for pain and tell any doctor she is on lithium before starting a thiazide diuretic or an ACE inhibitor; she should keep well hydrated, and report tremor, ataxia, slurred speech, vomiting or diarrhoea at once as toxicity signs.

The phase sets the target. In acute mania the target trough is higher, 0.8 to 1.2 mmol/L, and it steps down to 0.6 to 1.0 mmol/L for maintenance; toxicity appears reliably above 1.5 mmol/L (Yatham 2018; Maudsley 2021). The twelve-hour trough and the 5-to-7-day recheck after a dose change are the two most-tested sampling facts, developed in full in the lithium-monitoring topic of these mood-block notes.

0.6 to 1.0	0.8 to 1.2	12	1.5
MAINTENANCE LITHIUM (MMOL/L)	ACUTE MANIA TARGET (MMOL/L)	TROUGH SAMPLING (HOURS POST-DOSE)	TOXICITY THRESHOLD (MMOL/L)

RULE **Draw lithium as a twelve-hour trough and counsel against NSAIDs.** The **12-hour** post-dose sample is the only interpretable level; NSAIDs, thiazides and ACE inhibitors raise the level toward toxicity.

TRAP **Checking a lithium level at the wrong time.** A non-trough sample drawn a few hours post-dose reads falsely high and invites a wrong dose cut; standardise to 12 hours every time.

INDIA

Lithium carbonate is cheap and heavily prescribed in India as Licab and the controlled-release Intalith CR, and the serum assay is inexpensive and widely available. The practical failure point is the twelve-hour trough discipline in a busy outpatient department, so counsel the patient to attend fasting in the morning before the day's dose and to note the time of the last tablet. Over-the-counter NSAID use for musculoskeletal pain is common and unsupervised, which makes the no-NSAID counselling a genuine safety instruction, not a formality.

37.3 Vignette 3: suspected serotonin syndrome on an SSRI plus tramadol, reasoned through the Hunter criteria

The decision. This vignette is a **recognition and emergency-management** problem: identify the syndrome from a combination of a serotonergic antidepressant and a serotonergic analgesic, apply the diagnostic rule, take the first management step, and separate it from its dopamine-blocker mimic. The management sequence and the discriminator are verified (Maudsley 2021; Kaplan and Sadock 2024).

WORKED EXAMPLE

Case: a 52-year-old man on sertraline (Serta) for depression is given tramadol for acute back pain and within hours becomes agitated, sweaty and febrile at 39 degrees Celsius, with dilated pupils, a tachycardia of 130, brisk lower-limb reflexes and sustained ankle clonus. Reasoning: sertraline plus tramadol is a two-drug serotonergic combination, and tramadol is itself weakly serotonergic, so this is the classic precipitant of serotonin syndrome. Apply the Hunter Serotonin Toxicity Criteria: in a patient on a serotonergic agent, the diagnosis is met by any one of spontaneous clonus; inducible clonus with agitation or diaphoresis; ocular clonus with agitation or diaphoresis; tremor plus hyperreflexia; or hypertonia plus temperature above 38 degrees Celsius plus ocular or inducible clonus. This patient has spontaneous clonus, which alone satisfies the Hunter criteria. Resolution: the first and most important step is to stop all serotonergic agents at once (both the sertraline and the tramadol); then give supportive care with intravenous fluids and active cooling for the hyperthermia, sedate with a benzodiazepine for agitation and neuromuscular hyperactivity, and in this moderate-to-severe case give cyproheptadine (Ciplactin, or Practin), a 5-HT2A antagonist, orally as the serotonin-antagonist antidote, a common regimen being an initial 12 mg then 2 mg every two hours if symptoms persist, to a ceiling around 32 mg in 24 hours. Most cases resolve within about 24 hours of stopping the trigger.

The NMS differential is the point. Serotonin syndrome and neuroleptic malignant syndrome share hyperthermia, rigidity, autonomic instability and altered consciousness, so the examiner rewards the one discriminator: serotonin syndrome follows a serotonergic drug, comes on rapidly over hours, and shows clonus with hyperreflexia; neuroleptic malignant syndrome follows a dopamine-blocker, comes on slowly over days, and shows lead-pipe rigidity with hyporeflexia and a markedly raised creatine kinase, often above 1000 units per litre (Maudsley 2021). The wider acute-emergency management frame is set out in the Perinatal/women's mental health and emergency psychiatry notes.

clonus	hours	12 then 2
THE HUNTER ANCHOR AND NMS DISCRIMINATOR	SEROTONIN-SYNDROME ONSET AFTER TRIGGER	CYPROHEPTADINE (MG, INITIAL THEN Q2H)

RULE **Stop the serotonergic drugs first, then support, sedate and give cyproheptadine.** Clonus with hyperreflexia in a patient on a serotonergic agent is serotonin syndrome until proven otherwise.

TRAP **Missing serotonin syndrome when an SSRI meets tramadol, or mislabelling it as NMS.** Tramadol is serotonergic; clonus and hyperreflexia (not lead-pipe rigidity) separate serotonin syndrome from its dopamine-blocker mimic.

INDIA

Tramadol is casually co-prescribed for musculoskeletal pain across Indian practice, so the highest-risk everyday scenario is a patient already on an antidepressant who is given tramadol. Cyproheptadine is freely available in India as an oral antihistamine (commonly stocked as Ciplactin or Practin), which makes the specific antidote easy to obtain once moderate-to-severe serotonin syndrome is recognised.

37.4 Vignette 4: treatment-resistant depression up the augmentation ladder

The decision. This vignette is an **escalation-discipline** problem: before augmenting, prove the depression is genuinely resistant and not merely under-treated, then climb the augmentation ladder in the guideline order. Every guideline opens the treatment-resistant depression pathway with a mandatory review of adequacy and diagnosis before any escalation (CANMAT 2016; BAP 2015; Gautam 2017).

WORKED EXAMPLE

Case: a 40-year-old woman with a major depressive episode that has not remitted despite an SSRI (escitalopram) followed by an SNRI (venlafaxine). Reasoning: first confirm this is true resistance, defined as failure of at least two adequate antidepressant trials in the current episode, each at an adequate dose for an adequate duration (response judged at 4 weeks and again at 6 to 8 weeks). Confirm each trial actually reached a therapeutic dose and was taken long enough, and confirm adherence, because most apparent resistance is pseudoresistance from an inadequate dose, an inadequate duration, poor adherence or a wrong diagnosis; review the diagnosis for a missed bipolar disorder, psychotic depression, or an organic or substance cause. Resolution: with two genuinely adequate failures confirmed, augment rather than endlessly switch. The first-line augmentation moves are to add lithium (Licab) 600 to 1200 mg/day titrated to a therapeutic serum level, or to add an atypical antipsychotic such as aripiprazole 2 to 15 mg/day or quetiapine (Qutipin) 150 to 300 mg/day (CANMAT 2016; BAP 2015). If augmentation fails, the next tier is the glutamatergic and neurostimulation options: add intranasal esketamine (Spravato) to an SSRI or SNRI for patients who have failed at least two adequate antidepressant trials, monitoring blood pressure and dissociation, or refer for electroconvulsive therapy, which is considered for patients who have not responded to other treatments and is the treatment of choice in severe, psychotic or high-suicide-risk depression.

The ladder in order. Optimise and confirm adequacy and adherence, review the diagnosis, then augment with lithium or an atypical (first-line augmentation), then move to esketamine or ECT. Lithium augmentation has the best evidence in older people, and CANMAT places aripiprazole, brexpiprazole, quetiapine and lithium among the first-line adjuncts, with esketamine reserved for at least two failed trials (BAP 2015; CANMAT 2016). The staging systems (Thase-Rush, Maudsley staging method) and the full ladder are developed in the treatment-resistant depression topic; the ECT technique itself is in the ECT and neurostimulation notes.

STEP	ACTION	AGENT / DOSE (VERIFIED)
1	**Confirm adequacy and adherence, review diagnosis**	Two adequate trials at therapeutic dose, judged at 4 and 6 to 8 weeks; exclude bipolar, psychotic, organic and substance causes
2	Optimise the current antidepressant	Raise a low or marginal dose to a recommended therapeutic dose first
3	**First-line augmentation: lithium or an atypical**	Lithium 600 to 1200 mg/day (to therapeutic serum level); aripiprazole 2 to 15 mg/day; quetiapine 150 to 300 mg daily
4	Glutamatergic or neurostimulation	Intranasal esketamine added to an SSRI/SNRI after 2 failed adequate trials; or ECT

The treatment-resistant depression ladder as applied in the vignette: confirm resistance and adherence, optimise, augment with lithium or an atypical, then esketamine or ECT (CANMAT 2016; BAP 2015). Highlighted steps are the board-critical moves.

RULE **Prove adequacy and adherence before you augment.** Two adequate trials must fail in the current episode; then augment with lithium or an atypical before moving to esketamine or ECT.

TRAP **Stopping at response instead of remission, or escalating over pseudoresistance.** Response without remission relapses; an inadequate dose, an inadequate duration or a missed bipolar diagnosis is under-treatment, not resistance.

GOOD TO REMEMBER

- **Vignette 1, antidepressant choice:** comorbid pain plus prior SSRI sexual dysfunction reasons to duloxetine (Duzela) 60 mg/day (treats pain and mood, CANMAT first-line SNRI) or bupropion (Bupron) 150 to 300 mg/day (lowest sexual-dysfunction rate); never a second SSRI for a class-effect adverse event.
- **Vignette 2, lithium initiation:** baseline renal (eGFR/creatinine), thyroid (TSH), calcium, weight, ECG where indicated, and pregnancy test; maintenance target 0.6 to 1.0 mmol/L (acute mania 0.8 to 1.2); draw a twelve-hour trough; counsel no NSAIDs, and caution with thiazides and ACE inhibitors.
- **Vignette 3, serotonin syndrome:** SSRI plus tramadol, Hunter criteria met by spontaneous clonus; stop all serotonergic agents first, then support and cool, benzodiazepine, then cyproheptadine (Ciplactin/Practin) 12 mg then 2 mg every 2 hours; clonus and hyperreflexia (not lead-pipe rigidity) distinguish it from NMS.
- **Vignette 4, treatment-resistant depression:** confirm two adequate failed trials and adherence, review the diagnosis, then augment with lithium 600 to 1200 mg/day or an atypical (aripiprazole 2 to 15 mg/day, quetiapine 150 to 300 mg/day), then esketamine (Spravato) or ECT.

HOLD THIS

The four clinical moves: match the antidepressant to the comorbidity and the prior intolerance (duloxetine for pain, bupropion for sexual sparing); start lithium on a full baseline work-up with a twelve-hour trough and no-NSAID counselling; in serotonin syndrome stop the serotonergic drugs first and give cyproheptadine; and in resistant depression prove adequacy and adherence before augmenting with lithium or an atypical and then esketamine or ECT.

38 . Consolidate: mnemonic, retrieval and synthesis

This is the closing topic of the mood pharmacotherapy block, and its job is not to add new drug facts but to **consolidate** the ones already taught into a form you can retrieve cold in an examination. Two evidence-based study moves do the heavy lifting: a single master **mnemonic** that chains the whole chapter into four movements so nothing is dropped, and **active recall** against a map you can redraw from memory. The pharmacology and the algorithms are all upstream; here they are re-indexed for retrieval.

The board does not reward a resident who can recognise a fact when prompted; it rewards one who can **generate** it under time pressure. That is why this topic is built around retrieval, not re-reading: the mnemonic is the retrieval cue, the recall prompts are the practice, and the synthesis map is the whole chapter compressed to one page you rebuild without looking. Everything below points back to a topic taught in full elsewhere in these notes.

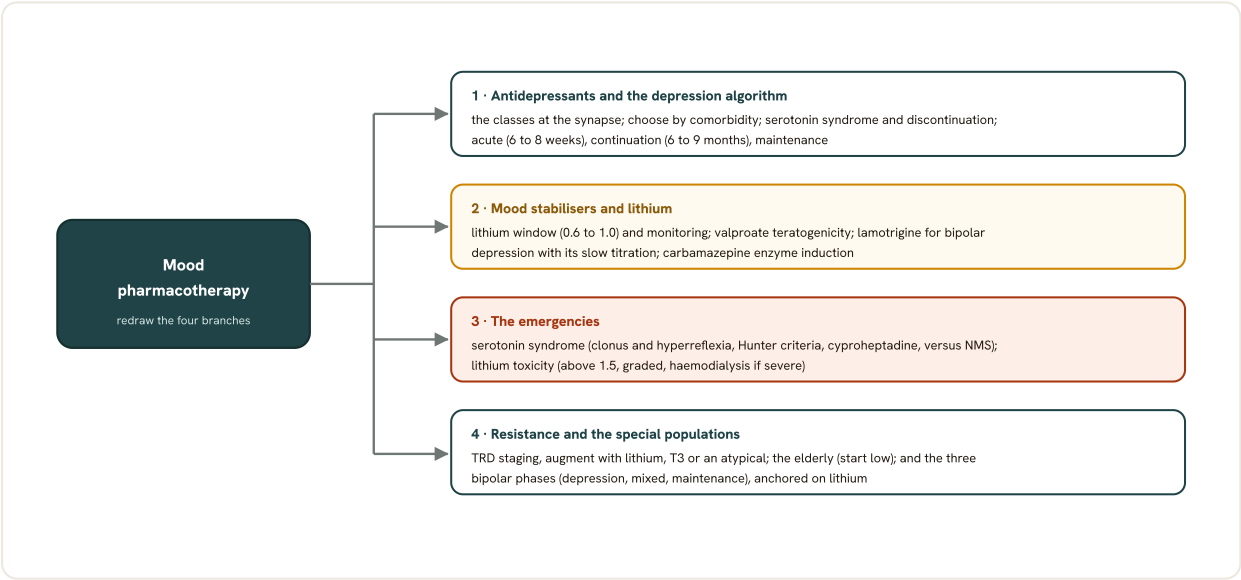


Fig 12.17 The whole chapter at a glance, framed for retrieval: cover the branches and redraw them from memory. The four branches are the antidepressants and the depression algorithm; the mood stabilisers and lithium with their monitoring and teratogenicity; the emergencies (serotonin syndrome and lithium toxicity); and treatment resistance with the special populations and the three bipolar-management phases.

38.1 The master mnemonic: chaining the whole chapter

One handle, four movements. The entire pharmacotherapy block hangs on the Step-2 seed you planted at the outset, and this is its payoff. Hold the whole chapter as **"A SNoM LiVeS, then CALM the STORM, then climb the LADDER"**. The first beat is the antidepressant classes and the depression algorithm; the second is lithium and the mood stabilisers with their monitoring and teratogenicity; the third is the two pharmacological emergencies; the fourth is treatment

resistance, augmentation and the bipolar-phase management. Each capitalised letter is a slot that expands into a full topic, and every fact chained below is verified against the source that owns it (Maudsley 2021; Stahl 2021; CANMAT 2016; CANMAT 2018; Yatham 2018).

MNEMONIC

A SNoM LiVeS, then CALM the STORM, then climb the LADDER

A SNoM is the antidepressant classes and the depression algorithm. **A**ntidepressants classify by synaptic action: SSRIs (SERT block, first-line, escitalopram **10 to 20 mg/day**), **S**NRIs (SERT plus NET, venlafaxine **75 to 225 mg/day** with dose-related blood-pressure rise), **N**aSSA/**N**DRI (mirtazapine, an alpha-2 antagonist that sedates; bupropion, a noradrenaline-dopamine reuptake inhibitor that spares sexual function and lowers the seizure threshold), the **o**lder tricyclics and **M**AOIs (reserved, dangerous, the tyramine and serotonergic hazards), and the **M**ultimodal and glutamatergic agents (vortioxetine, ketamine/esketamine). The depression algorithm is treat by phase to **remission**: acute review every **1 to 2 weeks**, judge by **2 to 4 weeks**, continuation at the same acute dose for **6 to 9 months**, maintenance **2 years or longer** if recurrent (CANMAT 2016). **LiVeS** is the mood stabilisers: **Li**thium (maintenance level **0.6 to 1.0 mmol/L**, twelve-hour trough, specific anti-suicide effect, first-trimester Ebstein signal), **V**alproate (serum **50 to 100 microg/mL**, the highest-risk teratogen: neural-tube defects, major-malformation rate around **10 percent**, dose-related IQ and autism harm, avoided in women of childbearing potential), lamotrigine (the depression pole, titrate **25 to 200 mg/day** slowly for the rash), the Stabiliser antipsychotics and carbamazepine (serum **4 to 12 mg/L**, enzyme induction, HLA-B*1502). **CALM the STORM** is the two emergencies: serotonin syndrome (clonus, hyperreflexia, autonomic instability, altered mental state, rapid over hours; stop the drug and give cyproheptadine) and lithium toxicity (coarse tremor and ataxia, toxic above **1.5 mmol/L**; stop, rehydrate with saline, dialyse if severe). **The LADDER** is treatment resistance and the bipolar phases: prove adequacy first (dose, duration, adherence, diagnosis), then switch, augment (lithium to **0.6 to 1.0 mmol/L**, or an atypical), combine, neuromodulate (ECT); and treat bipolar by phase (mania: lithium/valproate/an atypical, stop the antidepressant; bipolar depression: quetiapine, lurasidone, lithium, lamotrigine, never an antidepressant alone; maintenance: continue what worked, lithium level **0.6 to 1.0 mmol/L**).

RULE **Classify first, then treat by phase and polarity.** A SNoM LiVeS names the drug; CALM the STORM and the LADDER name what to do when it goes wrong or fails.

TRAP **Reciting the mnemonic without the numbers.** The letters are a scaffold; the exam marks fall on the doses, the serum levels and the monitoring intervals hung on each letter, so rehearse the figures, not just the acronym.

38.2 Retrieval practice, cover the answers

Practise generating, not recognising. The single most efficient consolidation move is **active recall**: close the notes and force the fact out, then check. What follows is a set of answer-free prompts spanning the four bands of the chapter. Use them as **retrieval practice**: read a prompt, say or write the full answer aloud from memory, and only then reveal the source topic to mark yourself. The prompts print no answers by design; that is the point of **cover the answers** practice. Space the repetitions across sittings rather than massing them.

RETRIEVAL PRACTICE, COVER THE ANSWERS

1. Name the primary synaptic action of each antidepressant class (SSRI, SNRI, TCA, MAOI, NaSSA, NDRI, multimodal, glutamatergic), and the one signature adverse effect or interaction that belongs to each.
2. State the four phases of the unipolar depression algorithm with the review interval, the response-judging point, the continuation duration and the maintenance duration, and say what defines the end of the acute phase.
3. Give the first-line agents for bipolar depression and state the one thing you never do with an antidepressant in bipolar disorder.
4. Recite the tyramine (cheese-reaction) food list for a patient on an irreversible MAOI, and the two washout intervals when switching to and from an MAOI or fluoxetine.
5. State lithium's molecular target and mechanism, its maintenance and acute serum ranges, the sampling rule (when the level is drawn), and the two anti-suicide claims attached to it.
6. List the lithium monitoring schedule: the trough timing, the recheck interval after a dose change, the ongoing level interval once stable, and the thyroid and renal monitoring intervals.
7. Give the drugs that raise and the drugs that lower the lithium level, and name the teratogenic signal and the trimester it belongs to.
8. State valproate's serum range, its full adverse-effect set, and the complete teratogenicity picture (structural, neurodevelopmental and its dose-dependence) with the prescribing rule that follows.
9. Give the lamotrigine titration and the one drug interaction that forces you to halve the schedule, and name the pole and phase lamotrigine is best for.
10. State carbamazepine's serum range, its three signature hazards, and the effect of its autoinduction on the level.
11. Recite the serotonin syndrome triad, the one sign that discriminates it from neuroleptic malignant syndrome, and the four-step management sequence.
12. Give the lithium toxicity level bands (mild, moderate, severe), the matching clinical features, the classic precipitants, and the four-step management including the dialysis indication.
13. State the definition of treatment-resistant depression, the four adequacy checks you clear before escalating, and the order of the switch-augment-combine-neuromodulate ladder.
14. Name the best-evidenced augmentation agents and the target lithium level for lithium augmentation.
15. Lay out the three bipolar phases (mania, depression, maintenance) with the first-line agents for each and the maintenance lithium level.

TRAP **Re-reading the notes and mistaking familiarity for mastery.** Recognising a fact on the page is not the same as retrieving it under a stem; only cover-the-answers recall trains the generation the board tests.

38.3 The synthesis map: redraw from memory

Rebuild the chapter on one page. The final consolidation move is to draw the whole-chapter **synthesis map** and then **redraw from memory** until it comes out clean. The map is a single

node, the mood pharmacotherapy block, with four branches, each a movement of the master mnemonic. Branch one is the antidepressants and the depression algorithm (the class map keyed to synaptic action, and the acute-continuation-maintenance phases). Branch two is the mood stabilisers and lithium (lithium initiation, monitoring, toxicity and teratogenicity, then valproate, carbamazepine, lamotrigine and the stabiliser antipsychotics). Branch three is the emergencies (serotonin syndrome and lithium toxicity, each with its discriminator and first management step). Branch four is treatment resistance and the special populations (the adequacy work-up and the augmentation ladder, the three bipolar phases, and prescribing in pregnancy and old age). Draw the four branches from the central node, hang the two or three load-bearing numbers on each leaf, and repeat the exercise cold until nothing is missing; the leaves you cannot fill are exactly the topics to revisit.

HOLD THIS

A SNoM LiVeS, then CALM the STORM, then climb the LADDER: four movements, four branches, one page you can redraw from memory.

GOOD TO REMEMBER

- **Branch 1 (antidepressants and the algorithm):** classify by synaptic action, then treat by phase to remission, continuation **6 to 9 months**, maintenance **2 years or longer** if recurrent (CANMAT 2016).
- **Branch 2 (stabilisers and lithium):** lithium maintenance **0.6 to 1.0 mmol/L** at a twelve-hour trough; valproate **50 to 100 microg/mL**, the highest-risk teratogen; lamotrigine for the depressive pole, titrated slowly (CANMAT 2018; Maudsley 2021).
- **Branch 3 (emergencies):** serotonin syndrome is clonus plus hyperreflexia (stop the drug, cyproheptadine); lithium toxicity is coarse tremor and ataxia above **1.5 mmol/L** (stop, saline, dialyse if severe) (Maudsley 2021).
- **Branch 4 (resistance and special populations):** prove adequacy (dose, duration, adherence, diagnosis) before you switch, augment, combine or neuromodulate; treat bipolar by phase and never give an antidepressant alone in bipolar depression (CANMAT 2016; Yatham 2018).
- **The retrieval rule:** generate the fact from a cue and space the repetitions; recognition on re-reading is not the skill the examination tests.

INDIA

For the Indian postgraduate examination, lead every management answer with CANMAT (CANMAT 2016 for depression, CANMAT 2018 and Yatham 2018 for bipolar disorder), then name the Indian Psychiatric Society position (Gautam et al. 2017 for depression, Grover and Avasthi 2017 for bipolar disorder), then note BAP and NICE where they converge (BAP 2015; NICE 2014). The Indian brands are learnt one drug at a time in the individual topics, Indian brand first: for example escitalopram (Nexito or S-Citadep), sertraline (Serta or Daxid), lithium carbonate (Licab or Intalith), sodium valproate (Valprol or Encorate), lamotrigine (Lamitor or Lametec) and quetiapine (Qutipin). Lithium remains a mainstream first-line stabiliser in Indian practice.

Previously asked

Mood pharmacotherapy is examined heavily and at the level of the individual drug: the SSRIs, the SNRIs, lithium, ketamine and the newer antidepressants have each come as standalone short notes, and the management of resistant depression and of refractory bipolar illness recurs as both a short note and the tail of a long essay. The reliable pattern is that every long mood question ends in a guideline-anchored drug plan, and a drug-specific note (a class, an agent, a monitoring rule, an adverse effect) can be asked on its own. The genuine questions on record are grouped by band below. The classification, the clinical syndromes and the neurobiology that these drugs treat are developed in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes.

HOW THIS TERRITORY IS ACTUALLY TESTED

- **Antidepressant classes and agents.** "SSRI antidepressants", "SNRI antidepressants" and "newer antidepressants" have each been asked as 10-mark notes, and "the recent advances in depression and development of antidepressants" as a longer question, so each class must be ready with its mechanism, its representative agents, its adverse-effect signature and its place. "Antidepressants in epilepsy with depression" tests the drug choice in a comorbidity. Prepare the class map, the individual agents and the comorbidity-driven selection. short note and essay, recurring

- **Serotonin syndrome and drug-induced states.** A case of a patient on an antidepressant and an antipsychotic who develops involuntary movements has been asked as a diagnose-investigate-manage question, and serotonin syndrome sits behind any antidepressant-combination scenario. Prepare serotonin syndrome (the Hunter criteria, the discrimination from NMS, the management) and the drug-induced movement disorders by cross-reference. case question, recurring

- **Rapid-acting and novel agents.** "The use of ketamine in depression" has come as a standalone note, so the NMDA mechanism, the rapid effect, the esketamine indication and the monitoring must be exam-ready, and the glutamatergic and other novel agents are worth a line. short note

- **Lithium and the mood stabilisers.** "Lithium" is a classic 10-mark note (mechanism, indications, the therapeutic range, monitoring, toxicity and the organ effects), and "carbamazepine" recurs across the papers. Prepare lithium in full, and valproate, carbamazepine and lamotrigine with their monitoring and their signature risks (valproate teratogenicity, lamotrigine and Stevens-Johnson). short note, recurring

- **Treatment resistance and bipolar management.** "The management of resistant depression" and "the management of treatment-resistant depression" have both come as standalone questions, and "the conceptual overview of bipolar spectrum disorder with the management of treatment-refractory bipolar II" and "the clinical features, differential diagnosis and management of bipolar depression" as essays. Prepare the TRD staging and augmentation ladder, and the three dedicated bipolar-management topics (bipolar depression, mixed episodes and maintenance), guideline-first. essay and short note, recurring

Prepare this material to be prescribed and monitored, not just recited: the class map, the dose-anchored good-to-remember boxes, the lithium monitoring and toxicity figures, the serotonin-syndrome differential and the guideline-anchored selection and management topics in these notes are built to the way the block is examined. The mood classification, the clinical syndromes and the neurobiology live in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes; the ECT and neurostimulation technique lives in the ECT and neurostimulation notes; the full clinical suicide risk assessment lives in the Somatic-symptom, sexual, impulse-control disorders and suicide notes; and the wider perinatal and emergency frames live in the Perinatal/women's mental health and emergency psychiatry notes.

Quick review

The whole subject in one table	
ANTIDEPRESSANT CLASSES	Classify by the primary synaptic action: reuptake inhibitors (SSRI at SERT, SNRI at SERT and NET, TCA at both plus H1/M1/alpha-1 blockade), enzyme inhibitors (irreversible MAOI, reversible moclobemide), receptor-acting (mirtazapine NaSSA, bupropion NDRI), multimodal (vortioxetine, agomelatine, trazodone) and glutamatergic (ketamine, esketamine). The site predicts the tolerability and the dangerous interactions.
SSRIS	First-line, broadly equal in efficacy; differ in half-life, interactions and adverse-effect emphasis. Fluoxetine (long half-life, activating), sertraline (broadest), escitalopram and citalopram (cleanest, dose-dependent QTc, citalopram capped at 40 mg/day), paroxetine (short half-life, anticholinergic, worst discontinuation, avoid in pregnancy), fluvoxamine (OCD, CYP1A2). Class effects: GI upset, sexual dysfunction, hyponatraemia/SIADH in the elderly, bleeding with NSAIDs, early activation.
SNRIS AND TCAS	SNRIs: venlafaxine (dose-dependent noradrenergic effect and blood-pressure rise, marked discontinuation), desvenlafaxine, duloxetine (neuropathic pain). TCAs: reuptake blockade plus off-target H1/M1/alpha-1 (the adverse effects); dangerous in overdose (quinidine-like cardiotoxicity, QRS widening, seizures), so weigh the suicide risk; amitriptyline, imipramine, clomipramine (OCD), nortriptyline (best tolerated).
MAOIS	Irreversible non-selective (phenelzine, tranylcypromine) or reversible RIMA (moclobemide, safer). Tyramine (cheese) reaction gives a hypertensive crisis; never combine with a serotonergic drug (serotonin syndrome). Washout: at least two weeks off an MAOI before a serotonergic drug; about one week off most SSRIs/SNRIs (two off a TCA) before an MAOI; five weeks off fluoxetine before an MAOI.
MIRTAZAPINE, BUPROPION, NEWER	Mirtazapine (NaSSA): sedation and weight gain (more at low dose), minimal sexual dysfunction, for depression with insomnia and poor appetite. Bupropion (NDRI): activating, low sexual dysfunction, smoking cessation, lowers the seizure threshold (avoid in seizure and eating disorders). Newer: vortioxetine and vilazodone (multimodal), agomelatine (melatonergic, needs LFT monitoring), trazodone (SARI, priapism), tianeptine.

The whole subject in one table	
SEROTONIN SYNDROME VS NMS	Serotonin syndrome: rapid onset from a serotonergic combination; clonus, hyperreflexia, tremor, hyperthermia, hyperactive bowel sounds, mydriasis; Hunter criteria; stop the agent, supportive care, cyproheptadine. NMS: slow onset from a dopamine blocker; lead-pipe rigidity, hyporeflexia, marked CK rise; dantrolene, bromocriptine. The pivot is clonus and hyperreflexia (serotonin) versus lead-pipe rigidity (NMS).
KETAMINE, DISCONTINUATION	Ketamine and esketamine (NMDA antagonists): rapid effect within hours via AMPA and synaptogenesis; esketamine (intranasal) for treatment-resistant depression and MDD with acute suicidality, given under observation for dissociation and blood pressure; effect is transient. Discontinuation syndrome (FINISH: flu-like, insomnia, nausea, imbalance, sensory zaps, hyperarousal): worst with paroxetine and venlafaxine, least with fluoxetine; taper slowly, it is not addiction.
CHOOSING AND THE PHASES	First-line agents are equal in efficacy, so choose by comorbidity, adverse-effect profile, past response, safety and cost (CANMAT lead; IPS and NICE agree). Acute phase: treat to remission over 6 to 8 weeks, review by 2 to 4 weeks. Continuation: the SAME acute dose for 6 to 9 months. Maintenance: 2 years or longer for recurrent or high-risk depression. Psychotic depression needs an antidepressant plus an antipsychotic, or ECT.
LITHIUM: DOSE AND MONITORING	Mechanism: inositol depletion and GSK-3 inhibition; renally excreted, sodium-linked, narrow therapeutic index. Range: acute mania 0.8 to 1.0 (up to 1.2), maintenance 0.6 to 0.8 (up to 1.0), elderly 0.4 to 0.6 mmol/L. Sample as a 12-hour trough; recheck 5 to 7 days after a dose change; renal and thyroid function 6-monthly. Baseline: renal, thyroid, calcium, ECG, pregnancy, weight.
LITHIUM: TOXICITY AND ORGANS	Toxicity (dehydration, NSAIDs, thiazides, ACE inhibitors precipitate): mild 1.5 to 2.0 (coarse tremor, GI, lethargy), moderate 2.0 to 2.5 (confusion, ataxia, dysarthria), severe above 2.5 (seizures, coma, renal failure); stop, saline, haemodialysis for severe. Organs: nephrogenic DI and long-term CKD (watch eGFR trend), hypothyroidism and goitre (thyroxine, keep lithium), hypercalcaemia, benign T-wave changes, acne and psoriasis, fine tremor. Ebstein anomaly first-trimester (small but raised). Interactions that RAISE the level: NSAIDs, thiazides, ACE inhibitors and ARBs.
VALPROATE, CARBAMAZEPINE, LAMOTRIGINE	Valproate: anti-manic and maintenance (not bipolar depression alone); hepatotoxicity and PCOS; CRITICAL teratogenicity (neural-tube and neurodevelopmental risk), so avoid in women of childbearing potential without a pregnancy-prevention programme. Carbamazepine: potent CYP3A4 autoinducer (oral-contraceptive failure), hyponatraemia, blood dyscrasias, HLA-B*1502 SJS screen. Lamotrigine: for bipolar depression and

The whole subject in one table	
	maintenance (weak for mania); slow titration, HALVED with valproate; stop for a serious or mucosal rash (Stevens-Johnson).
TRD AND AUGMENTATION	TRD: failure of at least two adequate antidepressant trials, but exclude pseudoresistance first (dose, duration, adherence, missed bipolarity); Thase-Rush and Maudsley staging; STAR-D showed remission falls with each step. Ladder: optimise, switch, augment (lithium the classic and anti-suicidal, T3, an atypical, the best evidence), combine, then ECT, esketamine or neuromodulation.
BIPOLAR MANAGEMENT BY PHASE	Acute mania: stop any antidepressant; first-line lithium, quetiapine, valproate, or an atypical (aripiprazole, asenapine, risperidone, cariprazine), combination for severe. Bipolar depression: quetiapine, lurasidone, lithium, lamotrigine, olanzapine-fluoxetine, cariprazine; never an antidepressant alone (manic switch). Mixed episodes: valproate, asenapine, cariprazine, olanzapine, ECT; antidepressants avoided; lithium relatively weaker. Maintenance: lithium anchors (anti-suicidal), quetiapine, valproate, lamotrigine for the depressive pole, LAI for non-adherence.
ECT, NEUROMODULATION, PSYCHOTHERAPY	ECT: first-line in the emergencies (severe, psychotic or treatment-resistant depression, high suicide risk, food refusal, catatonia, pregnancy), rapid and effective; technique elsewhere. rTMS: non-invasive, for treatment-resistant depression. VNS: later-line, slow. DBS: experimental. Psychotherapy: CBT, IPT and behavioural activation are first-line in mild-to-moderate depression alone and combined with medication in severe depression.
SPECIAL POPULATIONS AND SUICIDE	Elderly: somatic and cognitive presentation, vascular depression; start low and go slow but still reach an adequate dose; prefer an SSRI (watch hyponatraemia, falls, the QTc cap), avoid TCAs; ECT works well in severe late-life depression. Suicide: mood disorders carry the highest risk (severe, mixed, early illness, early recovery); lithium is anti-suicidal; avoid a large TCA supply; counsel early antidepressant activation.

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The pharmacology is grounded in the standard prescribing and psychopharmacology sources (the source hierarchy below), with the Maudsley Prescribing Guidelines and Stahl as the depth bar for the mechanisms, doses, serum levels and monitoring, and the management is guideline-first (CANMAT leading, with the Indian Psychiatric Society, the British Association for Psychopharmacology and NICE). Every dose, serum level, therapeutic range, monitoring interval, teratogenicity fact, drug interaction and first-line recommendation has been checked against these sources; anything that could not be confirmed was omitted and flagged rather than guessed. Each journal PMID here was verified against PubMed this build, matched on title, first author

and year; identifiers that resolved to the wrong paper were corrected or dropped. The classic sources seeding the field (Cade's 1949 report of lithium in mania, Schou's lithium work) are named in the prose by author and year.

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PART VI

VI

Substance Use Disorders: By Substance, Treatment and Relapse Prevention

Substance use across the major drugs: the syndromes, the treatments, and how relapse is prevented.

01 General concepts and assessment

02 Alcohol use disorder

03 Opioid use disorder

04 Other substances of misuse

05 Psychosocial treatment and relapse prevention

06 Anti-craving and aversive pharmacotherapy

07 Apply and consolidate

PAPER II

Substance use disorders

Six sections . one complete notes document

This material gathers the substance use disorders into one document, by substance and by treatment. The first band is **general concepts and assessment**: the dependence syndrome and harmful use, the neurobiology of addiction and the reward pathway, tolerance and withdrawal, the screening instruments and their cut-offs, dual diagnosis and harm reduction. The second band is **alcohol use disorder**: the pharmacology, the withdrawal spectrum with the CIWA-Ar and the benzodiazepine protocol, delirium tremens, Wernicke encephalopathy and Korsakoff syndrome, alcoholic hallucinosis, the medical complications and the laboratory markers. The third band is **opioid use disorder**: overdose and naloxone, withdrawal and the COWS, opioid substitution with buprenorphine and methadone, antagonist relapse prevention and detoxification. The fourth band is **the other substances of misuse**: cannabis, the stimulants, tobacco, the sedative-hypnotics, the inhalants, hallucinogens and caffeine, the behavioural addictions, and the special populations. The fifth band is **psychosocial treatment and relapse prevention**: motivational interviewing, the stages of change, the Marlatt relapse-prevention model, brief interventions, the twelve-step groups and contingency management. The sixth band is **anti-craving and aversive pharmacotherapy**: disulfiram, naltrexone, acamprosate and the guideline-anchored choice between them. The examinable skill is the safe, guideline-anchored assessment and treatment of each substance: which scale and which cut-off, which withdrawal regimen at what dose, which emergency behind which sign, and which treatment for which patient and stage.

HOW TO USE THESE NOTES

Read the six bands as one continuous account of how substance use disorder is assessed and treated. The **general** band builds the frame: the dependence syndrome, the reward-pathway neurobiology and the screening scales with their verified cut-offs. The **alcohol** and **opioid** bands teach each substance by its intoxication, its withdrawal and its complications, and carry the core emergencies, the alcohol-withdrawal and Wernicke management on one side and opioid overdose and substitution on the other. The **other substances** band covers cannabis, the stimulants, tobacco and the sedative-hypnotics in working depth and the rest compactly. The **psychosocial** band teaches motivational interviewing, the stages of change and the Marlatt model as the SUD-core skills, and the **anti-craving** band teaches disulfiram, naltrexone and acamprosate and how to choose between them. Every management recommendation is guideline-anchored, led by the BAP guidelines with the Indian Psychiatric Society, NICE and WHO positions stated, on the where-to-treat, target-by-phase, modes-of-treatment spine; every named drug ends with a **Good to remember** box giving the mechanism, the signature caution and the one dose, and every named emergency ends with one giving the feature, the discriminator and the first step. Figures declare one axis and code it in colour: **petrol** marks structure and the neutral case, **coral** marks the trap or the danger, and **marigold** highlights the number to hold; the screening and withdrawal scales are reproduced as the actual instruments, credited to their sources. Several boundaries are stated up front: the reward-pathway anatomy is taught in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and cross-referenced here; the wider psychosis boundary in the Other psychotic disorders, delusional syndromes and catatonia notes; the wider delirium and emergency frame and substance use in pregnancy in the Perinatal and emergency psychiatry notes; the NDPS Act and the medico-legal frame in the Mental health legislation and forensic psychiatry notes; the wider psychotherapy technique in the Psychotherapies notes; and the wider amnestic frame in the Dementias and the Neuropsychiatry of systemic disease notes. This is doctor-facing revision, so the full technical vocabulary is used, brand names lead with the Indian brand, and every dose, scale cut-off, thiamine regimen and first-line recommendation is verified against a source or omitted and flagged.

General concepts and assessment

1 · Dependence syndrome and harmful use

The whole of the substance-use chapter turns on one distinction, and this is where it is drawn: the difference between a pattern of use that is *damaging* a person (**harmful use**) and a pattern that has captured them (the **dependence syndrome**). Get this pair right and every downstream question, from which scale to reach for to whether a person needs assisted withdrawal, follows. Examiners love it because it is a criterion-count item: they will ask what the criteria are, how many are needed, over what period, and how the old ICD-10 list maps onto the newer ICD-11 concept. The construct is not arbitrary. The dependence syndrome descends directly from Edwards and Gross's 1976 description of the alcohol dependence syndrome, which is why the same clustering of features reappears across every substance class.

Why it matters clinically. Naming dependence rather than harmful use changes the plan: dependence implies a physiological withdrawal risk, a need to consider assisted withdrawal and relapse-prevention pharmacotherapy, and a much higher chance of relapse, whereas harmful use is often addressed with brief, motivation-based intervention alone. The reward-pathway biology that underlies the **salience** and **compulsion** at the heart of the syndrome is developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and is not re-derived here.

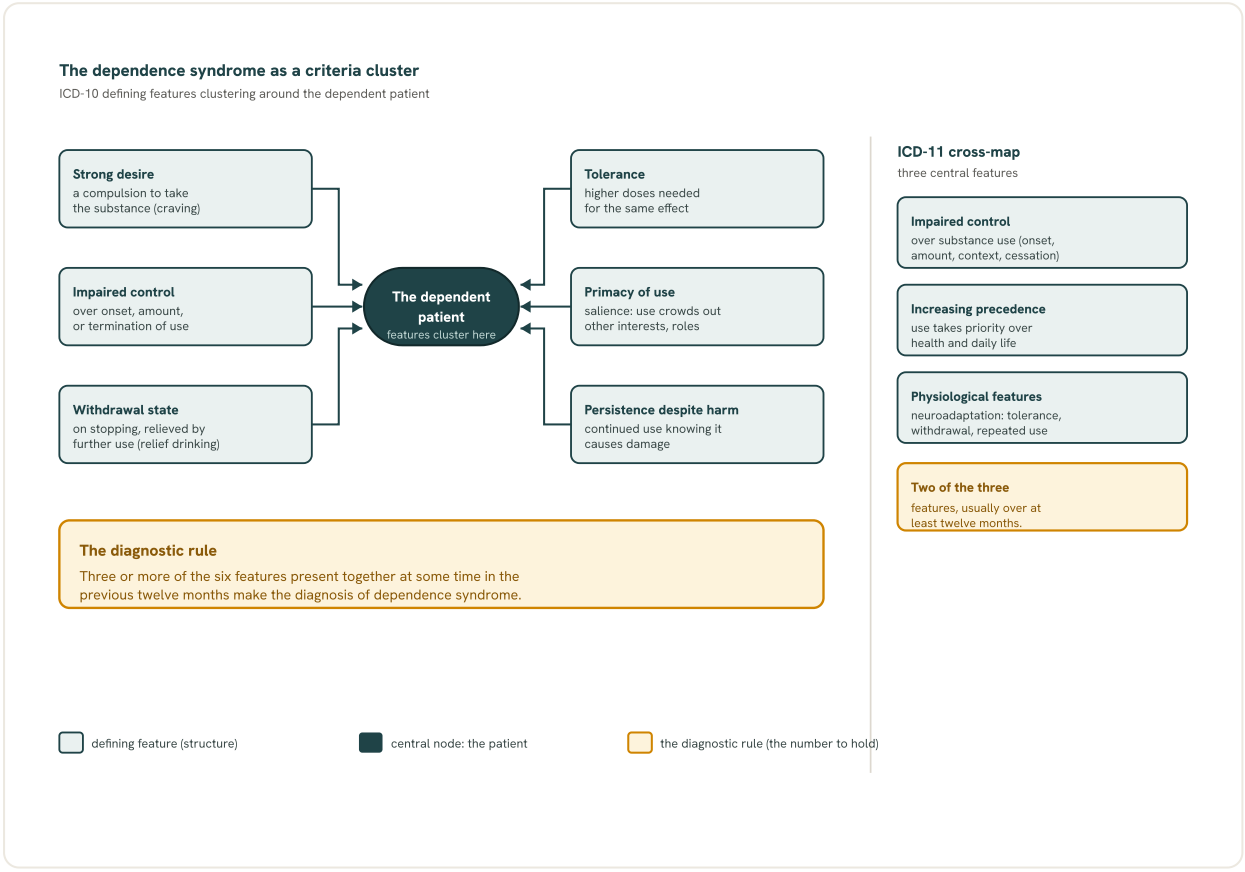


Fig 13.1 The dependence syndrome: the criteria cluster and the ICD-11 cross-map. In ICD-10 the dependent patient sits at the centre of six defining features: a strong desire or compulsion to use, impaired control, a physiological withdrawal state, tolerance, primacy or salience of use over other interests, and persistence despite clear harm. The rule to hold, in the marigold chip, is that three or more of these clustering together at some time in the previous twelve months make the diagnosis. ICD-11 reduces this to three central features, requiring two of three: impaired control, increasing precedence of use, and physiological features of neuroadaptation (tolerance, withdrawal, or repeated use to relieve or avoid withdrawal).

1.1 The two ICD-10 categories: harmful use is damage, dependence is capture

Harmful use (F1x.1). Harmful use is a pattern of psychoactive substance use that is actually causing damage to health, where the damage may be to **physical health** (for example alcoholic hepatitis, or a bloodborne infection from injecting) or to **mental health** (for example a substance-induced depressive episode) (WHO 1992; Shorter Oxford 2018). The harm must be real and demonstrable, not merely disapproved of by others: social or legal consequences alone do not make the diagnosis. Critically, in ICD-10 harmful use and dependence are mutually exclusive at any one time; if dependence is present, that is the diagnosis and harmful use is not coded alongside it.

Dependence syndrome (F1x.2). The dependence syndrome is a cluster of behavioural, cognitive and physiological phenomena that develop after repeated use, in which the substance takes on a far higher priority for the person than behaviours that once had greater value (WHO 1992). It is the more severe, self-perpetuating end of the spectrum, and it is defined by counting criteria, not by quantity consumed. A person can drink heavily and be harmful-use only; another can drink less but meet dependence.

RULE **Count the criteria, not the units.** Dependence is diagnosed by the clustering of the defining features, never by how much a person drinks or uses; a modest intake with three clustering features is dependence, a large intake without them is not.

1.2 The icd-10 dependence definition: three or more of six, clustering within a 12-month period

The counting rule. A diagnosis of the **icd-10 dependence** syndrome is made if **three or more** of six defining features have been experienced or exhibited together at some time during the previous **12 months** (WHO 1992; Shorter Oxford 2018). Three is the threshold and twelve months is the window; both are examinable and both are frequently mis-stated. The features must cluster, meaning present together within that year, not scattered across a lifetime.

The six features. They are: a strong desire or sense of **compulsion** to take the substance; impaired control over its use (onset, termination or level of use); a physiological withdrawal state on cessation or reduction; evidence of tolerance; the **primacy** of use, that is progressive neglect of alternative pleasures or interests plus increasing time spent obtaining, using or recovering from the substance; and persistence despite clear evidence of overtly harmful consequences. This is the criterion set to hold cold, and the concept figure lays out all six as a cluster (Fig 13.1).

ICD-10 DEPENDENCE CRITERION (THREE OR MORE WITHIN 12 MONTHS)	WHAT IT MEANS CLINICALLY
1. Strong desire or sense of compulsion	Craving; a felt drive to use, often triggered by cues.
2. Impaired control	Difficulty controlling onset, termination or level of use; using more or longer than intended.
3. Physiological withdrawal state	Characteristic withdrawal on stopping or reducing, or using the substance (or a related one) to relieve or avoid it.
4. Tolerance	Increased doses needed to achieve the effect once produced by lower doses.
5. Primacy / salience	Progressive neglect of alternative pleasures and interests; more time to obtain, use or recover from the substance.
6. Persistence despite harm	Continued use despite clear evidence of overtly harmful physical or mental consequences.

The six ICD-10 (F1x.2) dependence features; any three clustering within a 12-month period make the diagnosis (WHO 1992).

MNEMONIC

WITHDRAWAL → but memorise as the "3 C's + 3": Compulsion, impaired Control, and Continued use despite harm, plus the physiological trio of tolerance, withdrawal, and salience.

The three cognitive-behavioural features (compulsion, impaired control, persistence despite harm) sit alongside the physiological and priority features (tolerance, withdrawal, primacy/salience). Any three of the six, clustering in a year, suffice.

HOLD THIS

ICD-10 dependence syndrome = three or more of six features (compulsion, impaired control, physiological withdrawal, tolerance, primacy/salience, persistence despite harm) clustering together at some time in the previous 12 months; count criteria, never units.

1.3 The seven criteria question: why the count is six, not seven, and where "seven" comes from

Six, not seven. A recurring trap is the "**seven criteria**" phrasing. ICD-10 dependence has **six** defining features; the answer to "how many dependence criteria in ICD-10?" is six, with a threshold of three. The number seven belongs to a different classification: the older DSM-IV substance *dependence* also listed seven criteria, and DSM-5 substance use disorder collapsed abuse and dependence into a single list of eleven criteria (with two or more needed, and a severity gradient of two to three mild, four to five moderate, six or more severe). If a stem says "seven criteria" it is testing whether you can keep the systems apart.

Keep the systems distinct. ICD-10 keeps harmful use and dependence as two separate categories; DSM-5 merged them into one dimensional disorder. This is the single most common point of confusion, so anchor to it: ICD-10 = harmful use plus a six-feature dependence syndrome; DSM-5 = one substance use disorder with eleven criteria; the phrase "seven criteria" is the DSM-IV dependence relic.

TRAP **Reciting seven criteria for ICD-10 dependence.** ICD-10 dependence has six features (threshold three); "seven criteria" is DSM-IV dependence, and DSM-5 has eleven for a single substance use disorder.

1.4 Tolerance and the physiological withdrawal state: neuroadaptation, not addiction by itself

Tolerance. Tolerance is the need for increasing doses to achieve the effect once produced by lower doses, reflecting neuroadaptation of receptor systems. It is one of the two physiological features and, on its own, does not equal dependence: a patient on chronic opioid analgesia or a benzodiazepine may show tolerance and a withdrawal state (physical dependence) without the compulsion, impaired control and salience that define the syndrome (DSM-5-TR 2022, which is explicit that prescribed-drug tolerance and withdrawal are normal responses and do not by themselves indicate addiction).

The physiological withdrawal state. This is the characteristic, substance-specific syndrome appearing on cessation or reduction, or the use of the same or a closely related substance to

relieve or avoid it (the "relief use" clause). The quality and severity of withdrawal are set by the substance class, and avoidance of withdrawal becomes a powerful driver of continued use. The detailed time-courses and management of alcohol, opioid and sedative withdrawal are developed in the withdrawal and management topics; here the point is only that physiological features are one arm of the syndrome, not the whole of it.

PEARL

Physical dependence (tolerance plus a withdrawal state) is not the same as the dependence syndrome. A person can be physically dependent on a legitimately prescribed drug without addiction; the syndrome needs the behavioural core, compulsion, impaired control and salience, as well.

1.5 Primacy and salience: the behavioural heart of the syndrome

Salience of drug use. Salience, also called primacy, is the feature in which the substance takes priority over behaviours that once mattered more: work, relationships, health and other pleasures are progressively neglected, and more and more of the day is given to obtaining, using and recovering from the substance. In Edwards and Gross's original description this "narrowing of the repertoire" and salience of drink-seeking was the signature of the syndrome, and it remains the feature that most distinguishes dependence from heavy but still-controlled use.

Compulsion and impaired control. The two other behavioural features are the strong desire or compulsion to use (craving) and impaired control over onset, termination and level of use. Together, compulsion, impaired control and salience form the psychological core of the syndrome; tolerance, withdrawal and persistence-despite-harm form the reinforcing shell around it. This is exactly the split that carries into ICD-11.

RULE **Salience is the discriminator.** When the substance has climbed above health, work and relationships in a person's priorities, you are looking at dependence, not harmful use, however modest the reported quantity.

1.6 The cross-map to ICD-11: three central features, two of three needed

The ICD-11 dependence concept. ICD-11 keeps dependence but streamlines the six ICD-10 features into three central features, requiring **two or more** of them (WHO ICD-11 CDDR 2024). The **icd-11 criteria** for dependence are: impaired control over substance use (onset, frequency, intensity, duration, termination, context); increasing precedence of substance use over other aspects of life, that is salience, such that use continues or escalates despite harm; and physiological features indicative of neuroadaptation, namely tolerance, withdrawal, or repeated use to relieve or prevent withdrawal (note that physiological features apply only to certain substances).

The time frame. ICD-11 features are usually evident over at least 12 months, but the diagnosis may be made if use is continuous (daily or almost daily) for at least 3 months. So the six ICD-10 criteria collapse cleanly: compulsion folds into impaired control, primacy/salience becomes

"increasing precedence", and tolerance plus withdrawal become the single "physiological features" arm. Two of these three make ICD-11 dependence.

ICD-10 DEPENDENCE (SIX; NEED THREE)	ICD-11 DEPENDENCE (THREE CENTRAL; NEED TWO)
Strong desire / compulsion	**Impaired control over substance use**
Impaired control	
Physiological withdrawal state	**Physiological features of neuroadaptation (tolerance or withdrawal)**
Tolerance	
Primacy / progressive neglect (salience)	**Increasing precedence of use over life (salience)**
Persistence despite overtly harmful consequences	Subsumed within the above features and their harm clause

How the six ICD-10 dependence features map onto the three central ICD-11 features; ICD-11 needs two of three (WHO 1992; ICD-11 CDDR 2024).

1.7 ICD-11 harmful pattern of use: harm to others is now explicit

The renamed category. ICD-10 "harmful use" becomes ICD-11 harmful pattern of use. Its essential feature is a pattern of continuous, recurrent or sporadic use that has caused clinically significant damage to a person's physical or mental health *or has resulted in behaviour leading to harm to the health of others* (ICD-11 CDDR 2024). The explicit inclusion of harm to others (for example harm from drink-driving or violence during intoxication) is the key ICD-11 change from ICD-10, which framed harm as being to the user's own health only.

The time frame. The harmful pattern must be evident over at least 12 months if use is episodic, or at least 1 month if use is continuous (daily or almost daily). ICD-11 also adds an intermediate risk category, a "single episode of harmful use", below the harmful-pattern threshold, which has no ICD-10 equivalent.

COMMON TRAP

Do not confuse ICD-11 "harmful pattern of use" (a diagnosis requiring demonstrable harm to health) with "hazardous use", which is a risk-level term for a pattern that increases the risk of harm but has not yet caused it. Hazardous use sits in the ICD-11 risk factors chapter, not among the substance-use disorders.

1.8 Screening at the harmful-use end: AUDIT, CAGE and where the cut-offs sit

Why screen here. Harmful and hazardous use are precisely where brief intervention works and where screening instruments earn their place, because these patterns are common, often unrecognised, and reversible before dependence is entrenched. Two instruments dominate the exam. The full instrument forms are reproduced in the scales gallery, so only what they are and their cut-offs are given here.

The two to hold. The AUDIT (Alcohol Use Disorders Identification Test) is a 10-item WHO screen; a score of **8 or more** indicates hazardous or harmful drinking, and NICE advises a comprehensive assessment for anyone scoring above 15. The CAGE is a four-item bedside screen

(Cut down, Annoyed, Guilty, Eye-opener) taking one to two minutes; a score of **2 or more** positive answers is clinically significant and warrants fuller assessment (NICE 2011). Dependence-severity and withdrawal-severity scales (SADQ, CIWA-Ar) belong to the withdrawal topics, not to screening.

3 of 6 ICD-10 DEPENDENCE THRESHOLD, WITHIN 12 MONTHS	**2 of 3** ICD-11 DEPENDENCE CENTRAL FEATURES	**8** AUDIT HAZARDOUS OR HARMFUL-USE CUT-OFF	**2** CAGE POSITIVE-ANSWER CUT-OFF

INDIA

India carries a very large substance-use treatment gap: most people meeting dependence criteria never reach formal care, and services concentrate in the government de-addiction centres and a handful of Drug De-addiction Programme (DDAP) units rather than in general practice. The legal frame is the Narcotic Drugs and Psychotropic Substances Act, 1985 (Act 61 of 1985, in force 16 September 1985; the medico-legal detail is developed in the Mental health legislation and forensic psychiatry notes), which lists cannabis, cocaine, opium, poppy straw and 76 scheduled psychotropics including diazepam, pentazocine and phenobarbital. The practical consequence for diagnosis is that the harmful-use category matters greatly here: brief, motivation-based intervention delivered by trained non-specialist workers, closing the gap at the point where use is damaging but dependence is not yet fixed, is the strategic priority the IPS substance-use guidelines emphasise (IPS 2014). Buprenorphine is the workhorse of Indian opioid-agonist treatment precisely because methadone access is limited, and its induction detail belongs to the substitution topics.

WORKED EXAMPLE

A 34-year-old lorry driver reports drinking most evenings. He describes a strong pull to drink after work (compulsion), repeatedly drinking more than he plans (impaired control), morning shakes relieved by an early drink (a physiological withdrawal state with relief use), needing far more than before to feel the effect (tolerance), and having given up cricket and family evenings for drinking (salience). That is five of the six ICD-10 features clustering within the year, well past the threshold of three: this is the dependence syndrome, not harmful use, and the plan must consider assisted withdrawal and relapse prevention, not brief advice alone. Map it to ICD-11 and he meets all three central features; two would have sufficed.

GOOD TO REMEMBER

- **Dependence syndrome (ICD-10 F1x.2):** three or more of six features (compulsion, impaired control, withdrawal, tolerance, primacy/salience, persistence despite harm) clustering within 12 months; the discriminator from harmful use is salience, the substance climbing above health, work and relationships; first step on recognising it is to assess withdrawal risk and the need for assisted withdrawal.
- **Harmful use (ICD-10 F1x.1) / harmful pattern (ICD-11):** a pattern actually causing demonstrable damage to physical or mental health; the ICD-11 change is that harm to the health of others now counts too; the discriminator from dependence is the absence of the dependence cluster; first step is brief, motivation-based intervention.
- **ICD-11 dependence:** two or more of three central features (impaired control, increasing precedence/salience, physiological features of neuroadaptation); evident over 12 months, or 3 months if continuous daily use; the one number to hold is two of three.
- **The "seven" trap:** ICD-10 dependence has six criteria (threshold three); "seven criteria" is DSM-IV dependence; DSM-5 merged abuse and dependence into one substance use disorder with eleven criteria (threshold two, graded mild/moderate/severe).

2 · ICD-11 changes in substance use disorders

The **icd-11 changes** to the substance use disorders are the single most exam-friendly restructuring in the whole chapter, because they turn the old two-box ICD-10 scheme (harmful use versus dependence) into a graded ladder that begins *before* any harm has occurred and rises through a discrete harm event to an entrenched pattern to full dependence. The examiner tests this as a discrimination task: given a vignette, can you place the drinker or the drug user in the right **icd-11 substance** category, and can you say why it is not the neighbouring one. The two genuinely new pieces are the **single episode of harmful use** (a one-off harm event, not a settled pattern) and **hazardous use** (increased risk but no harm yet, and deliberately *not* a mental disorder at all). This is a nosology topic, so the payload is criteria and boundaries; the reward-pathway mechanics behind why the ladder exists sit in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes, the substance-induced psychotic boundary in the Other psychotic disorders, delusional syndromes and catatonia notes, and the NDPS medico-legal frame in the Mental health legislation and forensic psychiatry notes.

How to use this page. Fix the four rungs of the ladder first, in order (hazardous use, episode of harmful use, harmful pattern, dependence), then the discriminators that separate each rung from the one above and below it, then the ICD-10-to-ICD-11 crosswalk, then how ICD-11 lines up against the DSM-5-TR single dimensional use disorder. The one clause that carries most of the marks is the boundary between an **episode of harmful use** and a harmful *pattern*: a single discrete harm event versus harm from a use pattern running over roughly twelve months.

2.1 The old ICD-10 dichotomy this replaces

Two boxes: harmful use and dependence. ICD-10 gave each substance class a small fixed set of clinical conditions, of which the two the examiner cares about were **harmful use** (F1x.1) and the dependence syndrome (F1x.2), alongside acute intoxication, withdrawal, withdrawal with delirium, psychotic disorder and the amnesic syndrome (Companion to Psychiatric Studies). Harmful use required actual damage to physical or mental health from the substance; below that

threshold ICD-10 offered nothing to code, so the person who was drinking dangerously but had not yet come to harm fell through the classification entirely. Dependence was operationalised from Edwards and Gross's **alcohol dependence syndrome** (1976) as a cluster requiring three or more of six features over the past year. The whole scheme was therefore a two-step: harm, or the syndrome, and nothing in between or before.

GOOD TO REMEMBER

- **ICD-10 dependence syndrome (the discriminator against harmful use):** three or more of six features (compulsion/craving, impaired control, physiological withdrawal, tolerance, salience/neglect of alternatives, persistence despite harm) for at least one month or repeatedly within twelve months; the feature to hold is that dependence needs the *cluster*, whereas harmful use needs only demonstrated *harm*; the source is Edwards & Gross (1976).

2.2 The ICD-11 restructuring: a graded ladder

Four rungs instead of two boxes. The core of the **icd-11 changes** is that each substance class (6C40 alcohol, 6C43 opioids, 6C41 cannabis, and so on) now carries a graded set of disorders due to substance use, and the WHO in ICD-11 identifies acute intoxication, harmful use, dependence syndrome, withdrawal state (with or without delirium), substance-induced psychotic disorder, substance-induced amnesic disorder and the residual categories (Maudsley Prescribing Guidelines, ICD-11 CDDR). What is new is that "harmful use" itself has been *split* into two levels, a discrete **episode of harmful use** and a settled **harmful pattern of use**, and a pre-harm category, hazardous use, has been added outside the mental-disorders chapter entirely. Read as a ladder, an icd-11 substance presentation climbs: hazardous use (risk, no harm, not a disorder) then episode of harmful use (one harm event) then harmful pattern of use (harm from a pattern) then dependence (the neuroadaptive syndrome).

RUNG	ICD-11 CATEGORY (ALCOHOL CODE)	THE ONE-LINE DISCRIMINATOR
1. Hazardous use	QE10 (Chapter 24, not a disorder)	**Risk of harm appreciably raised, but no harm has yet occurred; a health-behaviour problem, not a mental disorder**
2. Episode of harmful use	6C40.0	**A single discrete episode of use has caused clinically significant harm to the user's health or, via intoxicated behaviour, to others**
3. Harmful pattern of use	6C40.1 (episodic/continuous)	**Harm arises from a recurrent or continuous pattern of use, generally over at least 12 months**
4. Dependence	6C40.2 (with course specifiers)	**Two of three core features (impaired control, increasing precedence, neuroadaptation); the internal driven syndrome, not merely its harms**

The ICD-11 ladder for each substance class, alcohol codes shown; the reward-circuit basis for the climb is in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes (ICD-11 CDDR).

RULE **Grade by harm and pattern, not by drug alone.** The ICD-11 category is fixed by whether harm has occurred (none = hazardous; some = harmful) and whether it comes from a single episode or a sustained pattern, then by whether the dependence features are present, in that order.

2.3 The single episode of harmful use (new)

A one-off harm event, coded before a pattern is established. The **single episode of harmful use** (6C40.0 for alcohol) is diagnosed when a *single* episode of use of a psychoactive substance has caused clinically significant damage to the person's physical health (for example a bloodborne infection from one instance of intravenous self-administration), or mental health (a substance-induced mood disturbance), or has led, through intoxicated behaviour, to harm to the health of others (an assault, or a road traffic accident from impaired driving) (ICD-11 CDDR). There must be a clear causal link between the harm and that episode, and the harm must not be better explained by another condition. Crucially, this category exists precisely so that a clinician can code a first, discrete harmful event *without* having to assert a pattern that the history does not yet support; if no information about the pattern of use is available, an **episode of harmful use** may be coded until evidence of a pattern emerges, at which point the diagnosis is revised upward to harmful pattern or dependence. It is a deliberate hook for early, low-intensity intervention.

TRAP **Coding a single harm event as a harmful pattern.** One discrete harmful episode is 6C40.0 (episode of harmful use); "harmful pattern" needs a recurrent or continuous pattern over roughly twelve months. Reserve the pattern code for when the history actually shows one.

GOOD TO REMEMBER

- **Episode of harmful use (the diagnosis):** a single episode of substance use causing clinically significant harm to the user's physical or mental health, or to others via intoxicated behaviour; the discriminator from harmful pattern is *single/discrete versus recurrent-or-continuous*; the first-management step is a brief low-intensity intervention, and the code is revised upward once a pattern is shown.

2.4 Harmful pattern of use, and the 12-month boundary

Harm from a pattern, not from one occasion. The harmful pattern of use (6C40.1, specified as episodic or continuous) is assigned when the harm to physical or mental health results from a *known episodic or continuous pattern* of substance use and all other requirements are met. ICD-11 sets the operational threshold explicitly: substance use is generally considered to follow a pattern if there has been at least episodic or intermittent use over a period of **at least 12 months** (ICD-11 CDDR). This is the boundary the examiner probes. Below the pattern threshold but with a single demonstrable harm you are at "episode of harmful use"; above it, with harm attributable to the ongoing pattern, you are at "harmful pattern"; and if the neuroadaptive dependence features are present you climb again to dependence regardless of how the harm is distributed.

GOOD TO REMEMBER

- **Harmful pattern of use (the diagnosis):** clinically significant harm arising from a recurrent (episodic) or continuous pattern of use, the pattern generally running over at least twelve months; the discriminator downward is the single-episode category, upward is the presence of dependence features; specify episodic or continuous.

2.5 Hazardous use: risk without harm, and not a disorder

The pre-harm rung, deliberately outside the mental-disorders chapter. Hazardous use (QE10 hazardous alcohol use, QE11 hazardous drug use) is the genuinely conceptual novelty: a pattern of use that appreciably increases the risk of harmful physical or mental health consequences, to the user or to others, to a degree warranting attention and advice from health professionals, but where *no overt harm has yet occurred* (ICD-11 CDDR). Because there is as yet no harm and no syndrome, ICD-11 does *not* classify it as a mental or behavioural disorder at all; it is placed in Chapter 24, among "problems associated with health behaviours" (factors influencing health status or contact with health services). The raised risk may come from the frequency of use, the amount per occasion, a risky route of administration, or the context of use, and the pattern often persists despite the person's awareness of it. Its clinical point is to license a coded screening-and-brief-advice contact before any damage is done, exactly the population that an AUDIT score in the hazardous band identifies.

TRAP **Treating hazardous use as a mild substance use disorder.** Hazardous use is *not* a mental disorder in ICD-11; it lives in Chapter 24. The moment demonstrable harm appears, the person moves out of QE10/QE11 and into the 6C4x harmful-use categories.

PEARL

The cleanest way to hold the split: hazardous use is *risk, no harm, not a disorder*; episode of harmful use is *harm from one occasion*; harmful pattern is *harm from a pattern*; dependence is *the syndrome, whatever the harm*. The single question that sorts the first two from the last two is simply: has harm actually occurred yet?

2.6 The ICD-11 dependence syndrome: two of three

Streamlined to three core features, and the harms stripped out. ICD-11 dependence is defined by three core features, of which *two or more* must usually be present together over at least twelve months, or if use is continuous (daily or almost daily) for at least three months (ICD-11 CDDR). The three are: (a) *impaired control* over substance use (onset, frequency, intensity, duration, termination, context); (b) *increasing precedence* of substance use over other aspects of life, so that use continues or escalates despite harm; and (c) *physiological features of neuroadaptation*, that is tolerance, withdrawal on cessation, or repeated use to relieve or prevent withdrawal. Two structural moves distinguish this from ICD-10's six-item, three-required list: the criterion count is smaller and tighter, and the old "persistence despite harmful consequences" and craving are folded into precedence rather than standing as separate boxes. ICD-11 also warns explicitly that physiological features alone (tolerance and withdrawal from appropriately prescribed opioids for

cancer pain, say) do *not* make a dependence diagnosis; either impaired control or increasing precedence must also be present.

MNEMONIC

CPN: Control, Precedence, Neuroadaptation

Control impaired, substance takes **P**recedence over life, and **N**euroadaptation (tolerance/withdrawal): any *two* of these three, over roughly twelve months (or three months if near-daily), is ICD-11 dependence. Neuroadaptation on its own is never enough.

GOOD TO REMEMBER

- **ICD-11 dependence syndrome (the diagnosis):** two of three core features (impaired control; increasing precedence; physiological neuroadaptation = tolerance/withdrawal) present together, usually over twelve months or over three months if use is continuous; the discriminator from ICD-10 is the tighter three-feature/two-required structure; the trap-guard is that neuroadaptation alone does not qualify.

2.7 Course specifiers and the intoxication/withdrawal categories

Remission and pattern are now coded, not just noted. Beyond the four rungs, ICD-11 attaches structured specifiers that ICD-10 lacked. Dependence carries pattern-and-remission specifiers: current use (for alcohol, distinguished as continuous or episodic), early full remission (abstinent 1 to 12 months after a diagnosis), sustained partial remission and sustained full remission (more than 12 months) (ICD-11 CDDR). The acute states are retained and sharpened: substance intoxication and substance withdrawal each have their own codes, and withdrawal may be specified with perceptual disturbances or with delirium, which keeps the withdrawal-delirium (delirium tremens) presentation visible within the coding. The amnesic and psychotic sequelae become *substance-induced* amnesic disorder and substance-induced psychotic disorder. The effect is a scheme that records not just "which disorder" but "at what stage and in what state," which is what the graded ladder was designed to support.

2.8 ICD-11 versus DSM-5-TR: two philosophies

ICD-11 keeps categories; DSM-5 went dimensional. The two systems diverged deliberately. DSM-5 (and DSM-5-TR) *eliminated* the DSM-IV split of abuse and dependence and replaced it with a single overarching **substance use disorder** per drug, rated on a continuum from mild to severe by counting how many of eleven criteria are met, with two or more required for the diagnosis (DSM-5-TR 2022; Shorter Oxford Textbook of Psychiatry). ICD-11 kept a *categorical* structure but graded it into the ladder above, so that the two classifications no longer map one-to-one: a DSM-5 mild use disorder (two to three criteria) corresponds roughly to the ICD-11 harmful-pattern band, while moderate-to-severe DSM-5 disorder maps toward ICD-11 dependence (Kaplan & Sadock 2024). DSM-5 also folded craving in as a new criterion and dropped the old legal-problems criterion. The exam-usable summary: DSM-5 answers "how severe, on one scale," while ICD-11 answers "which category on the harm-and-dependence ladder."

FEATURE	ICD-11	DSM-5-TR
Overall structure	Categorical, graded ladder	**Single dimensional use disorder per drug**
Sub-harm risk category	Hazardous use (Chapter 24, not a disorder)	**None (no pre-harm category)**
Harm level	Episode of harmful use / harmful pattern of use	**Captured within mild/moderate use disorder**
Dependence / severe end	Dependence: 2 of 3 core features	**Severity by count of 11 criteria (2+ = disorder)**
Craving	Within "increasing precedence"	**A separate, explicitly added criterion**

The two classifications answer different questions; the crosswalk is approximate, not one-to-one (DSM-5-TR 2022, Kaplan & Sadock 2024, ICD-11 CDDR).

2.9 Screening scales that map onto the ICD-11 rungs

The instruments sort people onto the ladder. The graded structure is clinically usable because the standard screens read out roughly where a person sits. The AUDIT (10 items, each 0 to 4, maximum 40) flags **a score of 8 or more** as hazardous or harmful alcohol use, exactly the QE10-to-6C40.1 zone (Maudsley Prescribing Guidelines). The CAGE (four items) takes **2 or more** positive answers as identifying a problem drinker, quick enough for a busy clinic at one to two minutes. The SADQ (Severity of Alcohol Dependence Questionnaire, 20 items scored 0 to 3, maximum 60) grades dependence severity itself and informs the size of the withdrawal benzodiazepine regimen. The instrument forms are reproduced centrally in the scales gallery; here only the verified cut-offs matter.

8	2	12 months
AUDIT HAZARDOUS/HARMFUL CUT-OFF (MAX 40)	CAGE POSITIVE-SCREEN THRESHOLD (OF 4)	USE-PERIOD DEFINING A HARMFUL PATTERN

GOOD TO REMEMBER

- **AUDIT (scale):** 10 items, 0 to 4 each, maximum 40; the discriminator is a score of 8 or more, suggesting hazardous or harmful use; the cut-off to hold is 8.
- **CAGE (scale):** 4 items; the discriminator is 2 or more positive answers identifying a problem drinker; the number to hold is 2, in a 1 to 2 minute screen.

2.10 Anti-craving pharmacotherapy as the ladder's treatment end

The dependence rung is where relapse-prevention drugs are anchored. The classification is not just descriptive: the dependence category is the one that indicates maintenance anti-craving pharmacotherapy after medically assisted withdrawal, so the highest rung and the drug decision are linked. The three long-established agents for alcohol dependence are acamprosate (Acamprol), naltrexone (Nodict or Naltima) and disulfiram (Esperal or Dizone), all used with psychosocial support (BAP 2026, NICE 2011, Maudsley Prescribing Guidelines). Naltrexone reduces craving and heavy drinking but must not be started within a week of any opioid use, because it precipitates opioid withdrawal in an opioid-dependent person; disulfiram is an

aversive agent reserved for motivated, abstinence-goal, supervised patients and started at least 24 hours after the last drink; acamprosate maintains abstinence and is safe in liver disease but needs renal caution. The full withdrawal and opioid-substitution detail is owned by the other Day-13 treatment topics; here the point is only that the ICD-11 dependence category is the gate to these drugs.

GOOD TO REMEMBER

- **Naltrexone (Nodict/Naltima):** opioid-receptor antagonist reducing craving and heavy drinking; the signature caution is precipitated opioid withdrawal, so start only after at least one opioid-free week; oral maintenance **50 mg/day**.
- **Acamprosate (Acamprol):** glutamatergic NMDA-modulating anti-craving agent to maintain abstinence; the caution is renal impairment; dose **1998 mg/day** (666 mg three times daily) if over 60 kg, 1332 mg/day if under.
- **Disulfiram (Esperal/Dizone):** aldehyde-dehydrogenase inhibitor giving an aversive reaction with alcohol; reserve for motivated, supervised, abstinence-goal patients and start at least 24 hours after the last drink; dose **250 to 500 mg/day**.

INDIA

The ICD-11 ladder matters more in India than in most settings because of the sheer **treatment gap**: the large majority of people with alcohol and drug use disorders never reach care, and the graded scheme is built to catch them earlier, at the hazardous-use and single-episode rungs, through brief interventions in general and primary care rather than only at the dependence end. Indian de-addiction practice has long run on the ICD tradition (the F1x harmful-use and dependence codes are what the standard Indian teaching texts use), so the shift is evolutionary: the familiar harmful-use/dependence pair simply gains a pre-harm rung (hazardous use) and a split of harmful use into episode and pattern. The de-addiction centre and the Drug De-addiction Programme model, and the IPS substance-use clinical practice guidelines, are the service context; the NDPS Act frame that governs who can hold and dispense controlled drugs (and constrains buprenorphine and opioid-substitution access) is cross-referenced to the Mental health legislation and forensic psychiatry notes. Anti-craving generics are affordable and widely stocked; lead with the Indian brand and verify it locally before naming one.

HOLD THIS

ICD-11 replaces the ICD-10 harmful-use/dependence dichotomy with a graded ladder: hazardous use (risk, no harm, a Chapter-24 health-behaviour problem, not a mental disorder), then a single episode of harmful use (one discrete harm event, 6C40.0), then harmful pattern of use (harm from a pattern over about 12 months, 6C40.1), then dependence (two of three core features, impaired control / increasing precedence / neuroadaptation, over 12 months or 3 months if near-daily, 6C40.2 with remission specifiers); DSM-5-TR instead uses one dimensional use disorder graded mild-to-severe by counting 2 or more of 11 criteria.

3 . The neurobiology of addiction

Why this leads the substance block. The **neurobiology of addiction** is the mechanistic spine that makes every later topic legible: it explains why tolerance escalates use, why abstinence hurts, why craving outlives detoxification, and why a relapse-prevention agent has anything to aim at.

Addiction is best understood not as a failure of will but as a learned **reward pathway** disorder in which a normal survival circuit is hijacked by drugs that flood it with **dopamine** more explosively than any natural reward can (Stahl's Substance Use 2020). The examiner reward is a small, high-yield set: the **mesolimbic** circuit from the **ventral tegmental** area to the **nucleus accumbens**, the dopamine surge that all drugs of abuse share, the **incentive-sensitisation** account of **craving**, and Koob and Volkow's three-stage cycle. Get this frame right and intoxication, withdrawal, negative affect and relapse all fall out of one diagram.

This fragment teaches the anatomy of reward, then the dopamine signal that unifies all drugs of abuse, then the incentive-sensitisation model that separates wanting from liking, and finally the three-stage addiction cycle that maps the whole disorder onto three brain networks. The deep monoamine and second-messenger anatomy of the reward-pathway circuit sits in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; here we teach the addiction application. This topic carries Fig 13.2, the reward-circuit and three-stage-cycle schematic.

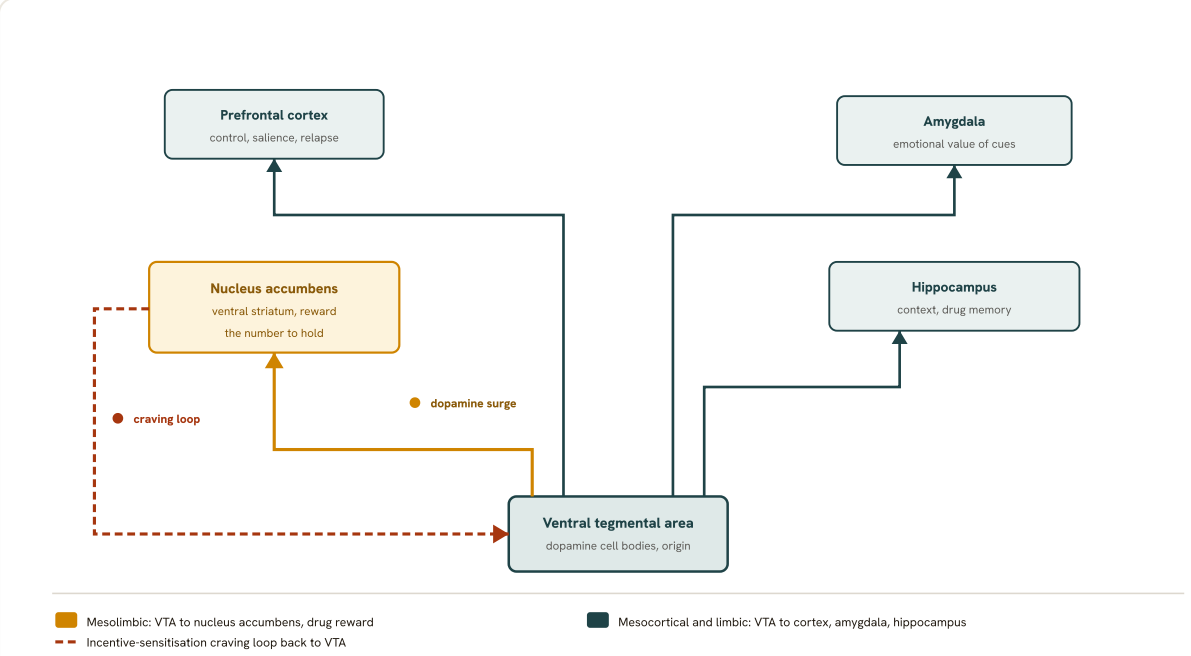


Fig 13.2 The mesolimbic reward circuit and the neurobiology of addiction. Dopamine cell bodies in the ventral tegmental area project along the mesolimbic tract to the nucleus accumbens, where drug reward drives a dopamine surge far larger than any natural reinforcer. Parallel projections reach the prefrontal cortex (control and salience), the amygdala (emotional value of drug cues) and the hippocampus (drug-associated context and memory). With repeated use the accumbens-driven incentive-sensitisation loop feeds back to the ventral tegmental area, so cues alone come to trigger craving even after the drug is stopped.

3.1 The mesolimbic reward pathway: the anatomy to hold

VTA to nucleus accumbens. The core of the reward system is the mesolimbic dopamine pathway, which runs from dopamine cell bodies in the ventral tegmental area (VTA) of the midbrain to the nucleus accumbens (NAc) in the ventral striatum (Stahl's Substance Use 2020; Kaplan and Sadock 2024). This projection is "central to reward": naturally rewarding activities such as a good meal or a major accomplishment cause fast, large increases in dopamine here, and drugs of abuse hijack the same wire (Stahl's Substance Use 2020). Two neighbouring dopamine

pathways round out the picture without being the reward core: the nigrostriatal pathway (substantia nigra to dorsal striatum), which the transition to compulsive, habit-like use recruits, and the mesocortical pathway (VTA to prefrontal cortex), which supplies the top-down control that addiction erodes (Stahl's Substance Use 2020). The VTA-NAc line is the phrase to reproduce; the amygdala links reward learning to it, and the prefrontal cortex regulates it from above.

RULE **One wire, hijacked.** The reward pathway is the mesolimbic dopamine projection from the ventral tegmental area to the nucleus accumbens; drugs of abuse do not build a new circuit, they seize the survival circuit that already exists.

3.2 The dopamine surge: the final common pathway of drug reward

All drugs of abuse raise accumbens dopamine. Whatever their molecular target, every major drug of abuse increases dopamine in the nucleus accumbens, either directly or indirectly (Stahl's Substance Use 2020). This shared endpoint is why chemically unrelated substances produce a common syndrome. The routes differ: stimulants block the dopamine transporter or release dopamine directly; opioids disinhibit VTA dopamine neurons by inhibiting the GABA interneurons that restrain them; nicotine directly stimulates nicotinic receptors on VTA dopamine neurons; alcohol and cannabinoids act more indirectly through GABA, glutamate and endocannabinoid modulation (Stahl's Substance Use 2020). Crucially, drugs raise dopamine "in a manner that is more explosive and pleasurable than that which occurs naturally," and it is the abrupt, large, phasic rise, not the mere presence of dopamine, that carries the reward and saliency signal (Stahl's Substance Use 2020).

DRUG CLASS	MOLECULAR TARGET	HOW ACCUMBENS DOPAMINE RISES
Stimulants (cocaine, amphetamines)	**Dopamine transporter (DAT)**	Blocks reuptake (cocaine) or drives release (amphetamine) at VTA-to-NAc terminals
Opioids	Mu-opioid receptor	**Disinhibits VTA dopamine neurons by inhibiting GABA interneurons**
Nicotine	Nicotinic receptor (alpha4 beta2)	Directly stimulates VTA dopamine neurons
Alcohol	Multiple (GABA, glutamate, opioid)	Facilitates GABAergic transmission and disinhibits dopamine indirectly
Cannabinoids	Cannabinoid CB1 receptor	Modulates dopamine signalling via CB1 in NAc and on GABA/glutamate terminals

Every drug of abuse converges on a dopamine rise in the nucleus accumbens by a different molecular route (Stahl's Substance Use 2020).

COMMON TRAP

Thinking dopamine equals pleasure. Dopamine encodes reward prediction and incentive salience ("wanting"), not the hedonic hit ("liking") itself, which is carried more by opioid and endocannabinoid signalling in accumbens hedonic hotspots. This distinction is the whole point of the incentive-sensitisation model below, and it is why craving can be intense while the drug no longer feels good.

3.3 Route and rate: why speed of onset drives addictiveness

Fast in, fast reward. The reinforcing effect of a drug is determined not only by how much dopamine it releases but by how fast the level rises, which is set by how quickly the drug enters the brain (Stahl's Substance Use 2020). Abrupt, large dopamine increases mimic the phasic firing that normally signals reward, so faster uptake means stronger reinforcement. This is why route of administration is a core addictiveness variable: intravenous injection and inhalation (smoking) give the fastest uptake, followed by snorting, then oral use (Stahl's Substance Use 2020). The same molecule is far more addictive smoked or injected than swallowed, which is the pharmacological logic behind harm-reduction shifts in route and behind the danger of smokable and injectable preparations.

3.4 Incentive sensitisation: wanting divorced from liking

The Robinson and Berridge model. The incentive-sensitisation theory (Robinson and Berridge) separates two dissociable psychological components that the folk model fuses: "liking," the hedonic pleasure a reward gives, and "wanting," the motivational pull toward it, technically termed **incentive salience** (Tasman 2015). Repeated drug exposure produces long-lasting sensitisation of the mesolimbic dopamine system, so the neural "wanting" signal grows and becomes attached to drug cues, while "liking" does not sensitise and often fades with tolerance. The result is the clinical paradox of addiction: the pull toward the drug becomes progressively more intense and cue-triggered even as the drug delivers less and less pleasure. This is the mechanistic account of pathological **craving**, especially the cue-evoked craving that survives detoxification and drives relapse long after withdrawal has passed.

Why cues matter clinically. Because incentive salience is stamped onto conditioned cues (people, places, paraphernalia, mood states), the sensitised "wanting" is reactivated by those cues rather than by an internal decision, which is why cue-exposure, environment change and stimulus control are built into relapse-prevention work (Tasman 2015). Incentive sensitisation is the bridge from the acute dopamine surge of first use to the durable, relapse-driving craving of established addiction.

MNEMONIC

WANT > LIKE

Incentive sensitisation = "wanting" (incentive salience, dopamine-driven, sensitises and attaches to cues) grows and outlasts "liking" (hedonic pleasure, opioid-driven, does not sensitise and fades with tolerance). Craving is sensitised wanting, not remembered liking.

3.5 The three-stage addiction cycle: the master framework

Binge, withdrawal, preoccupation. Koob and Volkow's cycle divides addiction into three recurring stages, each mapped to its own network and its own neurotransmitter shift (Kaplan and Sadock 2024). *Binge and intoxication* is the reward stage, driven by the basal ganglia, the nucleus accumbens and dorsal striatum, and dominated by the dopamine surge and positive reinforcement. *Withdrawal and negative affect* engages the extended amygdala (central amygdala, bed nucleus of the stria terminalis and the shell of the accumbens), where the brain stress systems, notably corticotropin-releasing factor and dynorphin, are recruited and reward is blunted, so the drug is now taken to relieve dysphoria (negative reinforcement). *Preoccupation and anticipation* is the craving stage, driven by the prefrontal cortex, orbitofrontal cortex, hippocampus and insula, where executive control fails and cue-triggered craving takes over (Kaplan and Sadock 2024).

Four neuroadaptations, one transition. The cycle summarises the transition to addiction as four combined changes: increased incentive salience, decreased reward, increased stress, and decreased executive function (Kaplan and Sadock 2024). Behaviourally, this is a progression from impulsive, positively reinforced use toward compulsive, negatively reinforced use driven by escape from a negative affective state (Stahl's Substance Use 2020).

STAGE	DOMINANT CIRCUIT	DRIVER / NEUROCHEMISTRY	REINFORCEMENT
Binge and intoxication	Basal ganglia (NAc, dorsal striatum)	**Dopamine surge; incentive salience**	Positive (pleasure/reward)
Withdrawal and negative affect	Extended amygdala (CeA, BNST, NAc shell)	**CRF and dynorphin up; reward down**	Negative (relief of dysphoria)
Preoccupation and anticipation	Prefrontal cortex, OFC, hippocampus, insula	**Executive dyscontrol; cue-driven craving**	Anticipatory (craving, relapse)

The three-stage addiction cycle, its networks, its neurochemistry and its reinforcement logic (Koob and Volkow, in Kaplan and Sadock 2024).

3.6 Opponent process: why abstinence turns painful

The b-process grows. The withdrawal stage is best explained by the opponent-process theory of motivation (Solomon and Corbit; Koob). Every hedonic state is automatically opposed by a counter-regulatory process: the positive drug response (the a-process) is fast, correlates with dose, and shows tolerance, while the opposing negative-affect response (the b-process) is slow to develop, slow to decay, and grows in magnitude with repeated exposure (Kaplan and Sadock 2024). With escalating use the b-process comes to dominate, so the baseline mood between doses drifts downward and the drug is increasingly taken not for euphoria but to cancel the withdrawal dysphoria the drug itself created. This "allostatic" resetting of the reward set-point is the neurobiology behind negative reinforcement and the persistence of use despite loss of pleasure.

3.7 Reactive versus reflective: the loss of top-down control

Bottom-up drive, top-down brake. A useful clinical shorthand splits the reward system into a reactive "bottom-up" component (VTA, nucleus accumbens and amygdala) that generates the

immediate pull toward pleasure or away from pain, and a reflective "top-down" component (prefrontal projections from the orbitofrontal, dorsolateral and ventromedial cortex, with the insula) that decides whether to act on that pull (Stahl's Substance Use 2020). In addiction the reactive system is sensitised and the reflective system is weakened, so cue-triggered drug-seeking is amplified at exactly the moment the brake is failing. This maps directly onto the preoccupation-anticipation stage and explains why insight and good intentions do not, on their own, prevent relapse.

HOLD THIS

All drugs of abuse converge on a dopamine surge in the nucleus accumbens via the mesolimbic pathway from the ventral tegmental area; repetition sensitises "wanting" (incentive salience) and recruits brain stress systems, moving the person through binge and intoxication, then withdrawal and negative affect, then preoccupation and anticipation, from positive to negative reinforcement.

3.8 Risk and the natural-reward comparison

Why not everyone who uses becomes addicted. The same cycle operates in all people, but the risk of moving from controlled, impulsive use to compulsive addiction is shaped by drug factors (the substance itself and its route and rate of uptake), genetics (many small-effect and epigenetic contributions, no single "addiction gene") and environment (early exposure, stress, deprivation, comorbid mental illness) (Stahl's Substance Use 2020). A useful examiner line: risk of *initiating* use is driven more by psychosocial factors, whereas risk of *progression* to addiction is driven more by neurobiological factors (Stahl's Substance Use 2020). The drug reward is pathological precisely because it is larger, faster and more reliable than natural rewards, so over time it out-competes food, work and relationships for the same circuit.

3	4	2
STAGES OF THE ADDICTION CYCLE	NEUROADAPTATIONS OF THE TRANSITION TO ADDICTION	DISSOCIABLE COMPONENTS: WANTING VS LIKING

3.9 The India frame: why the neurobiology is a treatment argument

From mechanism to access. In India the neurobiology of addiction is not an academic aside; it is the argument against moralising a disorder and for building services. The substance-use treatment gap is very large, with the great majority of people who are dependent never reaching any structured care, and the response is organised around a de-addiction and drug-de-addiction programme (DDAP) network of centres, the Indian Psychiatric Society substance-use clinical practice guidelines, and community and home-based delivery by trained non-specialist workers to reach the gap (IPS_CPG). The legal frame is the Narcotic Drugs and Psychotropic Substances Act (NDPS Act, Act 61 of 1985, in force 16 September 1985), which criminalises trafficking yet also provides for court-ordered detoxification, and whose access provisions govern how buprenorphine and methadone can be dispensed for opioid substitution. The full medico-legal detail of the NDPS Act sits in the Mental health legislation and forensic psychiatry notes; the point here is that the dopamine-hijack model reframes dependence as a brain disorder with

pharmacological targets rather than a vice, which is exactly what closing the treatment gap requires.

INDIA

The neurobiology carries directly into Indian practice on two fronts. First, buprenorphine (Indian brand Tidigesic; buprenorphine-naloxone as Suboxone or Bunorph) is the workhorse of opioid substitution precisely because it acts on the same mu-opioid step that disinhibits VTA dopamine, and its access is structured by the NDPS Act. Second, the incentive-sensitisation and opponent-process models are the teaching that lets a clinician explain to a family why relapse after months of abstinence is a cue-driven, sensitised-wanting phenomenon and not a moral failure, which is central to the non-confrontational, family-supported style the IPS guidelines recommend.

GOOD TO REMEMBER

- **Reward pathway (anatomy):** mesolimbic dopamine projection from the ventral tegmental area to the nucleus accumbens; amygdala adds reward learning, prefrontal cortex adds top-down control.
- **Dopamine surge (the discriminator):** all drugs of abuse raise accumbens dopamine by different molecular routes; the fast, phasic rise (set by route and rate of uptake) carries the reinforcement.
- **Incentive sensitisation (craving):** repeated use sensitises "wanting" (incentive salience, dopamine, cue-attached) which grows and outlasts "liking" (hedonic pleasure, opioid, fades); craving is sensitised wanting.
- **Three-stage cycle (the framework):** binge and intoxication (basal ganglia, dopamine, positive reinforcement); withdrawal and negative affect (extended amygdala, CRF and dynorphin, negative reinforcement); preoccupation and anticipation (prefrontal cortex, executive failure and cue-driven craving); the four neuroadaptations are increased incentive salience, decreased reward, increased stress and decreased executive function.

4 · Tolerance, withdrawal and neuroadaptation

Underneath every substance-use diagnosis sits a single physiology: the brain, exposed repeatedly to a drug, changes itself to oppose that drug, and those opposing changes are what a clinician meets as **tolerance** and, on cessation, as **withdrawal**. This topic is the mechanism chapter for the whole substance-use block. Examiners test it because it is where definitions, biology and clinical prediction meet: they will ask you to define the kinds of tolerance, to separate physical dependence from the dependence syndrome, to explain why the first fit of a drinker is rarely their worst, and to name the theory (allostasis) that ties reward loss to compulsive use. Get the vocabulary exact and the rest of the day, from why a benzodiazepine treats alcohol withdrawal to why successive detoxifications get more dangerous, follows without memorising each fact separately.

Why it matters clinically. The **neuroadaptation** that produces tolerance and withdrawal is also what makes withdrawal dangerous, predicts its time-course, and explains relapse long after the drug has cleared. Tolerance and a withdrawal state on their own are a normal, expected response to a chronically administered central nervous system drug and do *not* by themselves equal addiction (DSM-5-TR 2022). The reward-pathway and mesolimbic-dopamine anatomy on which all of this is built is developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and

Basic Psychopharmacology notes and is not re-derived here; the amnestic mechanism behind repeated-withdrawal brain injury is developed in the Dementias and neurocognitive disorders notes and the Neuropsychiatry of systemic and neurological disease notes.

4.1 Tolerance defined: the same dose does less, so more is needed

The core definition. Tolerance is the state in which, after repeated administration, a larger dose of a substance is required to produce the effect once achieved by a lower dose, or, equivalently, a given dose produces a progressively smaller effect (Kaplan and Sadock 2024; WHO ICD-11 CDDR 2024). It is a shift of the whole dose-response curve to the right. Tolerance is one of the physiological features of the dependence syndrome, but it is neither necessary nor sufficient for the syndrome on its own: a surgical patient on a stable opioid can be fully tolerant with no compulsion, salience or impaired control.

What it is not. Do not equate tolerance with the dependence syndrome or with addiction. Tolerance is a pharmacological adaptation; the syndrome adds a behavioural core (compulsion, impaired control, salience) on top of it. This distinction is the one DSM-5-TR is at pains to make, precisely so that prescribed-drug tolerance is not mislabelled as addiction.

4.2 The three mechanisms of tolerance: pharmacokinetic, pharmacodynamic and behavioural

The classification to hold. Kaplan and Sadock describe tolerance as arising through at least three distinct processes, and this taxonomy is a favourite short-answer item (Kaplan and Sadock 2024). **Pharmacokinetic (dispositional) tolerance** is adaptation of the drug-metabolising systems so the body clears the substance faster; for alcohol this is induction of hepatic and microsomal enzymes, so the same intake yields lower blood levels over time. **Pharmacodynamic (cellular) tolerance** is the most important: an adaptation of the nervous system itself so it can function despite high drug concentrations by resisting the drug's action at the cell, through receptor down-regulation, altered coupling and opposing changes in the balance of excitation and inhibition. **Behavioural (learned) tolerance** is where a person learns, through practice, to perform tasks effectively while under the drug's influence, so the observable impairment shrinks without the pharmacology changing.

Why the split matters. Pharmacodynamic tolerance is the one that generates the withdrawal state: because the cell has adapted *against* the drug, removing the drug leaves the adaptation unopposed, and the withdrawal syndrome is the adaptation showing through. Behavioural and pharmacokinetic tolerance do not, by themselves, produce a withdrawal state.

TYPE OF TOLERANCE	MECHANISM	WORKED ALCOHOL EXAMPLE
Pharmacokinetic (dispositional)	Faster metabolism / clearance of the drug (enzyme induction).	Hepatic and microsomal enzyme induction lowers blood alcohol for the same intake.
Pharmacodynamic (cellular)	Nervous system adapts to resist the drug's action at the cell.	GABA-A down-regulation and NMDA up-regulation let the brain function at high blood alcohol; this is what withdrawal unmasks.
Behavioural (learned)	Learned skill at performing while intoxicated; pharmacology unchanged.	The experienced drinker who walks a line at a level that would floor a novice.

The three mechanisms of tolerance; only pharmacodynamic (cellular) tolerance generates a physiological withdrawal state (Kaplan and Sadock 2024).

RULE **Pharmacodynamic tolerance is the one that bites.** Withdrawal is unopposed cellular (pharmacodynamic) adaptation; the more of it a substance produces, the more dangerous its withdrawal, which is why alcohol and sedatives, not opioids, kill in withdrawal.

GOOD TO REMEMBER

- **Tolerance:** more drug needed for the same effect (dose-response curve shifts right); three mechanisms, pharmacokinetic (faster clearance), pharmacodynamic/cellular (nervous-system resistance, the one that produces withdrawal), and behavioural (learned performance); it is one physiological feature of dependence, not the syndrome itself.

4.3 Cross-tolerance: tolerance to one drug carries to another in the same class

The definition. Cross-tolerance is the phenomenon whereby tolerance developed to one substance confers tolerance to a second, pharmacologically related substance the person may never have taken (Kaplan and Sadock 2024). It arises because the two drugs share a final common mechanism; once the cell has adapted against that mechanism, both drugs are resisted. Alcohol, benzodiazepines and barbiturates are all central nervous system depressants acting on the GABA-A system, so they show mutual cross-tolerance.

The two clinical consequences. First, cross-tolerance is exactly why a benzodiazepine treats alcohol withdrawal: the benzodiazepine substitutes at the same GABA-A system the brain has adapted around, and is then tapered. Second, a heavy drinker who stops will, in the short run, need a *higher* dose of another depressant such as a benzodiazepine for sedation. A separate danger is that two depressants taken together do not merely add but **potentiate**, so their combined depressant effect can be lethal even at individually modest doses. Note that cross-tolerance can be incomplete: between different opioids it is only partial, which is why equianalgesic switching lowers the dose.

COMMON TRAP

Do not assume tolerance to a drug's wanted effect means tolerance to its lethal effect. Tolerance to opioid euphoria and analgesia outruns tolerance to respiratory depression, so a person chasing the same high can reach a respiratory-arrest dose; and after a period of abstinence (for example release from custody or completed detoxification) tolerance falls fast, so a previously routine dose becomes fatal. This mismatch is the mechanism behind most opioid overdose deaths.

4.4 Physical dependence versus the dependence syndrome: two different things

Physical dependence. **Physical dependence** is the physiological state of adaptation in which a characteristic withdrawal syndrome appears on stopping, reducing or antagonising the drug; operationally it is tolerance plus a withdrawal state. It is a normal consequence of chronic administration of many central nervous system drugs and can exist without any addictive behaviour at all.

The dependence syndrome. The dependence syndrome (developed in the dependence-syndrome topic) is a behavioural-cognitive-physiological cluster in which the substance acquires abnormally high priority: compulsion, impaired control and salience sit alongside the physiological features. DSM-5-TR states plainly that the tolerance and withdrawal that once defined "dependence" are normal responses to prescribed centrally acting drugs and do not by themselves indicate the presence of an addiction (DSM-5-TR 2022). A patient stabilised on a long-term benzodiazepine or opioid analgesic is physically dependent but is not, on that ground alone, addicted.

TRAP **Calling a stable prescribed patient "addicted".** Tolerance and a withdrawal state are physical dependence, a normal drug adaptation; addiction needs the behavioural core (compulsion, impaired control, salience). Labelling the compliant chronic-pain or panic patient as addicted is a criterion error, not a clinical finding.

4.5 Withdrawal as neuroadaptation unmasked: mirror-image and relief use

The mirror-image principle. The withdrawal state is the substance-specific syndrome that appears on cessation or reduction. For many substances the withdrawal features are the mirror image of the drug's acute pharmacological effects (WHO ICD-11 CDDR 2024): a central nervous system depressant such as alcohol calms and sedates, so its withdrawal is hyperexcitable, with tremor, tachycardia, seizures and, at the extreme, delirium tremens; an opioid produces analgesia, pupillary constriction, constipation and euphoria, so its withdrawal produces pain, mydriasis, diarrhoea and dysphoria. This is the neuroadaptation showing through once the drug is removed: the opposing cellular changes that produced tolerance now have nothing to oppose.

Relief use. A key clinical rider is the "relief-use" clause: taking the same or a closely related substance to relieve or avoid withdrawal is itself a marker of the physiological arm of dependence, and avoidance of withdrawal becomes a powerful driver of continued use. The full time-courses and drug-specific management of alcohol, opioid and sedative withdrawal are developed in the withdrawal-management topics; here the point is only mechanistic.

PEARL

Read a withdrawal syndrome by inverting the intoxication. If you can recall what the drug does acutely, you can predict its withdrawal: the depressant's withdrawal is excitation (seizures, delirium), the stimulant's is a "crash" (hypersomnia, hyperphagia, dysphoria), and the opioid's is a flu-like autonomic storm that is distressing but, in the physically healthy adult, rarely life-threatening.

4.6 The molecular substrate: what actually adapts

Alcohol and sedatives. The prototype is the GABA-glutamate axis. Chronic alcohol enhances inhibitory GABA-A transmission and inhibits excitatory NMDA-glutamate transmission acutely; the brain compensates by down-regulating GABA-A receptors and up-regulating NMDA receptors. When alcohol is withdrawn, this leaves reduced inhibition and unopposed glutamatergic excitation, a hyperexcitable state that manifests as tremor, autonomic arousal and, if severe, seizures and delirium (Kaplan and Sadock 2024). Benzodiazepines and barbiturates share the GABA-A target, hence the cross-tolerance and the clinical use of benzodiazepines to cover alcohol withdrawal.

Opioids. Chronic mu-opioid receptor agonism drives receptor uncoupling and desensitisation and a compensatory up-regulation of the cyclic-AMP and locus-coeruleus noradrenergic systems; on withdrawal, the noradrenergic overshoot produces much of the autonomic storm, which is why the alpha-2 agonists clonidine and lofexidine, and the mixed benefit of an alpha-2A agonist added to substitution, blunt opioid-withdrawal severity. The receptor-level detail belongs to the substitution and withdrawal-management topics.

4.7 Allostasis and the anti-reward system: why the setpoint moves

From homeostasis to allostasis. The dominant modern framework, from Koob and Le Moal, reframes addiction as a failure not of homeostasis (return to a fixed setpoint) but of allostasis: the brain achieves stability through change, and repeated drug use shifts the hedonic setpoint itself to a new, lower baseline that can only be maintained by continued use (Tasman 2015, Koob; Kaplan and Sadock 2024). The "allostatic load" is the accumulating cost of these repeated adaptations. Addiction, in this model, is a spiral driven as much by the loss of a normal reward baseline as by the pursuit of a high.

The anti-reward / opponent-process arm. Reward systems are opposed by **anti-reward** systems whose job is to limit reward (an opponent-process concept). As tolerance and withdrawal develop, brain-stress systems are recruited: corticotropin-releasing factor and noradrenaline in the extended amygdala, and the dynorphin-kappa-opioid system in the ventral striatum, which reduces accumbal dopamine release. The result is a dual hit: a within-system dampening of dopaminergic reward (blunted, so more drug is needed) and a between-system recruitment of stress/anti-reward circuitry (so abstinence feels actively bad). This is the negative-reinforcement engine of the withdrawal/negative-affect stage of the three-stage cycle (binge/intoxication, withdrawal/negative affect, preoccupation/anticipation).

WORKED EXAMPLE

A person with severe alcohol use disorder says drinking no longer makes them feel good; it only stops them feeling terrible. That single sentence is the allostasis model in the room: the hedonic setpoint has dropped (within-system reward loss) and the CRF/noradrenaline/dynorphin anti-reward systems are recruited (between-system stress), so the drink now works by negative reinforcement, relieving a manufactured distress rather than producing pleasure. It also explains why anti-craving pharmacotherapy and relapse prevention, not just detoxification, are needed: clearing the drug does not restore the setpoint.

4.8 Kindling: why each successive withdrawal is worse

The definition. Kindling is the phenomenon whereby substance-withdrawal symptoms become progressively more severe with each repeated episode of withdrawal, so that a person who has withdrawn many times faces worse and more dangerous withdrawals than a first-timer, independent of how much they drink (WHO ICD-11 CDDR 2024; Becker 1998). It is best characterised for alcohol. Repeated cycles of intoxication and abrupt withdrawal sensitise the central nervous system, borrowing the term from the electrophysiological kindling in which repeated sub-threshold stimulation eventually triggers seizures. Each detoxification is not a clean reset; it lays down a sensitised substrate for the next.

The clinical corollaries. Kindling is why a history of multiple prior withdrawals or prior withdrawal seizures is a red flag that predicts a more complicated course, why "just letting them dry out at home again" is dangerous in the multiply-detoxified drinker, and part of why aggressive, adequate benzodiazepine cover of each withdrawal matters, since under-treated withdrawals may worsen the next. The same repeated-cycle sensitisation is invoked for the paradoxical worsening seen in some benzodiazepine re-instatements (Maudsley Deprescribing Guidelines).

RULE **Count the prior withdrawals.** A history of repeated detoxifications or any prior withdrawal seizure predicts a more severe next withdrawal (kindling); treat such a patient's withdrawal as high-risk and cover it adequately, do not send them home to detox unassisted again.

2 of 3	8 to 10	3
ICD-11 DEPENDENCE CENTRAL FEATURES (IMPAIRED CONTROL, SALIENCE, NEUROADAPTATION)	CIWA-AR SCORE AT OR ABOVE WHICH TO MEDICATE ALCOHOL WITHDRAWAL	MECHANISMS OF TOLERANCE (PHARMACOKINETIC, PHARMACODYNAMIC, BEHAVIOURAL)

4.9 Where tolerance and withdrawal enter diagnosis and screening

The neuroadaptation arm of the criteria. In ICD-11, tolerance, withdrawal and relief use are collapsed into a single "physiological features indicative of neuroadaptation" criterion, one of the three central features of dependence, of which two are needed (WHO ICD-11 CDDR 2024). So on their own, tolerance and withdrawal contribute one of three; the behavioural features (impaired control, increasing precedence/salience) supply the rest. A crucial rider is that the physiological features apply only to certain substances, so their absence (as in some stimulant or hallucinogen use) does not exclude dependence.

Scales that touch this. Withdrawal severity is quantified for management, not diagnosis: the **CIWA-Ar** for alcohol withdrawal and the **COWS** for opioid withdrawal, both taught with their cut-offs in the withdrawal-management topics and reproduced in the scales gallery. At the screening end, the AUDIT (a score of 8 or more flags hazardous or harmful drinking) and CAGE identify problem use before dependence is entrenched. The severity-of-dependence instruments (for example the SADQ for alcohol) index the physiological adaptation this topic describes; their cut-offs belong to the withdrawal topics.

MNEMONIC

"PK-PD-B" for the three tolerances, and "mirror, relief, kindle" for withdrawal

Tolerance splits into PharmacoKinetic (faster clearance), PharmacoDynamic (cellular resistance, the withdrawal-maker), and Behavioural (learned). Withdrawal is the Mirror image of intoxication, drives Relief use, and Kindles (worsens) with each repeated episode.

INDIA

The mechanistic picture has a sharp Indian edge. India carries a very large substance-use treatment gap, with most people meeting dependence criteria never reaching formal care, and services concentrated in government de-addiction centres and Drug De-addiction Programme (DDAP) units rather than general practice (IPS 2014). Kindling is the reason this matters clinically here: the multiply-detoxified drinker who has cycled through unassisted or under-resourced withdrawals repeatedly arrives with a sensitised, higher-risk withdrawal, so adequate benzodiazepine cover and parenteral thiamine before any glucose load are not optional. The legal frame is the Narcotic Drugs and Psychotropic Substances (NDPS) Act, 1985, whose scheduling shapes access to controlled agents; the medico-legal detail is developed in the Mental health legislation and forensic psychiatry notes. On the neuroadaptation-reversal side, buprenorphine (Indian brand Tidigesic; buprenorphine-naloxone as Suboxone) is the workhorse of Indian opioid-agonist treatment because it substitutes at the adapted mu-opioid receptor while capping respiratory risk, and its induction detail belongs to the substitution topics.

GOOD TO REMEMBER

- **Cross-tolerance:** tolerance to one drug carries to a related drug sharing the mechanism (alcohol / benzodiazepines / barbiturates via GABA-A); it is why a benzodiazepine treats alcohol withdrawal; combined depressants potentiate and can be lethal; between opioids it is only partial (lower the dose when switching).
- **Physical dependence:** tolerance plus a withdrawal state; a normal adaptation to chronic centrally acting drugs; not the same as addiction, which needs the behavioural core; the first management step on stopping is to assess and cover withdrawal risk.
- **Kindling:** withdrawal severity rises with each repeated withdrawal episode, best characterised for alcohol; the discriminator of a high-risk withdrawal is the count of prior detoxifications or a prior withdrawal seizure; the first step is to treat the next withdrawal as high-risk with adequate cover.
- **Allostasis / anti-reward:** repeated use lowers the hedonic setpoint (within-system reward loss) and recruits CRF, noradrenaline and dynorphin-kappa stress systems (between-system anti-reward), driving use by negative reinforcement; the corollary is that detoxification alone does not restore the setpoint, so relapse-prevention pharmacotherapy is needed.

GOOD TO REMEMBER

- **Naltrexone (Indian brands Naltima, Nodict):** a mu-opioid receptor antagonist; oral 50 mg/day is a first-line anti-craving agent in alcohol use disorder (blunting alcohol's reward, an allostasis-relevant target); the signature caution is that giving it to a current opioid user precipitates an acute withdrawal, so an opioid-free window (about 7 to 10 days) is mandatory before starting; not itself a treatment for the physiological withdrawal state.

HOLD THIS

Withdrawal is pharmacodynamic (cellular) neuroadaptation unmasked, so it mirrors intoxication and worsens with each repeated episode (kindling); tolerance and a withdrawal state are physical dependence, a normal drug adaptation, and are not addiction until the behavioural core (compulsion, impaired control, salience) is present.

5 · Screening instruments for substance use

Most people with a substance problem never volunteer it, and most present for something else entirely, so the substance-use disorders are found by *asking in a structured way*, not by waiting for a confession. That is the whole logic of screening: short, validated **questionnaire**s that a clinician (or the patient) can complete in a couple of minutes to flag the person who needs a fuller assessment. Examiners love this topic because it is pure recall of numbers: they will ask how many items an instrument has, what it screens for, and above all its **cut-off** score. A wrong cut-off is the classic dropped mark, so the whole of this topic is built around getting four numbers cold: AUDIT 8, CAGE 2, DAST-10 3, and the ASSIST risk bands.

Why it matters clinically. Screening earns its place precisely at the hazardous-and-harmful end, where the problem is common, under-recognised and still reversible by brief, motivation-based intervention before dependence is entrenched. A positive screen is never a diagnosis; it is a trigger for assessment. This is where India's substance-use treatment gap is most tractable, because a validated instrument in a non-specialist's hands catches the drinker or user long before they would ever reach a de-addiction centre. The full instrument forms are reproduced in the

scales gallery figure (Fig 13.3), so this topic teaches what each instrument is and how it is scored, not the item wording.

Box 10

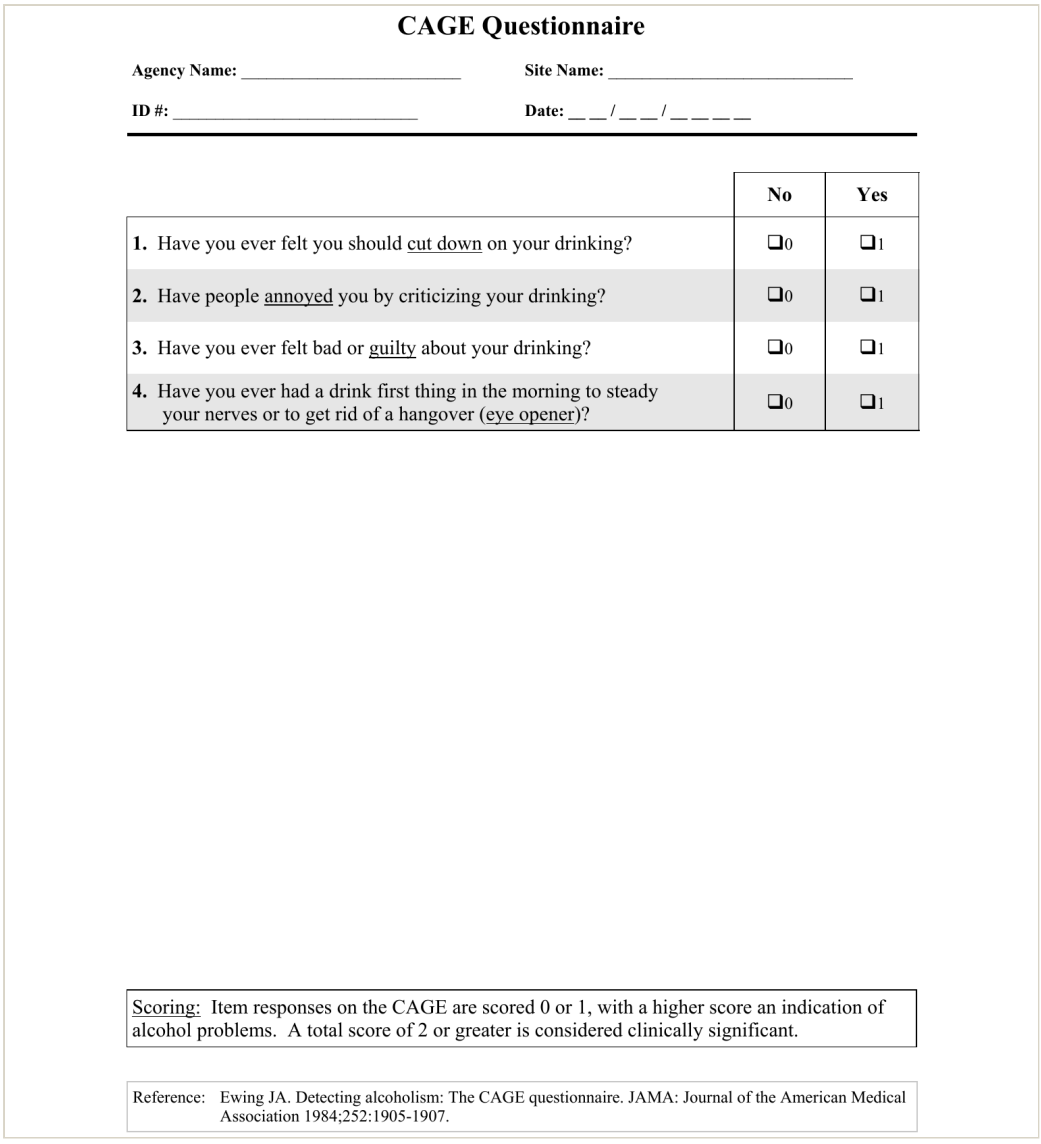
The Alcohol Use Disorders Identification Test: Self-Report Version

PATIENT: Because alcohol use can affect your health and can interfere with certain medications and treatments, it is important that we ask some questions about your use of alcohol. Your answers will remain confidential so please be honest.
Place an X in one box that best describes your answer to each question.

Questions	0	1	2	3	4	
1. How often do you have a drink containing alcohol?	Never	Monthly or less	2-4 times a month	2-3 times a week	4 or more times a week	
2. How many drinks containing alcohol do you have on a typical day when you are drinking?	1 or 2	3 or 4	5 or 6	7 to 9	10 or more	
3. How often do you have six or more drinks on one occasion?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
4. How often during the last year have you found that you were not able to stop drinking once you had started?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
5. How often during the last year have you failed to do what was normally expected of you because of drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
7. How often during the last year have you had a feeling of guilt or remorse after drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
8. How often during the last year have you been unable to remember what happened the night before because of your drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
9. Have you or someone else been injured because of your drinking?	No		Yes, but not in the last year		Yes, during the last year	
10. Has a relative, friend, doctor, or other health care worker been concerned about your drinking or suggested you cut down?	No		Yes, but not in the last year		Yes, during the last year	
					Total	

The AUDIT, self-report version: 10 items, each scored 0 to 4 (total 0 to 40); the examinable cut-off is 8 or more for hazardous or harmful use.

Reproduced from WHO AUDIT manual (WHO/MSD/MSB/01.6a, 2001); free for non-commercial reproduction per the WHO copyright grant.



CAGE Questionnaire

Agency Name: _____ **Site Name:** _____

ID #: _____ **Date:** __ __ / __ __ / __ __ __ __

	No	Yes
1. Have you ever felt you should cut down on your drinking?	❑0	❑1
2. Have people annoyed you by criticizing your drinking?	❑0	❑1
3. Have you ever felt bad or guilty about your drinking?	❑0	❑1
4. Have you ever had a drink first thing in the morning to steady your nerves or to get rid of a hangover (eye opener)?	❑0	❑1

Scoring: Item responses on the CAGE are scored 0 or 1, with a higher score an indication of alcohol problems. A total score of 2 or greater is considered clinically significant.

Reference: Ewing JA. Detecting alcoholism: The CAGE questionnaire. JAMA: Journal of the American Medical Association 1984;252:1905-1907.

The CAGE questionnaire: four yes/no items (Cut down, Annoyed, Guilty, Eye-opener), each 0 or 1; a total of 2 or more is clinically significant.

CAGE questionnaire (Ewing JA, JAMA 1984); reproduced with acknowledgement, non-commercial use, per the Bowles Center permission.

DAST-10 (TYPESET, NOT REPRODUCED)	VERIFIED STRUCTURE AND CUT-OFF
Instrument	Drug Abuse Screening Test, 10-item version (Skinner 1982)
Items	10 yes/no items; drug use excluding alcohol and tobacco, past 12 months; item 3 is reverse-scored; total range 0 to 10
Cut-off / bands	**3 or more warrants assessment; 0 none, 1 to 2 low, 3 to 5 moderate, 6 to 8 substantial, 9 to 10 severe (Skinner)**

DAST-10: typeset structure and verified cut-off only; the form is permission-required and is not reproduced (Skinner HA. The Drug Abuse Screening Test. Addict Behav. 1982;7(4):363-71; © 1982 Harvey A. Skinner / CAMH).

WHO ASSIST V3.1 (TYPESET, NOT REPRODUCED)	VERIFIED STRUCTURE AND RISK BANDS
Instrument	Alcohol, Smoking and Substance Involvement Screening Test, interviewer-administered, 10 substance classes (Humeniuk et al., WHO 2010)
Items	8 questions per substance; a Substance Involvement (SI) score is summed from questions 2 to 7
Risk bands	**Most substances: 0 to 3 lower, 4 to 26 moderate, 27 or more high. Alcohol: 0 to 10 lower, 11 to 26 moderate, 27 or more high**

WHO ASSIST: typeset structure and verified bands only; verbatim reproduction requires WHO Press permission (Humeniuk R, et al. The ASSIST: manual for use in primary care. Geneva: WHO; 2010. ISBN 978 92 4 159938 2).

Fig 13.3 The substance-use screening instruments: AUDIT, CAGE, DAST and ASSIST. The AUDIT and CAGE are shown as their actual open, freely reproducible forms: the AUDIT is the 10-item WHO alcohol screen (each item 0 to 4, total 0 to 40, cut-off 8 or more), and the CAGE is the four-item bedside screen (Cut down, Annoyed, Guilty, Eye-opener, cut-off 2 or more). The DAST-10 and the WHO ASSIST are permission-required instruments and so are given as typeset structure and verified cut-offs only, not reproduced: the DAST-10 is the 10-item non-alcohol drug screen with a cut-off of 3 or more, and the ASSIST is the WHO all-substance screen whose per-substance Substance Involvement score sorts the person into lower, moderate or high risk (0 to 3, 4 to 26, 27 or more for most substances; 0 to 10, 11 to 26, 27 or more for alcohol) and directs the matched intervention.

5.1 What a screening instrument is (and is not): screen, do not diagnose

The purpose. A **screening instrument** is a brief, standardised tool designed to identify people who are likely to have a problem and who therefore warrant fuller assessment; it trades depth for speed and reach (Clinical Methods in Psychiatry 2024). Screening instruments such as the AUDIT, DAST and CAGE are deliberately over-inclusive: they favour sensitivity so as not to miss cases, accepting some false positives that the follow-up assessment will sort out.

The contrast with diagnostic instruments. A screen only sorts people into "assess further" versus "reassure"; the diagnosis is made afterwards against ICD-11 or DSM-5-TR criteria (the criterion sets are developed in the dependence-syndrome topic). Reading a positive screen as a diagnosis is the single commonest misuse of these tools.

RULE **A screen triggers assessment, never a diagnosis.** A score over the cut-off means "ask more", not "this person has a substance use disorder"; the diagnosis is always made against the criterion set, not the questionnaire.

5.2 The AUDIT: the 10-item WHO alcohol screen and its cut-off of eight

What it is. The AUDIT (Alcohol Use Disorders Identification Test) is the standard alcohol screen, developed by the WHO in the late 1980s for the early detection of **hazardous** and **harmful** drinking across settings (Kaplan & Sadock 2024; Maudsley 2021). It is a **10-item** self-report **questionnaire**, each item scored 0 to 4, giving a total of 0 to 40, and takes under five minutes with no professional training. Its three domains are structured: items 1 to 3 cover the quantity and frequency of alcohol consumed, items 4 to 6 the signs and symptoms of dependence, and items 7 to 10 the behaviours and problems of harmful use (Maudsley 2021).

The cut-off. A score of **8 or more** is the standard threshold, suggestive of hazardous or harmful drinking (Kaplan & Sadock 2024; Maudsley 2021). It is quite sensitive, at least in men; lower cut-offs (7 in women, adolescents and older adults) improve detection in those groups, and a threshold of 10 buys more specificity. NICE advises a comprehensive specialist assessment for anyone scoring more than 15 (NICE 2011). The abbreviated **audit**-C uses only the first three consumption items (score 0 to 12) for rapid consumption screening.

AUDIT BAND (TOTAL SCORE)	INTERPRETATION	ACTION
0 to 7	Low risk	Reinforce; no intervention needed
8 to 15	Hazardous / increasing risk	Brief advice / simple brief intervention
16 to 19	Harmful / higher risk	Brief intervention plus monitoring / referral
20 to 40	Possible dependence	Refer for specialist / diagnostic assessment

The AUDIT score bands; the single examinable number is the cut-off of 8 for hazardous or harmful use (Kaplan & Sadock 2024; Maudsley 2021; NICE 2011).

GOOD TO REMEMBER

- **AUDIT:** 10-item WHO alcohol screen, each item 0 to 4, total 0 to 40; cut-off **8 or more** = hazardous or harmful drinking; NICE refers >15 for comprehensive assessment; domains are consumption (Q1-3), dependence (Q4-6), harm (Q7-10); AUDIT-C = the first 3 consumption items.

5.3 The CAGE: the four-item bedside screen and its cut-off of two

What it is. The CAGE (Ewing 1984) is the classic ultra-brief bedside alcohol screen, four yes/no questions taking one minute or less (Kaplan & Sadock 2024; Tasman). The acronym is the whole instrument: **C**ut down (have you ever felt you should cut down?), **A**nnoyed (have people annoyed you by criticising your drinking?), **G**uilty (have you ever felt bad or guilty about your drinking?), and **E**ye-opener (have you ever had a drink first thing in the morning to steady your nerves or cure a hangover?). Each "yes" scores 1, for a total of 0 to 4.

The cut-off. A score of **2 or more** is clinically significant and strongly suggests an alcohol problem warranting fuller assessment; a score of 1 or more warrants follow-up (Kaplan & Sadock 2024). The trade-off is deliberate: a threshold of 2 is more specific, a threshold of 1 more sensitive. CAGE's weakness is that it detects established problem drinking well but is poor at picking up the early, hazardous drinking that brief intervention most helps, which is exactly where the AUDIT is stronger. The **cage**-AID variant extends the four questions to cover other drugs.

MNEMONIC

CAGE = Cut down · Annoyed · Guilty · Eye-opener

Four questions, one point each; two or more positive answers is the cut-off that flags a likely alcohol problem. The Eye-opener item (a morning drink) is the one most specific for dependence.

GOOD TO REMEMBER

- **CAGE:** 4-item bedside alcohol screen (Cut down, Annoyed, Guilty, Eye-opener), each 1 point; cut-off **2 or more** positive answers is clinically significant; good for established problem drinking, weak for early hazardous use; CAGE-AID extends it to other drugs.

5.4 The DAST-10: the drug-abuse counterpart and its cut-off of three

What it is. The DAST (Drug Abuse Screening Test, Skinner 1982) is the drug-use analogue of the AUDIT, screening for problems related to *non-alcohol* psychoactive drugs (illicit and prescription misuse) over the past 12 months (Clinical Methods in Psychiatry 2024). The widely used short form, the DAST-10, is a **10-item** yes/no **questionnaire** where most items score 1 for "yes" (one reverse-scored item scores 1 for "no"), giving a total of 0 to 10; longer 20-item and 28-item versions also exist.

The cut-off. On the DAST-10 a score of **3 or more** is the usual threshold prompting further assessment, with higher scores grading the problem (1 to 2 low, 3 to 5 moderate, 6 to 8 substantial, 9 to 10 severe). Because it deliberately excludes alcohol and tobacco, the DAST is paired with the AUDIT for a full picture, or replaced by the ASSIST where a single all-substance tool is wanted.

GOOD TO REMEMBER

- **DAST-10:** 10-item yes/no drug-use screen (non-alcohol drugs, past year), total 0 to 10; cut-off **3 or more** = warrants assessment (3-5 moderate, 6-8 substantial, 9-10 severe); the drug counterpart of the AUDIT.

5.5 The WHO ASSIST: the all-substance screen with its per-substance risk bands

What it is. The ASSIST (Alcohol, Smoking and Substance Involvement Screening Test) is the WHO's single instrument covering *all* substance classes at once, developed for use in primary and general health care (Kaplan & Sadock 2024). It is an eight-question interviewer-administered **questionnaire** asking, for each substance (tobacco, alcohol, cannabis, cocaine, amphetamine-type stimulants, inhalants, sedatives, hallucinogens, opioids and "other"), about lifetime and recent use, urge, problems, failed control, and concern from others. It generates a **Specific Substance Involvement Score** (SSIS) for each substance, which sorts the person into a risk band that maps directly onto the intervention needed.

The bands. For most substances the SSIS bands are **0 to 3** lower risk (no intervention), **4 to 26** moderate risk (brief intervention), and **27 or more** high risk (more intensive treatment / referral). Alcohol is the one exception, where the lower-risk band runs 0 to 10 and the moderate band 11 to 26 (WHO ASSIST manual). The tiered structure is the point: the ASSIST does not just

detect, it directs the person straight to brief intervention or specialist referral. Shorter variants (ASSIST-Lite, the NIDA-Modified ASSIST) exist for rapid use.

ASSIST SSIS BAND	OTHER SUBSTANCES (SCORE)	ALCOHOL (SCORE)	LINKED ACTION
Lower risk	0 to 3	0 to 10	No intervention; feedback only
Moderate risk	4 to 26	11 to 26	Brief intervention
High risk	27 or more	27 or more	More intensive treatment / referral

The WHO ASSIST per-substance risk bands; note the alcohol lower-risk band runs to 10 whereas other substances cut at 3 (WHO ASSIST manual).

GOOD TO REMEMBER

- **ASSIST:** 8-question WHO all-substance screen giving a per-substance SSIS; bands **0-3 lower / 4-26 moderate / 27+ high** for most drugs, but **0-10 / 11-26 / 27+** for alcohol; the moderate band triggers brief intervention, the high band triggers referral.

5.6 Choosing the instrument: matching the screen to the question

The decision. The four instruments are not interchangeable, and the exam tests whether you know which to reach for. Reach for the *AUDIT* when the question is specifically about alcohol and you want to catch it early; the *CAGE* when you need a one-minute bedside screen and lifetime problem drinking is the concern; the *DAST* when the question is non-alcohol drug use; and the *ASSIST* when you want one tool across every substance class with a built-in link to the intervention.

The common thread. Every one is a screen, so every positive result routes to the same next step: a fuller, criterion-based assessment. The value added by the ASSIST and the AUDIT bands is that they also tell you *how intensively* to respond, which is why they suit stepped-care systems and the Indian treatment-gap context better than a bare yes/no screen.

INSTRUMENT	ITEMS	SCREENS FOR	CUT-OFF / BANDS
AUDIT	10	Hazardous / harmful alcohol use	**8 or more (NICE >15 refer)**
CAGE	4	Established problem drinking	**2 or more positive**
DAST-10	10	Non-alcohol drug problems	**3 or more**
ASSIST	8 (per substance)	All substance classes	**4-26 moderate / 27+ high (alcohol 11-26 / 27+)**

The four screens at a glance; the cut-off column is the one that earns or loses the mark (Kaplan & Sadock 2024; Maudsley 2021; WHO ASSIST manual).

8	2	3	27
AUDIT HAZARDOUS OR HARMFUL-USE CUT-OFF	CAGE POSITIVE-ANSWER CUT-OFF	DAST-10 CUT-OFF FOR FURTHER ASSESSMENT	ASSIST HIGH-RISK SSIS THRESHOLD

TRAP **Blurring the cut-offs.** The numbers are not the same: AUDIT is 8, CAGE is 2, DAST-10 is 3, and the ASSIST high-risk band is 27 (with alcohol's moderate band uniquely starting at 11, not 4). Swapping one cut-off for another is the classic dropped mark.

INDIA

Screening is the sharpest tool against India's substance-use treatment gap, where the large majority meeting dependence criteria never reach the government de-addiction centres or the Drug De-addiction Programme (DDAP) units that hold most formal services. The IPS substance-use guidelines therefore emphasise brief, motivation-based intervention delivered by trained non-specialist health workers, with a strategic shift toward community and home-based delivery (IPS 2014); a validated screen in a general-practice or primary-care hand is the entry point to that pathway. The AUDIT and ASSIST have been widely used in Indian primary-care and epidemiological work, and the WHO ASSIST's built-in brief-intervention link fits the non-specialist model well. The wider legal frame is the Narcotic Drugs and Psychotropic Substances Act, 1985, which shapes how opioid problems (buprenorphine being the workhorse of Indian opioid-agonist treatment) are managed once a screen has flagged them; that medico-legal detail is developed in the Mental health legislation and forensic psychiatry notes.

WORKED EXAMPLE

A 40-year-old man attends a general clinic for dyspepsia. The clinician administers the AUDIT: he scores 17, in the harmful band, so brief intervention plus monitoring is indicated rather than reassurance. Because he also mentions occasional sleeping-tablet use, the clinician adds the DAST-10, on which he scores 4 (moderate), prompting a fuller drug history. Neither score is a diagnosis; both are triggers. Had a single all-substance tool been wanted, the ASSIST alone would have covered both the alcohol and the sedative use and sorted each into its own risk band, pointing directly to brief intervention for the alcohol and assessment of the sedatives.

COMMON TRAP

Do not confuse a *screening* instrument with a *severity* scale. The AUDIT, CAGE, DAST and ASSIST answer "is there a problem worth assessing?"; the SADQ (dependence severity), CIWA-Ar (alcohol withdrawal severity), COWS (opioid withdrawal severity) and Fagerstrom (nicotine dependence) answer a different question and belong to the withdrawal and dependence-management topics, not to screening.

HOLD THIS

Four screens, four numbers: AUDIT 8 (10 items, alcohol), CAGE 2 (4 items, alcohol), DAST-10 3 (10 items, drugs), ASSIST 27 for high risk (8 questions per substance, alcohol moderate band uniquely 11-26); every positive screen triggers assessment, never a diagnosis.

6 · Dual diagnosis

Some patients do not fit into one clinic. A person can have both a substance use disorder *and* another mental disorder at the same time, and when they do, treating one and ignoring the other tends to fail both. This is the topic that names that situation, teaches how services have historically tried (and mostly failed) to handle it, and states the one management principle the exam wants: treat both together. The construct sits at the seam between the substance-use chapter and the rest of psychiatry, which is exactly why it is a favourite. The reward-pathway biology that makes psychiatric illness and substance use so intertwined is developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and is not re-derived here.

Why it matters clinically. Comorbidity is not the exception; among people with alcohol dependence roughly a third carry a second psychiatric diagnosis, and among those with drug dependence nearly half do (Farrell et al 2001, in the Companion). Miss it and you mis-diagnose, under-treat, and watch the person cycle through crisis presentations. The examinable spine is a triad: the **concept, models** of service delivery, and the integrated-treatment principle. Learn those three and the topic is yours.

6.1 The concept: a co-occurring substance use disorder plus another mental disorder

Definition. Dual diagnosis is the co-occurrence, in the same person, of a substance use disorder and at least one other mental disorder (WHO; Companion to Psychiatric Studies 2010). The term is used loosely and many textbooks prefer **comorbidity**: the Companion states explicitly that for its chapter the word comorbidity, rather than dual diagnosis, is used when one diagnosis is psychoactive substance use and the second a mental and behavioural disorder. The Shorter Oxford treats the two as synonyms and notes the modern move away from diagnostic hierarchies (which forced one label) toward recognising comorbidity, because comorbidity is very common (Kessler 2004). Hold both words; an examiner may use either.

What it is not. Dual diagnosis in current psychiatric usage means a mental disorder plus a substance use disorder. It no longer means, as it once did, a mental disorder co-occurring with intellectual disability; that older, stigmatising usage has been retired (Tasman). Keep the modern meaning.

RULE **Screen everyone, both ways.** Ask every psychiatric patient about substances and every substance-use patient about mental illness; comorbidity is the rule, not the exception, and it is routinely missed when only one door is opened.

GOOD TO REMEMBER

- **Dual diagnosis / comorbidity:** a substance use disorder plus a second mental disorder in the same person; the discriminator from a single diagnosis is that both independently need treatment; the first step on recognising it is to establish which came first and whether the second is truly independent or substance-induced.

6.2 How common, and which pairings: the numbers to hold

Base rates. Against a general-population psychiatric-diagnosis rate near 12%, comorbidity rises to **30%** in alcohol dependence and to **45%** in drug dependence (Farrell et al 2001; Companion). On inpatient psychiatric units, substance misuse is found in roughly 20% before drug screening and 35% after, reaching 65% in young, male, urban, lower-income groups. These are the figures examiners quote.

The classic pairings. Substance misuse is the single most prevalent comorbid condition in schizophrenia (cannabis and stimulants predominate); bipolar disorder carries a comorbidity rate around 35% (stimulants most common); antisocial personality disorder rises from a 5% population rate to 18% in substance users and up to 44% in injectors; and mood disorders before age 20 carry a four-fold increased risk of later substance misuse (Companion). ADHD, PTSD and anxiety disorders complete the common list.

COMORBID DISORDER	COMORBIDITY SIGNAL (FROM THE COMPANION)
Schizophrenia	The most prevalent comorbidity in schizophrenia; cannabis and amphetamines predominate; worse compliance, more violence, more relapse, poorer prognosis.
Bipolar disorder	Comorbidity rate around 35%; stimulants (cocaine, amphetamine) most common; mood stabilisers (lithium, valproate, carbamazepine) supported.
Antisocial personality disorder	5% population rate rises to 18% in substance users, up to 44% in IV drug users.
Mood disorders	Onset before age 20 gives a four-fold increased risk of later substance misuse.
PTSD	Substance misuse parallels PTSD development (self-medication of hyperarousal); sedative preference; a present-focused coping-skills model is best-tested.
ADHD	Adult ADHD drives comorbid misuse (usually stimulants); medication alone is inadequate for both.

The high-yield comorbid pairings and their signals; substance misuse is the commonest comorbidity in schizophrenia (Companion 2010).

6.3 Which came first: primary, secondary, and the self-medication question

The temporal question. In any comorbid case, ask which condition came first, because it changes both the label and the plan. An initial substance problem (through intoxication, withdrawal or chronic toxic effects) can produce a **substance-induced** psychiatric state; the Companion is firm that these drug-induced states are not true comorbidity and should be seen as secondary phenomena. Conversely, a primary psychiatric illness may be unmasked or precipitated by substances in a vulnerable person, or the two may share common risk factors. The substance-induced psychotic-disorder boundary is drawn in detail in the Other psychotic disorders, delusional syndromes and catatonia notes.

The self-medication hypothesis. One influential account holds that some patients use particular drugs for symptomatic relief, for example smoking to ease negative symptoms or cognitive deficits in schizophrenia, or sedatives to blunt PTSD hyperarousal (New Oxford; Kaplan & Sadock). The evidence is mixed: formal tests measuring the temporal sequence often fail to support pure self-medication, and shared vulnerability (a common pathophysiology or genetic risk) is at least as plausible (Kaplan & Sadock). Treat self-medication as a hypothesis to hold lightly, not a rule.

TRAP **Calling a substance-induced state a comorbidity.** A depressive or psychotic picture arising only during intoxication, withdrawal or chronic use is a secondary, substance-induced state, not independent comorbidity; re-assess after a period of abstinence before fixing the second diagnosis.

6.4 The three service models: sequential, parallel, integrated

The taxonomy. Historically, services for dual diagnosis have been organised in one of three ways (El-Mallakh 1998, the canonical treatment-models paper; Companion). In the sequential (or serial) model the two disorders are treated one after the other, in separate services, usually demanding abstinence before the mental illness is addressed. In the parallel model both are treated at the same time but by two different teams in two different services. In the integrated model both are treated together, in one setting, ideally by the same clinical team (El-Mallakh 1998). The three form a natural progression, and the exam wants you to name all three and to know which one wins.

Why sequential and parallel fail. Sequential treatment (the "get sober first, then we will treat the depression" stance) is associated with worse outcomes and higher attrition, because the untreated disorder undermines treatment of the other and the patient falls through the gap between services (IPS 2014). Parallel treatment is better but fragments care: two teams, two care plans, poor communication, and the patient ping-ponging between them with each service disowning the other's problem, exactly the confidence-and-training gap Johnson described, with psychiatric staff seeing substance users only in crisis and addiction staff lacking psychiatric experience (Companion).

MODEL	STRUCTURE	PROBLEM
Sequential / serial	One disorder treated, then the other; separate services; often abstinence-first.	Worse outcomes, high attrition; the untreated disorder sabotages the treated one.
Parallel	Both treated at once, but by two teams in two services.	Fragmented care; poor communication; each service disowns the other's problem.
Integrated	Both treated together, one setting, same team, one care plan.	The recommended model; the resource and training demand is the main barrier.

The three service-delivery models for dual diagnosis; integrated treatment is the recommended standard (El-Mallakh 1998; IPS 2014).

MNEMONIC

SPI: Sequential, Parallel, Integrated → "Same Place, one clinician In charge"

Three models, in order of increasing togetherness: Sequential = one then the other; Parallel = both at once but two teams; Integrated = both at once, one team, one plan. Integrated is the answer.

6.5 Integrated treatment: the recommended standard and its principles

The principle. Co-occurring substance use and mental illness require **integrated treatment** rather than serial treatment: address both conditions concurrently, in the same setting, with the same clinical team wherever possible (IPS 2014). This is the single most examinable line in the topic. It is the reason sequential and parallel models exist mainly as foils; the whole point of the taxonomy is to arrive at integration.

What integration contains. Drake and colleagues distilled nine key principles for this group: assertiveness (assertive outreach), close monitoring, integration, comprehensiveness, a stable living environment, flexibility, staged treatment, a longitudinal perspective, and optimism (Companion). Modern integrated programmes are staged and long-term, blend motivational interviewing with relapse prevention and psychosocial support, use a single care plan, and treat family work as a core component, not an add-on (IPS 2014). Pharmacotherapy for the mental disorder is used alongside substance-use pharmacotherapy within the same plan rather than being withheld until abstinence. The general motivational-interviewing frame is developed in the Psychotherapies, clinical assessment, MSE and nosology notes.

PEARL

Integrated does not mean abstinence-first. Withholding antidepressant or antipsychotic treatment until a patient stops using is a sequential-model reflex; in integrated care you start the psychiatric treatment and the substance-use work together, because each makes the other more achievable.

6.6 Pharmacology in the comorbid patient: pick agents that treat both, avoid ones that clash

Choose dual-purpose agents. Where one drug can serve both conditions, prefer it. In comorbid alcohol dependence with bipolar disorder, prefer naltrexone (Naltima or Nodict; oral opioid antagonist, **50 mg/day** for alcohol, titrated from 25 mg) as the anti-craving agent (BAP). Where alcohol-related liver disease limits hepatic metabolism, prefer acamprosate (Acamprol; **666 mg** three times daily) instead (BAP). In comorbid nicotine dependence, varenicline (Champix) helps both. Where comorbid depression coexists with nicotine dependence, bupropion (Bupron; 150 mg once daily for 3 days, then 150 mg twice daily) carries a dual indication (BAP; NICE). In comorbid ADHD with amphetamine use, prescription stimulants may improve ADHD and reduce use (NICE).

Watch the clashes. In comorbid depression after starting opioid agonist treatment, adopt watchful waiting: depression often remits within a month as the person stabilises, so do not rush an antidepressant; and avoid combining tricyclic antidepressants with methadone because of safety risks (WHO mhGAP 2016). The most dangerous single error is giving naltrexone to a

current opioid user (it precipitates acute withdrawal), so the opioid-free window and the substitution-versus-antagonist decision, developed in the opioid substitution topics, matter as much in the comorbid patient as in the pure one.

COMORBID PAIRING	PREFERRED AGENT	DOSE / LINE	SOURCE
AUD + bipolar disorder	**Naltrexone (Naltima / Nodict)**	50 mg/day PO, from 25 mg; first-line here	BAP
AUD + liver disease	**Acamprosate (Acamprol)**	666 mg three times daily	BAP
AUD + nicotine dependence	Varenicline (Champix)	Standard course; treats both	BAP
Nicotine + depression	Bupropion (Bupron)	150 mg OD x3 days then 150 mg BD	BAP / NICE
Opioid + depression on OST	**Watchful waiting**	Often remits within a month; avoid TCA + methadone	WHO mhGAP
Amphetamine + ADHD	Prescription stimulant	May improve ADHD and cut use	NICE

Pharmacological choices that treat both conditions or avoid a clash in the comorbid patient (verified against the day guideline supplement).

GOOD TO REMEMBER

- **Naltrexone (Naltima / Nodict):** oral opioid antagonist, 50 mg/day (from 25 mg) for alcohol craving and first-line where alcohol coexists with bipolar disorder; the signature caution is precipitated withdrawal if given to a current opioid user, so an opioid-free window is mandatory before starting.
- **Acamprosate (Acamprol):** 666 mg three times daily anti-craving agent acting on NMDA-glutamatergic transmission; preferred in comorbid alcohol-related liver disease because it is not hepatically metabolised.
- **Bupropion (Bupron):** 150 mg OD for 3 days then 150 mg BD for smoking cessation; dual indication when depression coexists; avoid where there is a seizure history or an eating disorder.

6.7 The India frame: the treatment gap, de-addiction services, NDPS and buprenorphine access

The gap and where care sits. India carries a very large substance-use treatment gap: most people meeting dependence criteria never reach formal care, and services concentrate in government de-addiction centres and Drug De-addiction Programme (DDAP) units rather than in general or psychiatric practice. For the dual-diagnosis patient this fragmentation is acute, because the addiction service and the psychiatric service are often physically and administratively separate, defaulting the system into a parallel or even sequential model when integrated care is what the patient needs. The IPS substance-use guidelines therefore push integrated, concurrent management with family work as a core component (IPS 2014).

The legal and access frame. The controlling statute is the Narcotic Drugs and Psychotropic Substances Act, 1985 (the medico-legal detail is developed in the Mental health legislation and forensic psychiatry notes). For opioid-agonist treatment the practical reality is that methadone

was not recommended by the Indian expert committee for de-addiction services, so buprenorphine (Tidigesic; buprenorphine-naloxone as Suboxone) is the workhorse of Indian OST, and its induction detail belongs to the substitution topics. Disulfiram (Esperal or Dizone; 250 to 500 mg/day) remains widely used for alcohol relapse prevention but must never be started in a still-drinking or cardiac patient.

INDIA

The Indian dual-diagnosis patient is where the treatment gap bites hardest: a person with, say, cannabis use and a first-episode psychosis may pass between a de-addiction centre and a psychiatry OPD with neither owning the whole picture, which is the parallel or sequential trap the IPS guidelines warn against. Because methadone is not part of the Indian de-addiction formulary, buprenorphine (Tidigesic) carries opioid-agonist maintenance; because de-addiction services are few, integrated care often has to be built inside a single general-hospital psychiatry unit rather than assumed across services. The strategic priority the IPS emphasises is integrated, family-inclusive, non-specialist-deliverable care that closes the gap at the point of first contact (IPS 2014).

6.8 Putting it together: assessment to plan in the comorbid patient

The clinical sequence. Detect (a low threshold, screening both ways), establish the temporal relationship and whether the second diagnosis is independent or substance-induced (re-assessing after abstinence where possible), then build a single integrated plan that treats both concurrently. Where a drug can serve both conditions, choose it; where an agent clashes, avoid it. Family work and psychosocial rehabilitation are part of the plan, not appendices to it. The wider delirium, emergency and pregnancy considerations for the intoxicated or withdrawing comorbid patient are developed in the Perinatal/women's mental health and emergency psychiatry notes.

30%	45%	3	50
COMORBIDITY RATE IN ALCOHOL DEPENDENCE	COMORBIDITY RATE IN DRUG DEPENDENCE	SERVICE MODELS: SEQUENTIAL, PARALLEL, INTEGRATED	NALTREXONE ANTI-CRAVING DOSE, MG PER DAY

WORKED EXAMPLE

A 26-year-old man is referred with paranoid delusions and near-daily cannabis use. The addiction centre wants him "clean first"; the psychiatry team wants him admitted for the psychosis. That split is the sequential-versus-parallel failure in miniature. The integrated answer: admit to one setting, treat the psychosis with an antipsychotic now (do not wait for abstinence), run motivational and relapse-prevention work for the cannabis in the same plan, involve the family, and re-assess whether the psychosis is independent or substance-related once he is stable. One team, one plan, both problems, from the outset.

COMMON TRAP

Do not let the two services each treat "their half" and disown the other; that is the parallel-model failure. And do not demand abstinence before starting psychiatric medication; that is the sequential-model failure. Both are the classic errors the integrated model was designed to correct.

HOLD THIS

Dual diagnosis = a substance use disorder plus another mental disorder; the three service models are sequential, parallel and integrated; integrated treatment (both disorders, concurrently, same setting, same team, one care plan) is the recommended standard, and sequential "get sober first" care is associated with the worst outcomes.

GOOD TO REMEMBER

- **Integrated treatment (the principle):** treat the substance use disorder and the comorbid mental disorder concurrently, in the same setting, with the same clinical team and a single care plan; the discriminator from parallel care is one team and one plan rather than two; the first step is to start both treatments together rather than sequencing them.
- **The three models:** sequential (one then the other, separate services, abstinence-first, worst outcomes), parallel (both at once but two teams, fragmented), integrated (both together, one team, recommended); the answer to "which model?" is integrated.

7 · Harm reduction

Not everyone who uses drugs can, or will, stop today, and **harm reduction** is the pragmatic clinical and public-health response to that reality: a set of policies and interventions that aim to reduce the *harms* of continued substance use for the individual, their family and society, without insisting on abstinence as the precondition for help (Companion to Psychiatric Studies; Tasman Psychiatry). It is not the opposite of abstinence-oriented treatment but the lowest, most inclusive tier of a **hierarchy of goals** that still runs all the way up to abstinence; **the whole point** is to keep a person alive and infection-free long enough to reach the higher rungs later. Synonyms you may meet are harm minimisation, risk reduction and risk minimisation (Tasman Psychiatry).

Why it matters clinically and in exams. Injecting drug use kills through two routes that harm reduction directly targets: blood-borne viral infection (HIV, hepatitis B and C) from shared injecting equipment, and fatal opioid overdose. Examiners test whether you can name the four flagship interventions (needle and syringe programmes, take-home naloxone, opioid substitution as harm reduction, and supervised consumption facilities), place opioid substitution treatment correctly as *both* a treatment and a harm-reduction measure, and state the naloxone rescue dose. The India device is genuine and heavy here: with a very large substance-use treatment gap, the NDPS legal frame, and buprenorphine as the OST workhorse, harm reduction is where Indian policy (through the National AIDS Control Organisation) has done its most concrete work.

7.1 The philosophy: reduce harm, do not require abstinence first

The core idea. Harm reduction accepts that abstinence is not achievable for every person at every moment and asks a different question: given that this person is using, how do we cut the damage? It reduces harm not only to the user but to family, friends and society generally (Tasman Psychiatry). Crucially it is *not* a rival to abstinence; the best models integrate a harm-reduction component with a use-reduction and an abstinence component in one framework, so that reducing either the quantity of use or the harm per use lowers total harm (Tasman Psychiatry).

The controversy. Harm reduction has been resisted where it is misread as condoning or legalising drug use. The counter-argument, and the exam-safe framing, is that it is a clinically salient goal of good medicine that keeps people alive and connected to services, and that it acts as a conduit into more comprehensive treatment rather than an alternative to it (Tasman Psychiatry; Kaplan & Sadock 2024).

RULE **Meet the patient where they are.** Offer harm-reduction measures to anyone who is still using; keeping a person alive and infection-free is the precondition for every later goal, not a reward for stopping.

7.2 The hierarchy of goals: harm reduction is the bottom rung, not a dead end

The ladder. The Companion sets out an explicit **hierarchy of therapeutic goals** for injecting drug users (Box 14.6): (1) reduce sharing of injecting equipment, (2) reduce injecting, (3) reduce street-drug use, (4) stabilise on substitute prescribing, (5) manage the features of the dependence syndrome, (6) reduce substitute prescribing, and finally (7) maintain abstinence from psychoactive drugs (Companion to Psychiatric Studies). The clinician works with whichever rung the patient can reach now, and the lower rungs are legitimate goals in their own right.

Why the order matters. The first and most urgent target is stopping needle-sharing, because that is the step that prevents the irreversible harm of HIV or hepatitis seroconversion; abstinence sits at the top precisely because it is the hardest and last-reached goal, not the entry requirement.

RUNG	GOAL	HARM TARGETED
1	**Reduce sharing of injecting equipment**	Blood-borne virus transmission
2	Reduce injecting (route shift)	Injecting-related infection, overdose
3	Reduce street-drug use	Unknown purity, overdose, crime
4	**Stabilise on substitute prescribing**	Illicit use, overdose, mortality
5	Manage dependence-syndrome features	Morbidity of dependence
6	Reduce substitute prescribing	Ongoing medication burden
7	Maintain abstinence	All substance-related harm

The Companion Box 14.6 hierarchy of therapeutic goals for injecting drug users; harm reduction occupies the lower, most urgent rungs, abstinence the top (Companion to Psychiatric Studies).

7.3 Needle and syringe programmes: clean needles as the first-line harm-reduction intervention

What it is. A needle and syringe programme (also called **needle exchange**) supplies sterile injecting equipment, and safe disposal for used equipment, to people who inject drugs, so that each injection can be done with **clean needles** rather than shared ones. Providing clean needles directly attacks the top rung of the hierarchy: the sharing of injecting equipment that transmits blood-borne viruses (Companion to Psychiatric Studies).

The evidence. Needle exchange has been one of the most controversial strategies, yet the research is broadly favourable: participation is associated with a reduction in the spread of blood-borne infections such as hepatitis and HIV, with cessation of syringe-sharing, and it acts as a conduit into more comprehensive treatment, drawing users into medical withdrawal and other services (Tasman Psychiatry; Companion to Psychiatric Studies). A prospective cohort found no evidence that needle-exchange participation causally transmits HIV, countering the early fear that it might concentrate high-risk users (Tasman Psychiatry). Strategies to cut HIV transmission in people who inject drugs therefore pair needle exchange with pre-exposure prophylaxis, medication-assisted treatment for opioid use disorder, and linkage to HIV care (Kaplan & Sadock 2024).

TRAP **Reading needle exchange as "enabling" drug use.** The evidence is that a needle exchange reduces viral transmission and pulls users into treatment; it does not increase drug use, and treating it as condoning addiction is the classic policy error.

GOOD TO REMEMBER

- **Needle and syringe programme:** supplies sterile equipment so injections use clean needles, not shared ones; targets the top rung (equipment-sharing); reduces HIV and hepatitis transmission and acts as a conduit into treatment; first management step to prevent irreversible blood-borne-virus harm.

7.4 Take-home naloxone: overdose prevention put in the community's hands

What it is. Naloxone is a short-acting mu-opioid antagonist that reverses opioid-induced respiratory depression. **Take-home naloxone** distribution is the harm-reduction strategy of supplying naloxone, with rescue-breathing and recovery-position training, to people who use opioids and to their significant others, so a bystander can reverse an overdose before an ambulance arrives (Maudsley 2021; BAP 2026). Because overdose is the most common cause of death in opioid use disorder, this is the single most life-saving harm-reduction measure for opioid users (Kaplan & Sadock 2024).

The rescue dose. The verified rescue regimen is intramuscular naloxone **0.4 to 2 mg**, repeated every 2 to 3 minutes up to a total of **10 mg**, or intranasal **4 mg** per spray repeated after 2 to 3 minutes (BAP 2026); take-home kits are commonly the **0.4 mg in 1 mL** ampoule or a prefilled device (WHO). The critical caution is that naloxone is short-acting: if the opioid taken is long-acting (methadone, sustained-release preparations) the antagonist can wear off before the agonist does, so **re-narcotisation** can recur and a further dose or infusion and continued observation are needed (Companion to Psychiatric Studies). Overdose risk is highest after any period of forced abstinence (post-detox, post-incarceration, after disengaging from OST) when tolerance has fallen, which is exactly when take-home naloxone should be provided (BAP 2026).

WORKED EXAMPLE

A man who injects heroin is found unresponsive with pinpoint pupils and a respiratory rate of 4. A trained family member gives intramuscular naloxone 0.4 mg, starts rescue breathing and places him in the recovery position; the breathing improves within a couple of minutes. Because the effect is short-lived, they call emergency services and keep him under observation, ready to repeat the dose, since the opioid outlasts the naloxone. The trained bystander and the take-home kit are the intervention that bought the time.

GOOD TO REMEMBER

- **Naloxone (take-home):** short-acting mu-opioid antagonist reversing opioid respiratory depression; rescue dose IM 0.4 to 2 mg, repeat every 2 to 3 min up to 10 mg, or intranasal 4 mg/spray; take-home kit typically 0.4 mg in 1 mL; short half-life means re-narcotisation with long-acting opioids, so observe and repeat; give to any current or recent opioid user, especially after detox or release from custody.

7.5 Opioid substitution as harm reduction: OST is a treatment and a harm-reduction measure at once

The dual identity. Opioid substitution treatment (OST) with methadone or buprenorphine is the pivot where treatment and harm reduction meet. Replacement pharmacotherapy on methadone or buprenorphine is explicitly considered a harm-reduction measure because it reduces the morbidity, mortality and crime of the injecting lifestyle, much as antihypertensives control but do not cure hypertension (Companion to Psychiatric Studies; Tasman Psychiatry). By substituting a prescribed oral or sublingual agonist for injected street opioid it moves the patient up rungs 3 and 4 of the hierarchy at once: off unknown-purity street drugs and off injecting.

The harm-reduction pay-off. OST is the most extensively evaluated treatment in the field; adequate-dose maintenance improves treatment retention, reduces illicit opioid use, and lowers the risk of HIV and hepatitis seroconversion and of overdose death, provided the person stays in treatment (Companion to Psychiatric Studies; Maudsley 2021). Buprenorphine adds a harm-reduction advantage of its own: as a partial agonist it has a ceiling on respiratory depression, making overdose less likely than with full-agonist methadone. Maintenance doses that actually suppress illicit use are needed: buprenorphine typically **16 mg/day** or more, methadone typically **60 to 120 mg/day** after slow induction (Maudsley 2021; NICE 2011).

GOOD TO REMEMBER

- **Buprenorphine (OST as harm reduction):** partial mu-agonist with a respiratory-depression ceiling; substitutes for injected street opioid, reducing injecting, overdose and blood-borne-virus risk; maintenance typically 16 mg/day or more; the Indian OST workhorse; the signature caution is precipitated withdrawal if started before objective withdrawal appears (COWS about 8 to 12).

GOOD TO REMEMBER

- **Methadone (OST as harm reduction):** full mu-agonist; reduces illicit use, mortality and crime as a harm-reduction measure; maintenance typically 60 to 120 mg/day after slow induction (start 20 to 30 mg/day, not more than 30 mg initially); the first two weeks of induction are the high-risk overdose window because of accumulation, so observe closely.

7.6 Supervised consumption facilities and other measures: the higher-threshold end of harm reduction

Supervised consumption. A **supervised consumption facility** (drug consumption room, supervised injection facility) provides a clean, monitored space where people inject or use their own drugs under staff observation, so an overdose can be reversed on the spot and equipment stays sterile. Modelling of Vancouver's supervised injection facility estimated it prevents HIV infections, and such facilities extend **overdose prevention** and blood-borne-virus prevention to the highest-risk users while acting as a further conduit into treatment (Tasman Psychiatry). Related higher-threshold approaches include supervised or daily-observed heroin-assisted treatment for people who fail standard OST, trialled positively in Switzerland, the Netherlands, Germany and Canada (Tasman Psychiatry).

Other harm-reduction measures. The continuum also includes education on safer injecting technique, HIV pre-exposure prophylaxis, testing and linkage to HIV and hepatitis care, and, for tobacco, nicotine harm reduction via safer nicotine delivery (Maudsley 2021; Kaplan & Sadock 2024). The common thread is that every measure keeps the person alive, uninfected and in contact with services.

PEARL

The four flagship harm-reduction interventions map neatly onto the two ways injecting kills: needle and syringe programmes and supervised consumption facilities attack blood-borne infection and unsafe injecting, while take-home naloxone and opioid substitution attack overdose death. Naming this two-axis structure is the clean way to answer an "outline harm reduction" question.

7.7 The Indian harm-reduction and policy context: NACO OST, NDPS and the treatment gap

The frame. India carries a very large substance-use **treatment gap**, with most people meeting dependence criteria never reaching formal care, which is concentrated in government de-addiction centres and Drug De-addiction Programme (DDAP) units rather than in general practice (IPS 2014). The controlling statute is the Narcotic Drugs and Psychotropic Substances (NDPS) Act, 1985, which schedules controlled drugs and shapes access to opioid agonists; its Section 64A allows diversion of an addict into treatment in lieu of conviction, a harm-reduction-flavoured legal provision (the medico-legal detail is developed in the Mental health legislation and forensic psychiatry notes).

Indian harm reduction in practice. The concrete national harm-reduction machinery sits with the National AIDS Control Organisation (NACO), whose targeted interventions for people who inject drugs deliver needle and syringe programmes and opioid substitution treatment as HIV-

prevention. Methadone in India is restricted to government OST clinics run under NACO and select institutional programmes (for example AIIMS NDDTC and NIMHANS), so it is referred to a licensed OST centre rather than prescribed in private practice (IPS 2014). Buprenorphine, usually the sublingual buprenorphine-naloxone 4:1 combination (Indian brands include Tidigesic; the combination as Suboxone or Bunorph), is the accessible workhorse of Indian opioid-agonist maintenance, inducted at 4 mg/1 mg once objective withdrawal appears and maintained at about 8 to 16 mg/day. The IPS emphasis on brief, motivation-based, non-specialist-deliverable care is itself a treatment-gap-closing strategy that complements the harm-reduction pathway (IPS 2014).

INDIA

Harm reduction in India is largely an HIV-prevention story routed through NACO's targeted interventions: needle and syringe programmes and opioid substitution treatment for people who inject drugs sit inside the national AIDS-control machinery rather than mainstream psychiatry, which is why buprenorphine (Tidigesic; buprenorphine-naloxone as Suboxone or Bunorph) rather than tightly restricted methadone is the accessible agent. Take-home naloxone is recommended for opioid-dependent people and their families (BAP 2026) but is not yet widely distributed here; the intranasal naloxone spray marketed for lay overdose reversal is where policy is moving. The NDPS Act, 1985 both restricts access and, through Section 64A treatment-in-lieu-of-conviction, offers a harm-reduction-adjacent diversion route.

0.4 to 2	4	16
IM NALOXONE RESCUE DOSE IN MG (REPEAT EVERY 2 TO 3 MIN, UP TO 10 MG)	BUPRENORPHINE-NALOXONE INDUCTION IN MG (4 MG/1 MG) AT OBJECTIVE WITHDRAWAL	BUPRENORPHINE MAINTENANCE TARGET IN MG/DAY OR MORE

RULE **OST is treatment and harm reduction.** Methadone or buprenorphine maintenance is the single measure that reduces injecting, overdose death and blood-borne-virus transmission at once, and it is the most evidence-based treatment in opioid use disorder.

COMMON TRAP

Do not treat harm reduction and abstinence as mutually exclusive. They are rungs of one hierarchy: harm reduction (clean needles, naloxone, substitution) keeps the person alive and in contact with services so that the higher goals, including abstinence, remain reachable. Insisting on abstinence as the entry ticket loses the very patients harm reduction is designed to save.

HOLD THIS

Four flagship harm-reduction interventions: needle and syringe programmes (clean needles, cut blood-borne-virus transmission), take-home naloxone (IM 0.4 to 2 mg for overdose prevention), opioid substitution treatment (methadone or buprenorphine, both treatment and harm reduction), and supervised consumption facilities; abstinence sits at the top of the hierarchy of goals, not at its entrance.

Alcohol use disorder

8 · The pharmacology of alcohol

Almost everything a psychiatrist does with a drinking patient rests on one small molecule and how the body handles it. **Alcohol pharmacology** is the grammar behind intoxication, the breathalyser reading, why the blood level falls at a fixed pace no matter how drunk the person is, why the chronic drinker metabolises faster, and why a "standard drink" is a fixed dose rather than a glass of any size. Examiners like this topic because it is clean and quantitative: they can ask you to name the two enzymes of the primary pathway, to state that **metabolism** is zero-order, to explain the microsomal route that appears on chronic use, and to convert a drink into units. Get the numbers cold and the clinical topics later in this block, the withdrawal time-course, the disulfiram reaction, the safe-drinking advice, follow from the same physiology.

Why it matters clinically. The reward and mesolimbic-dopamine anatomy on which alcohol's addictive pull is built is developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and is not re-derived here; this topic is the pharmacokinetics and molecular pharmacodynamics that every downstream management decision assumes. Zero-order kinetics is why you cannot "sober someone up" faster and why the level drops predictably in a collapsed drinker; the GABA and glutamate story is why alcohol is a central nervous system depressant and why its withdrawal, covered in the withdrawal-management topics, is a hyperexcitable mirror image; the units concept is the currency of every brief intervention and safe-drinking conversation.

8.1 Absorption: a small, fully miscible molecule the gut takes up fast

Where and how fast. Ethanol is a small, water-soluble molecule with no need for a transporter; it is taken up by simple diffusion, a little from the stomach but mostly and rapidly from the proximal small intestine, so gastric emptying is the main rate-limiter of **absorption** (Kaplan and Sadock 2024). An empty stomach speeds absorption and food, especially fat and protein, slows it by delaying emptying, which is why the same drink taken on an empty stomach produces a higher peak. Absorption from the skin is minimal in adults but can be significant in infants sponged with alcohol.

First-pass and the gastric enzyme. A fraction of a drink is oxidised before it ever reaches the systemic circulation, a first-pass effect occurring in the gastric mucosa and liver via gastric alcohol dehydrogenase. This gastric first-pass metabolism is lower in women (contributing, with a smaller volume of distribution, to higher blood levels for the same intake) and is reduced by some drugs, which is one reason a given amount of alcohol hits harder in certain patients.

8.2 Distribution: into total body water, straight across the barriers

Volume of distribution. Once absorbed, ethanol distributes widely and evenly into body water, with a volume of distribution of about **0.7 L/kg**, essentially the volume of total body water (KDT 2019). It crosses the blood-brain barrier efficiently, so brain concentration tracks blood concentration closely, and it crosses the placenta freely, the pharmacological basis of the fetal

alcohol effects developed in the Perinatal/women's mental health and emergency psychiatry notes.

Why body composition changes the level. Because alcohol sits in body water and not in fat, a person with less body water, women on average, and older or leaner patients, reaches a higher blood alcohol concentration for the same dose. The blood-to-breath partition is consistent enough (about 2100:1) that the breathalyser can read blood level from exhaled air, the medico-legal basis of the roadside test.

8.3 The primary metabolic pathway: two enzymes, alcohol to acetaldehyde to acetate

The sequence to memorise. Around 98% of ingested alcohol is oxidised in the liver, and the primary pathway is a two-step oxidation (KDT 2019; Kaplan and Sadock 2024). Step one: alcohol dehydrogenase (ADH), a cytosolic enzyme, oxidises ethanol to **acetaldehyde**, using NAD as cofactor. Step two: aldehyde dehydrogenase (ALDH), a mitochondrial enzyme, oxidises the toxic acetaldehyde to harmless acetate, again NAD-dependent. Acetate is then used peripherally. The whole of alcohol's therapeutics, from the disulfiram reaction to the East-Asian flushing response, turns on this single intermediate, acetaldehyde.

Why acetaldehyde is the pivot. Acetaldehyde is the noxious metabolite; when it accumulates, the person feels flushed, nauseated and unwell. Genetic variation in these enzymes explains population differences: an inactive ALDH variant common in East-Asian people lets acetaldehyde build up after a small drink, producing an aversive flush that lowers dependence risk. Blocking ALDH pharmacologically reproduces this on purpose, which is exactly how disulfiram (Indian brands Esperal, Dizone) works, detailed in the anti-craving and aversion topics.

GOOD TO REMEMBER

- **The primary pathway:** ethanol goes alcohol dehydrogenase (cytosolic, NAD-dependent) to acetaldehyde (the toxic intermediate), then aldehyde dehydrogenase (mitochondrial, NAD-dependent) to acetate; about 98% of a dose is metabolised in the liver; acetaldehyde accumulation is the feature behind both the disulfiram reaction and the East-Asian flush; disulfiram acts by inhibiting aldehyde dehydrogenase.

8.4 Zero-order kinetics: a fixed amount cleared per hour, whatever the level

The defining fact. Because the metabolising enzymes are saturated at ordinary drinking concentrations, alcohol is eliminated by zero-order kinetics: a constant *amount*, not a constant fraction, is cleared per unit time regardless of how high the blood level is (KDT 2019; Kaplan and Sadock 2024). The figure to hold is roughly **8 to 12 mL of absolute alcohol per hour**, which corresponds to falling by about one unit an hour and a blood-alcohol decline on the order of 15 to 20 mg/dL per hour. Contrast this with the first-order elimination of most drugs, where a constant proportion is removed and a half-life can be quoted; ethanol has no meaningful single half-life at intoxicating levels.

The clinical consequences. Three things fall straight out of zero-order handling. You cannot accelerate sobering-up (coffee, fresh air and fructose drips do not meaningfully change the fixed rate); the time to clear a large load is long and roughly predictable, which lets you estimate when a

level will reach zero; and small increases in intake produce disproportionately large and prolonged rises in level once the enzymes are saturated. Methanol is handled the same way (zero-order, but with a far longer effective clearance), which is why its toxicity is delayed and severe.

RULE **You cannot rush a zero-order drug.** Alcohol clears at a fixed amount per hour irrespective of the blood level, so nothing "sobers a person up" faster; management of the intoxicated patient is time, airway and supportive care, not stimulants.

COMMON TRAP

Do not quote a half-life for alcohol at intoxicating levels or reach for a first-order calculation. At ordinary drinking concentrations the pathway is saturated, so elimination is zero-order (a fixed amount per hour), and a half-life is not defined. Only at very low, sub-saturating concentrations does elimination start to look first-order.

8.5 The microsomal route: CYP2E1 and why the chronic drinker clears faster

The second pathway. Alongside alcohol dehydrogenase, a smaller share of alcohol is oxidised by the hepatic microsomal ethanol-oxidising system, chiefly the cytochrome CYP2E1 (KDT 2019). At low intake this route is minor, but it is *inducible*: regular heavy drinking up-regulates CYP2E1, so a chronic drinker metabolises alcohol faster than a naive person. This is the pharmacokinetic (dispositional) arm of tolerance developed in the Tolerance, withdrawal and neuroadaptation topic.

Why induction matters beyond alcohol. An induced CYP2E1 does not only clear alcohol; it changes the handling of other CYP2E1 substrates. The clinically dangerous example is paracetamol: in the chronic drinker, more paracetamol is shunted to its toxic metabolite (NAPQI), so hepatotoxicity occurs at lower doses and the "safe" paracetamol ceiling is reduced. Induction also alters the metabolism of drugs such as phenytoin and tolbutamide, and smoking further induces CYP2E1, adding to the interaction.

PEARL

Acute versus chronic alcohol have opposite effects on drug metabolism. Taken acutely, alcohol competes for and inhibits hepatic enzymes, so it can raise the level of a co-ingested drug; taken chronically, it induces them (notably CYP2E1), so it lowers steady-state levels and clears faster. The same patient can therefore be an inhibitor when drinking and an inducer when sober, which is why timing matters when you read an interaction.

8.6 Pharmacodynamics: a central nervous system depressant on GABA and glutamate

The dual molecular action. Alcohol is a central nervous system depressant, and its acute action has two arms on the brain's main fast-signalling systems (Kaplan and Sadock 2024). It *enhances* inhibitory transmission at the GABA-A receptor (the same target as benzodiazepines and barbiturates, hence their cross-tolerance and the use of a benzodiazepine to cover alcohol withdrawal), and it *inhibits* excitatory transmission at the NMDA subtype of glutamate receptor. The net effect is global central nervous system depression: anxiolysis and disinhibition at low

doses, sedation, ataxia and dysarthria as the level rises, and respiratory depression and coma at high levels.

Where withdrawal comes from. Chronic exposure drives the brain to compensate: it down-regulates GABA-A receptors and up-regulates NMDA receptors to keep functioning against the depressant load. When alcohol is removed, this leaves reduced inhibition and unopposed glutamatergic excitation, the hyperexcitable state that manifests as tremor, autonomic arousal, seizures and, at the extreme, delirium tremens. The dose-response and management of that state are developed in the withdrawal-management topics; here the point is only that intoxication and withdrawal are two faces of the GABA-glutamate adaptation.

GOOD TO REMEMBER

- **Alcohol pharmacodynamics:** a central nervous system depressant that enhances GABA-A (inhibitory) and inhibits NMDA-glutamate (excitatory) transmission; chronic use down-regulates GABA-A and up-regulates NMDA, and withdrawal is that adaptation unmasked (hyperexcitability, seizures, delirium tremens); the shared GABA-A target is why benzodiazepines show cross-tolerance and are first-line to cover alcohol withdrawal.

8.7 The unit and the standard drink: alcohol as a fixed dose

The definitions to hold. To count alcohol as a dose rather than a volume of liquid, two conventions are used. In the UK, one of the units of alcohol is 10 mL of pure ethanol (equivalently 8 g), so a 250 mL glass of 10% wine is 2.5 units (Companion to Psychiatric Studies). In the US, one standard drink contains 14 g of ethanol (about 17.7 mL, so 1.77 UK units); by design a 355 mL beer, a 150 mL glass of wine and a 44 mL shot of spirits each deliver about one US standard drink. Spain and Australia use a 10 g "drink". The point is that beverage strength, not glass size, sets the dose: spirits at 40% pack far more alcohol per millilitre than beer at 4 to 6%.

Where the number is used. Units are the working currency of every safe-drinking conversation, brief intervention and screening tool. They let you quantify weekly intake against low-risk guidance, convert a patient's self-report into a comparable figure, and score the consumption items of the AUDIT (developed with its cut-offs in the screening topics). Knowing that one unit is metabolised in roughly an hour ties the units concept back to the zero-order clearance in 8.4.

CONVENTION	DEFINITION OF ONE DRINK/UNIT	WORKED CONVERSION
UK unit	10 mL (8 g) of pure ethanol	250 mL of 10% wine = 2.5 units
US standard drink	14 g (17.7 mL) of ethanol = 1.77 UK units	355 mL beer = 150 mL wine = 44 mL spirit shot
Spain / Australia "drink"	10 g of ethanol	slightly larger than a UK unit, smaller than a US drink
Clearance anchor	about 1 unit per hour (zero-order)	lets you estimate time for a level to fall

Standard-drink and units conventions; beverage strength (not glass size) sets the dose, and clearance is about one unit per hour (Companion to Psychiatric Studies; KDT 2019).

8 to 12 mL	10 mL	14 g	0.7 L/kg
ABSOLUTE ALCOHOL CLEARED PER HOUR, ZERO-ORDER (ROUGHLY ONE UNIT)	PURE ETHANOL IN ONE UK UNIT (8 G)	ETHANOL IN ONE US STANDARD DRINK	VOLUME OF DISTRIBUTION (TOTAL BODY WATER)

8.8 The India lens: a large treatment gap, the NDPS frame and the de-addiction setting

The epidemiology and the gap. Alcohol is the dominant substance of concern in Indian psychiatric practice, and most people who meet dependence criteria never reach formal care, a very large substance-use treatment gap (IPS 2014). Services are concentrated in government de-addiction centres and Drug De-addiction Programme (DDAP) units rather than general practice, so a strategic shift toward community and home-based delivery using trained non-specialist workers is part of the Indian clinical-practice-guideline response. This is where the pharmacology becomes practical: brief interventions counted in units, safe-drinking advice keyed to the zero-order clearance, and screening keyed to the AUDIT are the front-line tools that scale.

The legal and prescribing frame. The controlling statute is the Narcotic Drugs and Psychotropic Substances (NDPS) Act, 1985, whose scheduling shapes access to controlled agents; the medico-legal detail is developed in the Mental health legislation and forensic psychiatry notes. On the drug side, the anti-craving and aversion agents used in Indian practice are available as familiar brands, disulfiram as Esperal or Dizone, naltrexone as Naltima or Nodict, acamprosate as Acamprol, with the buprenorphine story (Indian brand Tidigesic) belonging to the opioid-substitution topics.

INDIA

The metabolic facts have a direct Indian bedside payoff. Because clearance is fixed and slow (about one unit an hour), the intoxicated patient in a busy Indian emergency setting is managed by time and supportive care, not by any agent that claims to "sober up". Because chronic drinking induces CYP2E1, the malnourished chronic drinker who also takes paracetamol is at hepatotoxic risk at lower doses, a real hazard given over-the-counter availability. And because acetaldehyde is the pivot, disulfiram (Esperal, Dizone) is offered only to a motivated, abstinence-goal patient with a reliable family supervisor and started at least 24 hours after the last drink, a caution that fits the family-supervised model common in Indian de-addiction care (IPS 2014).

MNEMONIC

"ADH makes the poison, ALDH clears it"

Alcohol Dehydrogenase (ADH) makes acetaldehyde, the toxic intermediate; ALdehyde Dehydrogenase (ALDH) clears it to acetate. Disulfiram blocks the second enzyme, so the poison piles up, which is the whole reaction. Chronically, the microsomal CYP2E1 route is induced, so the seasoned drinker clears faster.

GOOD TO REMEMBER

- **Disulfiram (Indian brands Esperal, Dizone):** an aldehyde-dehydrogenase inhibitor that causes acetaldehyde to accumulate on drinking, producing an aversive flush-nausea-hypotension reaction lasting 1 to 4 hours; a maintenance option (250 to 500 mg/day) only in a motivated, abstinence-goal patient with a reliable supervisor, started at least 24 hours after the last drink; the signature caution is that it is dangerous in a still-drinking or cardiac patient and is never a withdrawal treatment.

HOLD THIS

Alcohol distributes into total body water (about 0.7 L/kg), is oxidised in the liver by alcohol dehydrogenase then aldehyde dehydrogenase (acetaldehyde is the toxic pivot), clears by zero-order kinetics at a fixed 8 to 12 mL of absolute alcohol per hour (about one unit), and induces CYP2E1 on chronic use; pharmacodynamically it is a central nervous system depressant that enhances GABA-A and inhibits NMDA-glutamate transmission.

9 · Alcohol withdrawal, CIWA-Ar and SADQ

Stopping alcohol in a physically dependent drinker unmasks a brain that has spent months opposing a depressant, and the result is a time-ordered, potentially lethal **withdrawal spectrum** that a psychiatrist must recognise, stage and treat. This is the first clinical management topic of the substance-use block and one of the highest-yield: examiners want the withdrawal time-course by the clock, the two severity instruments (the **CIWA-Ar** for the withdrawal state and the **SADQ** for dependence severity) with their exact action thresholds and bands, the choice between a symptom-triggered and a fixed-dose benzodiazepine schedule, the choice of agent, and the parenteral-thiamine-before-glucose rule. Get the numbers exact here and most of the day's viva follows.

Why it matters clinically. **Alcohol withdrawal** is the one substance withdrawal that routinely kills: untreated **delirium tremens** carries a mortality of the order of 10 to 20 per cent, and a withdrawal seizure or unrecognised Wernicke encephalopathy converts a routine detoxification into an emergency. The underlying neuroadaptation (down-regulated GABA-A, up-regulated NMDA-glutamate) is developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and is not re-derived here; the amnestic mechanism of Korsakoff sits in the Dementias and neurocognitive disorders notes and the Neuropsychiatry of systemic and neurological disease notes. Here the task is to read the syndrome off the clock and manage it by the number.

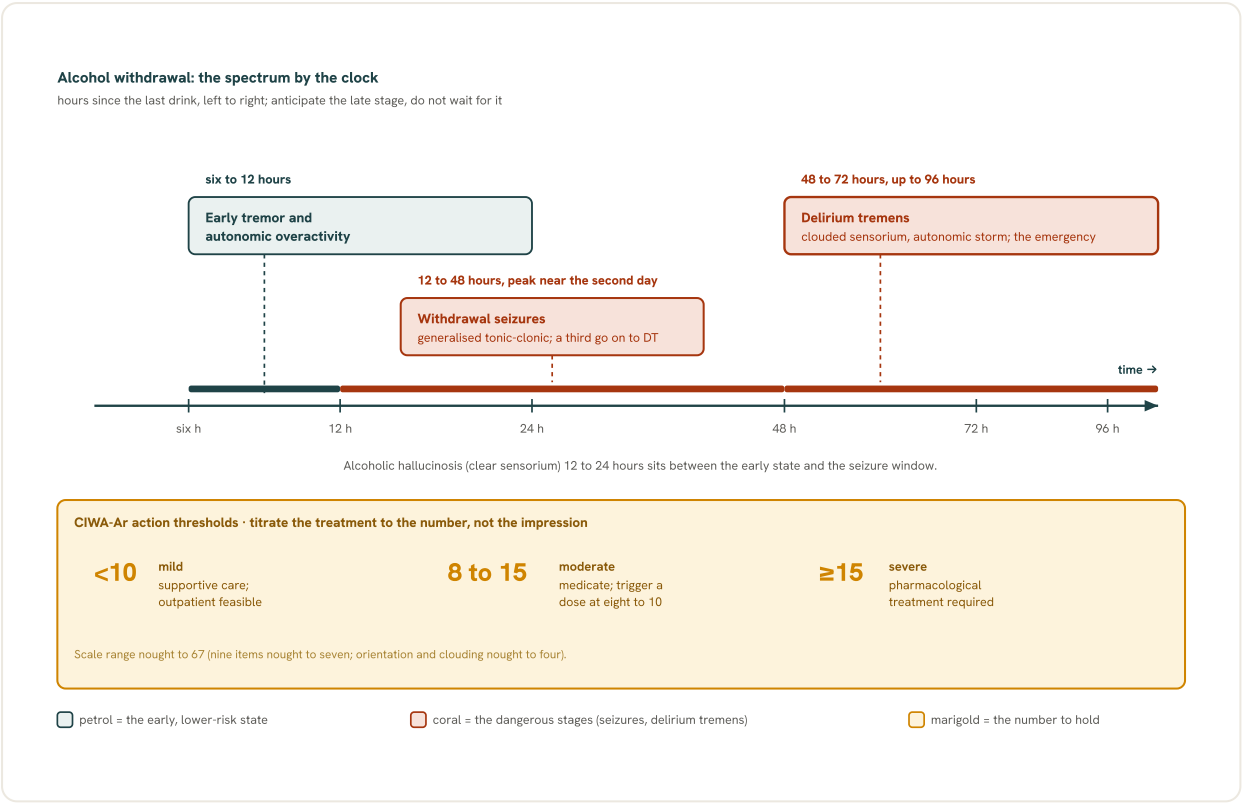


Fig 13.4 The alcohol-withdrawal spectrum read off the clock. Early tremor and autonomic overactivity begin at six to 12 hours, generalised withdrawal seizures cluster at 12 to 48 hours (peaking near day two, and about a third go on to delirium tremens), and delirium tremens, the high-mortality emergency, characteristically emerges at 48 to 72 hours and can extend to 96 hours; alcoholic hallucinosis in a clear sensorium sits at 12 to 24 hours in between. Stage the patient on the axis and treat forwards, titrating a long-acting benzodiazepine to the CIWA-Ar: under 10 is mild (supportive care), 8 to 15 moderate (medicate, with a symptom-triggered dose around a score of eight to 10), and 15 or more severe (pharmacological treatment required), on a scale that runs from nought to 67.

Clinical Institute Withdrawal Assessment of Alcohol Scale, Revised (CIWA-Ar)

Patient:_____ Date: _____ Time: _____ (24 hour clock, midnight = 00:00)

Pulse or heart rate, taken for one minute:_____ Blood pressure:_____

NAUSEA AND VOMITING -- Ask "Do you feel sick to your stomach? Have you vomited?" Observation.
0 no nausea and no vomiting
1 mild nausea with no vomiting
2
3
4 intermittent nausea with dry heaves
5
6
7 constant nausea, frequent dry heaves and vomiting

TACTILE DISTURBANCES -- Ask "Have you any itching, pins and needles sensations, any burning, any numbness, or do you feel bugs crawling on or under your skin?" Observation.
0 none
1 very mild itching, pins and needles, burning or numbness
2 mild itching, pins and needles, burning or numbness
3 moderate itching, pins and needles, burning or numbness
4 moderately severe hallucinations
5 severe hallucinations
6 extremely severe hallucinations
7 continuous hallucinations

TREMOR -- Arms extended and fingers spread apart. Observation.
0 no tremor
1 not visible, but can be felt fingertip to fingertip
2
3
4 moderate, with patient's arms extended
5
6
7 severe, even with arms not extended

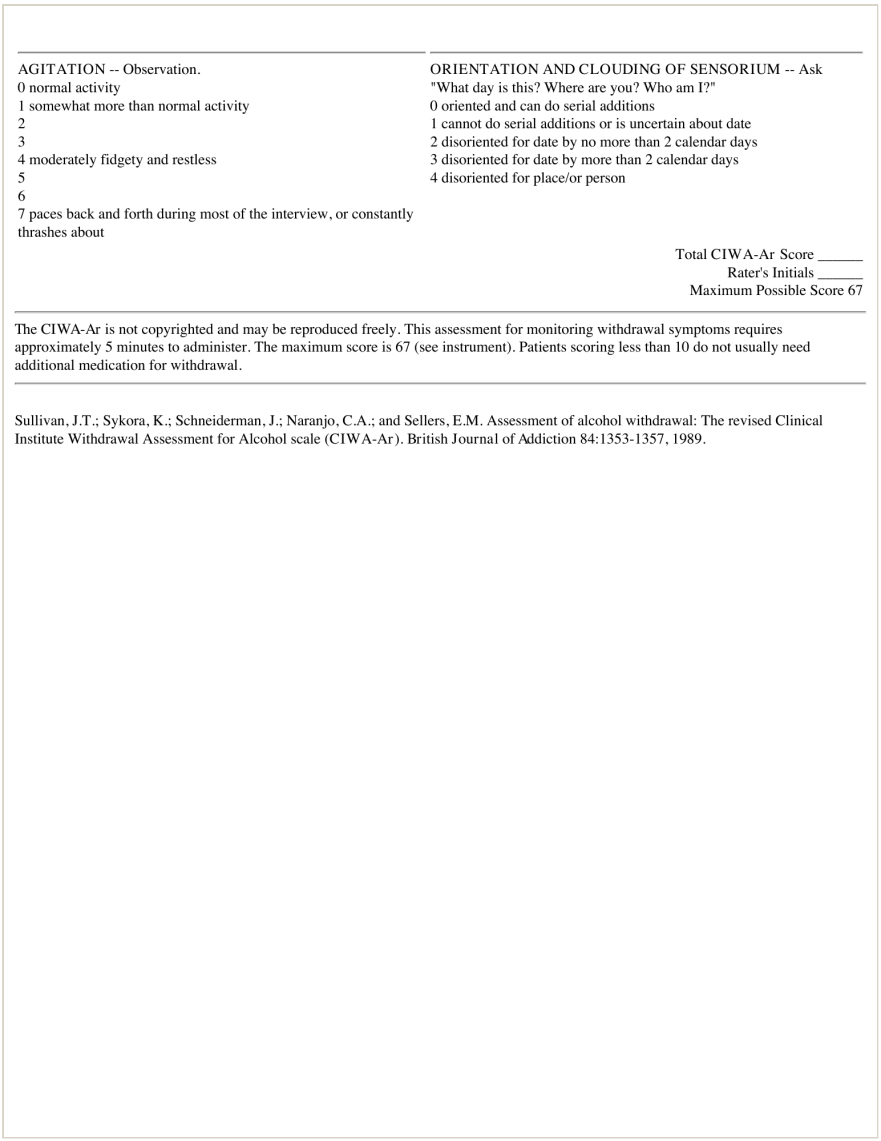
AUDITORY DISTURBANCES -- Ask "Are you more aware of sounds around you? Are they harsh? Do they frighten you? Are you hearing anything that is disturbing to you? Are you hearing things you know are not there?" Observation.
0 not present
1 very mild harshness or ability to frighten
2 mild harshness or ability to frighten
3 moderate harshness or ability to frighten
4 moderately severe hallucinations
5 severe hallucinations
6 extremely severe hallucinations
7 continuous hallucinations

PAROXYSMAL SWEATS -- Observation.
0 no sweat visible
1 barely perceptible sweating, palms moist
2
3
4 beads of sweat obvious on forehead
5
6
7 drenching sweats

VISUAL DISTURBANCES -- Ask "Does the light appear to be too bright? Is its color different? Does it hurt your eyes? Are you seeing anything that is disturbing to you? Are you seeing things you know are not there?" Observation.
0 not present
1 very mild sensitivity
2 mild sensitivity
3 moderate sensitivity
4 moderately severe hallucinations
5 severe hallucinations
6 extremely severe hallucinations
7 continuous hallucinations

ANXIETY -- Ask "Do you feel nervous?" Observation.
0 no anxiety, at ease
1 mild anxious
2
3
4 moderately anxious, or guarded, so anxiety is inferred
5
6
7 equivalent to acute panic states as seen in severe delirium or acute schizophrenic reactions

HEADACHE, FULLNESS IN HEAD -- Ask "Does your head feel different? Does it feel like there is a band around your head?" Do not rate for dizziness or lightheadedness. Otherwise, rate severity.
0 not present
1 very mild
2 mild
3 moderate
4 moderately severe
5 severe
6 very severe
7 extremely severe



AGITATION -- Observation.
0 normal activity
1 somewhat more than normal activity
2
3
4 moderately fidgety and restless
5
6
7 paces back and forth during most of the interview, or constantly thrashes about

ORIENTATION AND CLOUDING OF SENSORIUM -- Ask "What day is this? Where are you? Who am I?"
0 oriented and can do serial additions
1 cannot do serial additions or is uncertain about date
2 disoriented for date by no more than 2 calendar days
3 disoriented for date by more than 2 calendar days
4 disoriented for place/or person

Total CIWA-Ar Score _____
Rater's Initials _____
Maximum Possible Score 67

The CIWA-Ar is not copyrighted and may be reproduced freely. This assessment for monitoring withdrawal symptoms requires approximately 5 minutes to administer. The maximum score is 67 (see instrument). Patients scoring less than 10 do not usually need additional medication for withdrawal.

Sullivan, J.T.; Sykora, K.; Schneiderman, J.; Naranjo, C.A.; and Sellers, E.M. Assessment of alcohol withdrawal: The revised Clinical Institute Withdrawal Assessment for Alcohol scale (CIWA-Ar). British Journal of Addiction 84:1353-1357, 1989.

CIWA-Ar (Sullivan et al., 1989); public domain.

Fig 13.5 The CIWA-Ar (Clinical Institute Withdrawal Assessment for Alcohol, revised) as the actual clinician-rated form. Nine items are scored nought to seven and the tenth, orientation and clouding of sensorium, nought to four, for a maximum of 67; this is the observer-rated instrument that drives a symptom-triggered benzodiazepine regimen.

SEVERITY OF ALCOHOL DEPENDENCE QUESTIONAIRE (SADQ-C)[1]

NAME_____AGE_____No._____

DATE:

Please recall a typical period of heavy drinking in the last 6 months.

When was this? Month:…… Year……..

Please answer all the following questions about your drinking by circling your most appropriate response.

During that period of heavy drinking

1. The day after drinking alcohol, I woke up feeling sweaty.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS

2. The day after drinking alcohol, my hands shook first thing in the morning.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS

3. The day after drinking alcohol, my whole body shook violently first thing in the morning if I didn't have a drink.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS

4. The day after drinking alcohol, I woke up absolutely drenched in sweat.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS

5. The day after drinking alcohol, I dread waking up in the morning.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS

6. The day after drinking alcohol, I was frightened of meeting people first thing in the morning.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS

7. The day after drinking alcohol, I felt at the edge of despair when I awoke.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS

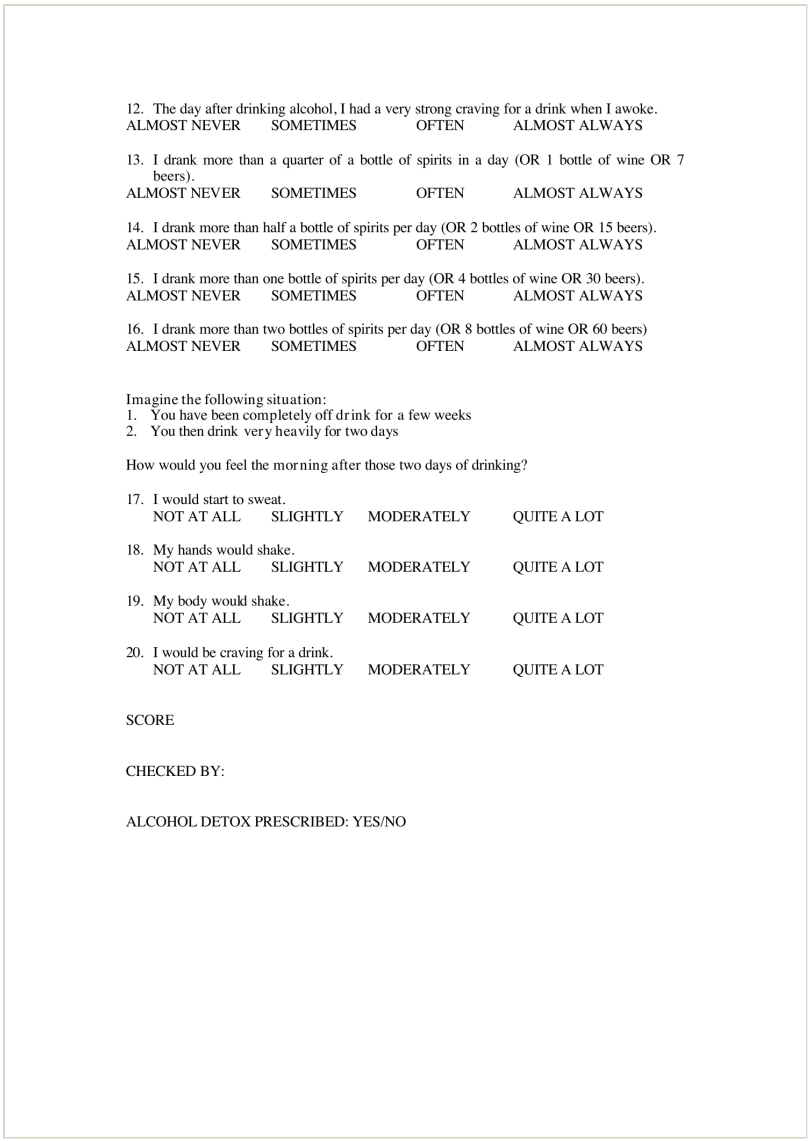
8. The day after drinking alcohol, I felt very frightened when I awoke.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS

9. The day after drinking alcohol, I liked to have an alcoholic drink in the morning.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS

10. The day after drinking alcohol, I always gulped my first few alcoholic drinks down as quickly as possible.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS

11. The day after drinking alcohol, I drank more alcohol to get rid of the shakes.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS

[1] Stockwell, T., Sitharan, T., McGrath, D.& Lang, . (1994). The measurement of alcohol dependence and impaired control in community samples. Addiction, 89, 167-174.



12. The day after drinking alcohol, I had a very strong craving for a drink when I awoke.
ALMOST NEVER SOMETIMES OFTEN ALMOST ALWAYS

13. I drank more than a quarter of a bottle of spirits in a day (OR 1 bottle of wine OR 7 beers).
ALMOST NEVER SOMETIMES OFTEN ALMOST ALWAYS

14. I drank more than half a bottle of spirits per day (OR 2 bottles of wine OR 15 beers).
ALMOST NEVER SOMETIMES OFTEN ALMOST ALWAYS

15. I drank more than one bottle of spirits per day (OR 4 bottles of wine OR 30 beers).
ALMOST NEVER SOMETIMES OFTEN ALMOST ALWAYS

16. I drank more than two bottles of spirits per day (OR 8 bottles of wine OR 60 beers)
ALMOST NEVER SOMETIMES OFTEN ALMOST ALWAYS

Imagine the following situation:
1. You have been completely off drink for a few weeks
2. You then drink very heavily for two days

How would you feel the morning after those two days of drinking?

17. I would start to sweat.
NOT AT ALL SLIGHTLY MODERATELY QUITE A LOT

18. My hands would shake.
NOT AT ALL SLIGHTLY MODERATELY QUITE A LOT

19. My body would shake.
NOT AT ALL SLIGHTLY MODERATELY QUITE A LOT

20. I would be craving for a drink.
NOT AT ALL SLIGHTLY MODERATELY QUITE A LOT

SCORE

CHECKED BY:

ALCOHOL DETOX PRESCRIBED: YES/NO

SADQ (Stockwell et al.); reproduced with acknowledgement, non-commercial use.

Fig 13.6 The SADQ (Severity of Alcohol Dependence Questionnaire) as the actual self-report form. Twenty items are each scored nought to three, for a maximum of 60; the SADQ indexes dependence severity before withdrawal (15 or less mild, 16 to 30 moderate, above 30 severe and an indication for inpatient detoxification), the complement to the CIWA-Ar, which measures the withdrawal state as it happens.

9.1 The withdrawal spectrum by the clock: a time-ordered emergency

The core sequence. The **withdrawal spectrum** unfolds in a predictable temporal order after the last drink, and the single most examinable fact is that order. Early autonomic overactivity and tremor begin at roughly **6 to 12 hours**; alcoholic hallucinosis (typically visual or tactile, in a clear sensorium) appears around 12 to 24 hours; generalised tonic-clonic withdrawal seizures (the classic "rum fits") cluster at roughly **12 to 48 hours**, peaking near the second day; and delirium tremens, the most dangerous stage, characteristically emerges at **48 to 72 hours** and can extend to 96 hours (Kaplan and Sadock 2024; Maudsley Prescribing Guidelines). Symptoms can begin before the blood alcohol level reaches zero.

Why the order matters. The sequence is not trivia: it lets you place a patient on the curve, anticipate what is coming, and decide setting and intensity. A tremulous, sweating patient at hour

eight is early; the danger window for seizures and delirium is still ahead, so this is precisely the patient in whom to start adequate benzodiazepine cover rather than to reassure and discharge.

STAGE	ONSET AFTER LAST DRINK	KEY FEATURES
Early / minor withdrawal	**6 to 12 hours**	Tremor of hands, tongue, eyelids; anxiety, agitation, insomnia; sweating, nausea, tachycardia, systolic hypertension, low-grade fever (autonomic overactivity).
Alcoholic hallucinosis	12 to 24 hours	Transient visual, tactile or auditory hallucinations in a *clear* sensorium (distinguishes it from delirium tremens); usually settles within 24 to 48 hours.
Withdrawal seizures ("rum fits")	**12 to 48 hours (peak near day two)**	Generalised tonic-clonic; often 2 to 6 in a cluster; about a third go on to develop delirium tremens; a first or focal fit needs investigation for another cause.
Delirium tremens	**48 to 72 hours (up to 96 hours)**	Clouding of consciousness and disorientation, vivid visual and tactile hallucinations, coarse tremor, gross autonomic storm (tachycardia, hypertension, fever, sweating); a medical emergency, 10 to 20 per cent mortality if untreated.

The alcohol withdrawal spectrum in temporal order; delirium tremens is the late, high-mortality stage and is the one to anticipate, not to wait for (Kaplan and Sadock 2024; Maudsley Prescribing Guidelines).

RULE **Place the patient on the clock, then treat forwards.** Read the hours since the last drink; adequate benzodiazepine cover started early prevents the seizures and delirium that come later, so you medicate the trajectory, not just the current score.

GOOD TO REMEMBER

- **Delirium tremens:** the criterion picture is clouding of consciousness plus disorientation, vivid visual and tactile hallucinations and a gross autonomic storm, onset 48 to 72 hours (up to 96 hours) after the last drink; the discriminator from alcoholic hallucinosis is the *clouded* sensorium; the first management step is to treat it as a medical emergency with generously titrated benzodiazepine (an antipsychotic only as adjunct, never alone) and to exclude infection and electrolyte derangement.
- **Alcohol withdrawal seizures:** the criterion feature is a generalised tonic-clonic fit 12 to 48 hours after the last drink, peaking near day two; the first step is a long-acting benzodiazepine (which both treats and prevents further fits) rather than a standard anticonvulsant; a focal or very late fit demands a search for another cause.

9.2 The CIWA-Ar: what it measures and why it is objective

What it is. The CIWA-Ar (Clinical Institute Withdrawal Assessment for Alcohol, revised) is a validated 10-item clinician-rated scale, completed in about five minutes, that quantifies

withdrawal severity so that treatment can be titrated to a number rather than to impression (Sullivan 1989; Tasman; Maudsley Prescribing Guidelines). Nine items (nausea and vomiting, tremor, paroxysmal sweats, anxiety, agitation, tactile disturbances, auditory disturbances, visual disturbances, headache) are each scored **0 to 7**, and the tenth item, orientation and clouding of sensorium, is scored **0 to 4**, giving a maximum total of **67**. The full instrument is reproduced in the scales gallery.

Why it is preferred. The CIWA-Ar is an *objective*, observer-rated scale (contrast the self-completed Short Alcohol Withdrawal Scale, SAWS), which is what makes it the standard tool for driving a symptom-triggered regimen: the same score means the same thing across raters and across time, so repeated scoring tracks the withdrawal and the effect of each dose.

9.3 CIWA-Ar action thresholds: the numbers that drive treatment

The thresholds to memorise. A score under **10** is mild withdrawal that usually needs supportive care only, and is the cut-off below which outpatient detoxification can reasonably be attempted with adequate support; scores of **8 to 15** are moderate and benefit from medication; a score of **15 or more** requires pharmacological treatment (Sullivan 1989; Foy 1988; Tasman). In a symptom-triggered regimen the operational trigger most guidelines use is to medicate when the CIWA-Ar reaches about **8 to 10** and to dose until it falls below 10 (IPS guidelines; BAP 2026). The higher the score, the more the risk: mortality in delirium tremens climbs sharply where the CIWA-Ar exceeds 25 with fever, marked tachycardia or seizures.

CIWA-AR SCORE	SEVERITY	ACTION
under 10	Mild	Supportive care usually sufficient; outpatient detoxification feasible with good support; medication optional.
8 to 15	Moderate	Symptomatic benefit from benzodiazepine; symptom-triggered dosing begins around a trigger of 8 to 10.
15 or more	Severe	Pharmacological treatment required; high-level supportive care and medical monitoring; consider inpatient setting.

CIWA-Ar action thresholds; the operative symptom-triggered trigger is a score of about 8 to 10, and 15 or more mandates medication (Sullivan 1989; Foy 1988; Tasman; IPS guidelines).

COMMON TRAP

Do not use the CIWA-Ar in a delirious, unco-operative or non-communicative patient, or in one with a language barrier or a co-existing head injury. The scale depends on the patient reliably reporting nausea, anxiety and perceptual disturbance and on assessable orientation; in established delirium tremens the score is unreliable and management shifts to clinical titration of benzodiazepine to light sedation, not to a CIWA-Ar number.

9.4 The SADQ: dependence severity, not withdrawal severity

What it is and what it is for. The SADQ (the **Severity of Alcohol Dependence Questionnaire**) is a 20-item self-report questionnaire, each item scored 0 to 3, giving a maximum total of **60**, that indexes the *severity of dependence* and thereby predicts how difficult a withdrawal is likely to be and how much medication it will need (Maudsley Prescribing Guidelines; Shorter Oxford Textbook of Psychiatry). The key conceptual point, and a favourite discriminator, is that the SADQ (also written **SAD-Q**) measures dependence severity *before* withdrawal, whereas the CIWA-Ar measures the withdrawal state as it happens: one sets the starting dose and setting, the other titrates the taper.

The bands. A SADQ score of **15 or less** is mild dependence, **16 to 30** is moderate, and a score **above 30** is severe dependence and is itself an indication for inpatient or residential detoxification (Maudsley Prescribing Guidelines; NICE 2011). The instrument is reproduced in the scales gallery.

SADQ SCORE	DEPENDENCE BAND	PRACTICAL IMPLICATION
15 or less	Mild	Often needs only small benzodiazepine doses or none; community detoxification usually feasible.
16 to 30	Moderate	Fixed-dose reducing benzodiazepine regimen, community or non-specialist inpatient setting.
above 30	Severe	An indication for inpatient / residential detoxification; higher starting doses; anticipate complications.

SADQ dependence-severity bands; a score above 30 flags severe dependence and points to inpatient detoxification (Maudsley Prescribing Guidelines; NICE 2011; Shorter Oxford Textbook of Psychiatry).

PEARL

Keep two questions separate. "How dependent is this person?" is answered before you start, by the SADQ (and by units per day and history of complications), and it sets the starting dose and the setting. "How bad is the withdrawal right now?" is answered repeatedly during detoxification by the CIWA-Ar, and it drives each dose. Mixing them up (using a SADQ to titrate, or a CIWA-Ar to decide inpatient versus outpatient in a currently sober patient) is a classic conceptual error.

9.5 Benzodiazepines: the first-line agent and why

The rule. A benzodiazepine is the first-line, gold-standard treatment for alcohol withdrawal (BAP 2026; IPS guidelines; NICE 2011; WHO mhGAP 2016). The reason is mechanistic: benzodiazepines show cross-tolerance with alcohol at the GABA-A receptor, so they substitute for the missing depressant at exactly the adapted target and are then tapered, and they are anticonvulsant, so they both relieve the withdrawal and prevent withdrawal seizures. Long-acting agents are preferred because their slow elimination self-tapers and gives a smoother course. WHO

mhGAP calls benzodiazepines the front-line medication and states plainly that antipsychotics must not be used as stand-alone treatment for alcohol withdrawal.

The guideline positions, in order. BAP names benzodiazepines the gold standard, preferring longer-acting agents (diazepam, chlordiazepoxide) except where hepatic metabolism is impaired (BAP 2026). The **Indian Psychiatric Society** offers a benzodiazepine (chlordiazepoxide or diazepam) as first-line, with chlordiazepoxide 25 to 50 mg orally every four to six hours as needed for uncomplicated withdrawal and a switch to lorazepam in hepatic compromise (IPS guidelines). NICE names chlordiazepoxide or diazepam as the preferred medication, reduced over 7 to 10 days (NICE 2011). WHO mhGAP recommends long-acting benzodiazepines limited to the first 3 to 7 days (WHO mhGAP 2016). None of these is contradicted here; benzodiazepine-first is verified across all four.

GOOD TO REMEMBER

- **Benzodiazepine (class):** first-line, gold-standard treatment for alcohol withdrawal; works by cross-tolerance at GABA-A and is anticonvulsant, so it treats symptoms and prevents seizures; prefer long-acting agents (diazepam, chlordiazepoxide) for a smoother, self-tapering course; the dose is titrated to the CIWA-Ar and reduced to zero over about 5 to 10 days.

9.6 Choice of agent: chlordiazepoxide and diazepam, and the hepatic switch

The default long-acting agents. For most patients the agent is chlordiazepoxide (the UK and Indian community workhorse) or diazepam; both are long-acting, cross-tolerant and anticonvulsant (BAP 2026; NICE 2011; IPS guidelines). Chlordiazepoxide is favoured for community detoxification because its lower euphoria and slower onset give it lower misuse potential than diazepam.

The hepatic-impairment switch. The one signature exception every candidate must know: in significant liver disease (and in the elderly, or where the oral route is unreliable) switch to lorazepam or oxazepam. These are metabolised by glucuronidation and have no active metabolites (unlike chlordiazepoxide and diazepam, whose long-lived active metabolites accumulate in hepatic failure and can cause oversedation and encephalopathy). Lorazepam 1 to 2 mg every four to six hours is the standard hepatic-compromise substitute (IPS guidelines); oxazepam is BAP's preferred agent in pregnancy for the same reason, an intermediate half-life with no active metabolite (BAP 2026). In severe liver impairment, avoid benzodiazepines with extensive hepatic metabolism altogether and monitor closely.

AGENT	WHEN TO USE	NOTE
Chlordiazepoxide (community default)	**Most uncomplicated withdrawal**	Long-acting, low misuse potential; UK and Indian first choice; reduce over 5 to 10 days.
Diazepam	Alternative long-acting; front-loading in severe risk	Long-acting active metabolites; smoothest course; used in front-loading regimens under close monitoring.
Lorazepam	**Hepatic impairment, elderly, unreliable oral route**	Glucuronidated, no active metabolite; does not accumulate in liver failure; 1 to 2 mg q4 to 6h.
Oxazepam	Hepatic impairment; BAP-preferred in pregnancy	Intermediate half-life, no active metabolite; hospitalise pregnant women for withdrawal.

Choice of benzodiazepine; the mnemonic exception is the LOT of glucuronidated agents (lorazepam, oxazepam, temazepam) in hepatic impairment (BAP 2026; IPS guidelines; NICE 2011).

MNEMONIC

LOT for the liver

Lorazepam, **O**xazepam, **T**emazepam are the glucuronidated benzodiazepines with no active metabolite, so they are the ones to reach for in hepatic impairment; the long-acting agents (chlordiazepoxide, diazepam) accumulate and oversedate the failing liver.

GOOD TO REMEMBER

- **Chlordiazepoxide (Librium):** the default long-acting benzodiazepine for alcohol withdrawal; a moderate-dependence fixed-dose schedule is about 20 mg four times daily on day one tapering to zero over roughly 5 days; low misuse potential makes it the community first choice; switch to lorazepam or oxazepam if the liver is compromised.
- **Lorazepam:** the hepatic-impairment substitute; glucuronidated with no active metabolite so it does not accumulate in liver failure; about 1 to 2 mg orally every four to six hours; also the practical choice when the oral route is unreliable (it can be given IM or IV).

9.7 Symptom-triggered versus fixed-dose: choosing the regimen

The two regimens. A **symptom-triggered** regimen gives a benzodiazepine only when the CIWA-Ar crosses a trigger (about 8 to 10), re-scoring every one to two hours and dosing until the score settles; a **fixed-dose** regimen gives a pre-set, tapering schedule regardless of moment-to-moment symptoms, with as-needed top-ups. Two randomised trials showed that symptom-triggered dosing shortens treatment duration and reduces the total benzodiazepine given compared with fixed dosing (Saitz 1994; Daeppen 2002; Tasman), but it depends on trained staff able to score reliably and frequently.

How to choose. The dividing line is monitoring capacity, not preference. NICE and the IPS position both direct that *community* and non-specialist settings use a *fixed-dose* reducing regimen (because reliable frequent scoring is not available and unsupervised as-needed dosing is unsafe), while symptom-triggered dosing is reserved for inpatient or specialist settings with adequate

monitoring and for patients without a history of complications (NICE 2011; IPS guidelines; BAP 2026). In practice symptom-triggered treatment often lasts only 24 to 48 hours before switching to an individualised fixed-dose taper.

FEATURE	SYMPTOM-TRIGGERED	FIXED-DOSE REDUCING
How dosed	Only when CIWA-Ar reaches trigger (about 8 to 10)	Pre-set tapering schedule, with PRN top-ups
Setting	**Inpatient / specialist, adequate monitoring**	**Community and non-specialist settings**
Requires	Trained staff, frequent reliable CIWA-Ar scoring	No moment-to-moment scoring; safer where monitoring is limited
Evidence signal	Shorter treatment, less total benzodiazepine (Saitz 1994; Daeppen 2002)	Predictable, standardised; preferred for outpatient safety

Symptom-triggered versus fixed-dose benzodiazepine regimens; the choice is decided by monitoring capacity, not clinician preference (NICE 2011; IPS guidelines; Tasman).

9.8 A worked fixed-dose chlordiazepoxide schedule

The rule of thumb. For a fixed-dose regimen the starting dose is estimated from the severity of dependence, using SADQ, units per drinking day and history: a rough guide is that consuming about 20 units a day suggests a starting dose near 20 mg four times daily, tapered to zero over 5 to 10 days (Maudsley Prescribing Guidelines). Mild dependence often needs very little or nothing; severe dependence usually needs inpatient care and a longer taper.

DAY	MODERATE DEPENDENCE (MG, CHLORDIAZEPOXIDE)	TOTAL (MG/DAY)
Day one	20 four times daily	**80**
Day two	15 four times daily	60
Day three	10 four times daily	40
Day four	5 four times daily	20
Day five	5 twice daily	10

A typical fixed-dose reducing chlordiazepoxide regimen for moderate alcohol dependence; severe dependence uses higher starting doses (for example a 200 mg first-day total) over a 7 to 10 day taper (Maudsley Prescribing Guidelines).

TRAP **Do not start the benzodiazepine while the patient is still intoxicated,** and do not taper faster than the schedule. Prescribing on top of alcohol risks respiratory depression; an over-rapid taper in a severely dependent or multiply-detoxified drinker re-opens the seizure and delirium window.

9.9 Parenteral thiamine before glucose: the non-negotiable

The rule. Every withdrawing or malnourished drinker at risk of Wernicke encephalopathy must receive parenteral thiamine before any intravenous glucose. Thiamine is the cofactor needed to metabolise glucose; giving a glucose load to a thiamine-deplete patient consumes the last of their

thiamine and can precipitate acute Wernicke encephalopathy (Maudsley Prescribing Guidelines; IPS guidelines). This is the single most tested management error on the topic.

The regimens. BAP recommends parenteral thiamine 300 to 1500 mg/day for 3 to 5 days for anyone with risk factors for Wernicke-Korsakoff, followed by an oral course, and treating established Wernicke encephalopathy as an emergency (BAP 2026). The IPS position gives parenteral thiamine 100 mg IM or IV daily for at least 3 to 5 days for prophylaxis, escalating to about 500 mg IV three times daily for 2 to 3 days if any Wernicke feature is present, then oral thiamine 100 mg/day for the duration of detoxification and at least 3 months (IPS guidelines). Wernicke encephalopathy is a thiamine-deficiency emergency in which the classical triad (confusion, ophthalmoplegia, ataxia) is complete in only about 10 per cent, so treat empirically on any single new neurological sign in a withdrawing patient; the amnestic Korsakoff endpoint is developed in the Dementias and neurocognitive disorders notes.

WORKED EXAMPLE

A malnourished man is brought in confused and unsteady 40 hours after his last drink; the intern sets up intravenous 5 per cent dextrose for presumed hypoglycaemia. The correct order is to give parenteral thiamine *first* (a Wernicke feature, ataxia, is already present, so an escalated regimen, for example 500 mg IV three times daily, is indicated), and only then the glucose. Reversing the order, glucose before thiamine, is the classic examination trap and can convert a treatable state into irreversible Korsakoff amnesia.

GOOD TO REMEMBER

- **Thiamine (parenteral, vitamin B1):** give it *before* any glucose in a malnourished or withdrawing drinker; prophylaxis is roughly 100 mg IM/IV daily (BAP: 300 to 1500 mg/day) for 3 to 5 days, escalated to about 500 mg IV three times daily for 2 to 3 days if any Wernicke feature appears, then a long oral course; the criterion trigger to treat empirically is a single new neurological sign, since the full triad is present in only about 10 per cent.

9.10 When benzodiazepines are not enough: seizures, delirium tremens and adjuncts

Seizures. After an alcohol withdrawal seizure, use a benzodiazepine (not a standard anticonvulsant) to prevent further fits; phenytoin does not prevent alcohol withdrawal seizures, and long-acting benzodiazepines are the meta-analytic winner for seizure prevention (WHO mhGAP 2016; Maudsley Prescribing Guidelines). A history of prior withdrawal seizures is an indication for long-acting benzodiazepine prophylaxis and for treating the withdrawal as high-risk.

Delirium tremens. Delirium tremens is a medical emergency needing generous, titrated benzodiazepine (often high doses, sometimes intravenous lorazepam or diazepam to light sedation) plus correction of electrolytes (magnesium, potassium, phosphate) and a search for infection; where agitation and hallucinations are not controlled by adequate benzodiazepine, add a dopamine antagonist (haloperidol) as an *adjunct*, never as monotherapy, watching for the lowered seizure threshold (IPS guidelines; BAP 2026). Carbamazepine or gabapentin can be

added or substituted where benzodiazepines are contraindicated or where past withdrawal seizures or benzodiazepine-misuse concerns apply (IPS guidelines; BAP 2026).

15	above 30	48 to 72 h
CIWA-AR SCORE AT OR ABOVE WHICH BENZODIAZEPINE TREATMENT IS REQUIRED	SADQ SCORE DEFINING SEVERE DEPENDENCE (INDICATION FOR INPATIENT DETOXIFICATION)	CHARACTERISTIC ONSET WINDOW FOR DELIRIUM TREMENS AFTER THE LAST DRINK

9.11 The India frame: treatment gap, NDPS and the de-addiction context

The clinical reality. India carries a very large substance-use treatment gap, with most people meeting dependence criteria never reaching formal care, and alcohol the commonest substance in de-addiction services (IPS guidelines). Care is concentrated in government de-addiction centres and Drug De-addiction Programme (DDAP) units and in the day care centre model rather than in general practice, so the psychiatrist is often the first and only clinician to stage a withdrawal correctly. The IPS position deliberately shifts brief, motivation-based interventions toward community and home-based delivery by trained non-specialist workers precisely to close that gap.

Access and law. The controlled status of benzodiazepines and of opioid agents sits under the Narcotic Drugs and Psychotropic Substances (NDPS) Act, 1985, whose scheduling shapes access; the medico-legal detail is developed in the Mental health legislation and forensic psychiatry notes. Indian brands the candidate should recognise for the relapse-prevention agents that follow detoxification are disulfiram (Indian brands Esperal, Dizone), naltrexone (Naltima, Nodict) and acamprosate (Acamprol); the withdrawal-management agents themselves are the generic benzodiazepines and parenteral thiamine above. A verified caution to carry forward: naltrexone must never be started in a current opioid user (it precipitates acute withdrawal) and needs an opioid-free window of about 7 to 10 days, a point developed in the opioid-substitution topics.

INDIA

Two India-specific management points recur in the viva. First, the parenteral-thiamine-before-glucose rule is not academic here: malnourished, multiply-detoxified drinkers presenting late to under-resourced services are exactly the Wernicke-risk population, and the IPS position specifies escalated parenteral thiamine on any Wernicke feature. Second, the fixed-dose chlordiazepoxide regimen is the default for community and non-specialist Indian settings because reliable frequent CIWA-Ar scoring for a symptom-triggered regimen is often unavailable; symptom-triggered dosing belongs to the inpatient de-addiction ward. Disulfiram (Esperal, Dizone) remains widely used in supervised, family-monitored abstinence programmes but is a relapse-prevention, not a withdrawal, agent and is started only after withdrawal is complete and at least 24 hours after the last drink.

HOLD THIS

Alcohol withdrawal runs on a clock (tremor and autonomic overactivity at 6 to 12 hours, seizures at 12 to 48 hours, delirium tremens at 48 to 72 hours); stage it with the CIWA-Ar (medicate at 8 to 10, treat at 15 or more) and the SADQ (severe above 30), cover it with a long-acting benzodiazepine (chlordiazepoxide or diazepam, or lorazepam/oxazepam if the liver is compromised) symptom-triggered inpatient or fixed-dose in the community, and give parenteral thiamine before any glucose.

10 · Delirium tremens and the substance-emergency differential

A patient stops drinking, and two or three days later becomes floridly confused, terrified, drenched in sweat, tachycardic and hallucinating. Recognising that picture as **delirium tremens** rather than a psychiatric decompensation, and separating it in a single beat from the other substance emergencies it mimics, is one of the highest-yield decisions on this block: get it right and you treat a reversible, high-mortality state; get it wrong and a treatable emergency is missed. Examiners want the onset window by the clock, the core clinical picture, the mortality figure, the parenteral-benzodiazepine-and-supportive plan, and the one discriminator that peels delirium tremens apart from Wernicke encephalopathy, alcoholic hallucinosis, opioid overdose and sedative-hypnotic withdrawal.

Why it matters clinically. **Delirium tremens** is the most severe form of alcohol withdrawal and the one that routinely kills. It is a clouded, fluctuating **confusion**al state with a gross **autonomic** storm, and its danger is that it is often missed early, dismissed as "simple withdrawal" until the patient is delirious and unstable. The underlying neuroadaptation (down-regulated GABA-A, up-regulated NMDA-glutamate) is developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and is not re-derived here; the amnestic mechanism of Korsakoff sits in the Dementias and neurocognitive disorders notes and the Neuropsychiatry of systemic and neurological disease notes; the wider delirium and restraint frame is in the Perinatal/women's mental health and emergency psychiatry notes. Here the task is to recognise the syndrome, treat it by the number, and run the emergency differential.

Discriminator the row you read across	Delirium tremens alcohol withdrawal	Wernicke encephalopathy thiamine deficiency	Alcoholic hallucinosis the clear-mind case	Opioid overdose the killable one	Sedative withdrawal benzo/barbiturate
Substance and timing	alcohol; 48 to 96 h after the last drink	thiamine lack; any time in a malnourished drinker	alcohol; 12 to 24 h, on continued use	opioid; acute, at the point of overdose	**timed to half-life:** short 12 to 24 h, long peaks at 5 to 8 days
Conscious-ness	clouded, fluctuating, disoriented (a delirium)	confused, but the eye and gait signs dominate	**clear and oriented, no clouding**	reduced, to coma	clouded if it reaches a delirium
Pupils	normal to dilated	normal	normal	**pinpoint (miotic), survive tolerance**	normal
Autonomic state	**gross storm: tachycardia, fever, sweating, hypertension**	no autonomic storm	minimal, if any	respiratory depression, not a sympathetic storm	overactivity, like alcohol withdrawal
The key sign what settles it in one look	clouded mind and autonomic storm together	**ophthalmoplegia or nystagmus with ataxia, no autonomic storm**	hallucinations in a clear sensorium	pinpoint pupils with failing respiration	delirium keyed to the agent's half-life
First management step	**parenteral benzodiazepine,** plus thiamine and supportive care	**IV thiamine at once, 500 mg three times daily**	reassure and observe; antipsychotic if it persists or distresses	**naloxone, with airway and ventilation support**	long-acting benzodiazepine or phenobarbital taper

shaded cell = the single best discriminator for that column

coral = opioid overdose, the reversible-in-minutes emergency

Fig 13.7 The substance emergencies discriminated. Read down the column, but the shaded cell is the one that settles each: delirium tremens is the clouded mind plus autonomic storm, Wernicke the eye signs and ataxia without a storm, alcoholic hallucinosis the clear sensorium, opioid overdose the pinpoint pupils with failing respiration, and sedative-hypnotic withdrawal the delirium timed to the agent's half-life. The first move follows straight from the discriminator: benzodiazepine, thiamine, reassurance, naloxone, or a long-acting taper.

10.1 What delirium tremens is: the criterion picture

The core state. Delirium tremens (DT, plural **DTs**) is an acute organic brain syndrome (a delirium) precipitated by cessation or a sharp reduction of heavy alcohol intake in a physically dependent drinker (Kaplan and Sadock 2024; Maudsley Prescribing Guidelines). The defining triad, and the thing to say first in a viva, is *clouded fluctuating consciousness*, *disorientation*, and a *gross autonomic storm*, on which vivid hallucinations are superimposed. It is not a functional psychosis: the sensorium is impaired, and that single fact drives most of the differential below.

The full clinical picture. The features cluster into four groups (Maudsley Prescribing Guidelines): clouding of consciousness with disorientation in time and place, poor attention span and distractibility; vivid, frightening visual and tactile hallucinations (the classic tactile hallucination of insects or small animals crawling over the skin, formication) with illusions; marked **autonomic** hyperactivity (tachycardia, hypertension, sweating, fever); and psychomotor agitation, coarse tremor, ataxia, insomnia with sleep-wake reversal, and dehydration with electrolyte imbalance. Prodromal night-time insomnia, restlessness and fear often precede the full state.

FEATURE CLUSTER	WHAT YOU SEE
Clouded consciousness	**Disorientation in time and place, fluctuating attention, distractibility (the delirium itself)**
Perceptual disturbance	Vivid, frightening visual and tactile hallucinations; formication (insects crawling on skin); illusions
Autonomic storm	**Tachycardia, hypertension, profuse sweating, fever (sympathetic overactivity)**
Psychomotor / other	Coarse tremor, agitation, ataxia, insomnia with sleep-wake reversal, dehydration and electrolyte derangement

The four feature-clusters of delirium tremens; the clouded sensorium plus autonomic storm is the criterion picture and separates it from alcoholic hallucinosis (Maudsley Prescribing Guidelines; Kaplan and Sadock 2024).

RULE **Clouded consciousness makes it delirium tremens.** Hallucinations in a clear sensorium are alcoholic hallucinosis; the moment consciousness clouds and the patient is disoriented with an autonomic storm, it is delirium tremens and a medical emergency.

10.2 The onset window and course: the 48-to-96-hour rule

Onset by the clock. Delirium tremens characteristically begins **48 to 96 hours** (2 to 4 days) after the last drink, later than the early tremor (6 to 12 hours), the hallucinosis (12 to 24 hours) and the withdrawal seizures (12 to 48 hours) that may precede it (Maudsley Prescribing Guidelines; Kaplan and Sadock 2024). The window is 2 to 4 days; the Maudsley Prescribing Guidelines give the peak at 3 to 4 days (72 to 96 hours). It is the *late* stage of the withdrawal spectrum, which is exactly why it must be anticipated in a tremulous patient at hour eight rather than waited for.

Course and who gets it. Delirium tremens develops in roughly **5 per cent** of patients admitted for alcohol withdrawal (the Maudsley Prescribing Guidelines 3 to 5%), compared with acute tremulousness in about a third; and in about **30 per cent** of alcohol-withdrawal seizure cases, delirium tremens follows the fit. The **course** once established is short, typically resolving over 3 to 7 days with treatment. Risk factors that should raise your guard: severe dependence, self-detoxification without medical cover, multiple previous withdrawal admissions, a past history of delirium tremens or withdrawal seizures, concurrent medical illness, and low potassium, low magnesium or thiamine deficiency (Maudsley Prescribing Guidelines).

GOOD TO REMEMBER

- **Delirium tremens (syndrome):** the criterion picture is clouded fluctuating consciousness plus disorientation plus a gross autonomic storm, with vivid visual and tactile hallucinations on top; onset 48 to 96 hours (2 to 4 days) after the last drink; develops in about 5 per cent of alcohol-withdrawal admissions; the discriminator from alcoholic hallucinosis is the *clouded* sensorium; the first management step is to treat it as a medical emergency with generously titrated parenteral benzodiazepine plus supportive care, and to give parenteral thiamine before any glucose.

10.3 Mortality: why untreated delirium tremens kills

The number to hold. Untreated delirium tremens carries a mortality of the order of **10 to 20 per cent** (Maudsley Prescribing Guidelines; Kaplan and Sadock give a range of 4 to 20%); with

prompt treatment this falls to roughly 5 per cent or less. Death is from cardiovascular collapse, hyperthermia, aspiration, infection, self-injury, or the complications of an untreated autonomic storm and its electrolyte derangement. Mortality rises sharply where the withdrawal is severe: a CIWA-Ar over **25** with concurrent fever, marked tachycardia (over 120) or seizures flags a patient who needs care escalated immediately.

48 to 96 h	5	10 to 20	25
ONSET OF DELIRIUM TREMENS AFTER LAST DRINK	PER CENT OF WITHDRAWAL ADMISSIONS WHO DEVELOP IT	PER CENT MORTALITY UNTREATED (MAUDSLEY)	CIWA-AR ABOVE WHICH MORTALITY CLIMBS WITH FEVER OR FITS

COMMON TRAP

The classic error is missing delirium tremens behind "simple withdrawal". A patient two to three days into an unsupervised detoxification who becomes agitated, confused and febrile is not decompensating psychiatrically and is not merely anxious: this is the late, lethal stage of the withdrawal spectrum. Treating it as agitation with an antipsychotic alone, without adequate benzodiazepine cover and without excluding infection and electrolyte derangement, is dangerous and misses the diagnosis.

10.4 Management of delirium tremens: the parenteral-benzodiazepine and supportive plan

The first step. The **management of delirium tremens** begins by treating it as a medical emergency: admit, ideally to a high-dependency or monitored setting, and consider intensive care (Maudsley Prescribing Guidelines; IPS guidelines). The mainstay is a benzodiazepine, given *parenterally* and titrated generously to light sedation, because the delirious patient cannot reliably take or absorb oral medication and needs rapid control of the autonomic storm. Escalate to intravenous lorazepam or intravenous diazepam, titrated to a lightly sedated, arousable state; established delirium tremens needs larger benzodiazepine doses than uncomplicated withdrawal (IPS guidelines; Maudsley Prescribing Guidelines). In the delirious patient the CIWA-Ar is unreliable (it depends on the patient reporting symptoms and being orientable), so dosing is by clinical titration, not by a score.

The supportive package. Alongside the benzodiazepine: give parenteral thiamine before any glucose load (see 10.5); actively correct fluid and electrolyte derangement (potassium, magnesium, phosphate); monitor pulse, blood pressure and temperature closely; and exclude the mimics and precipitants, particularly infection, head injury, hepatic encephalopathy and metabolic derangement, which can both cause and complicate the delirium. An antipsychotic (haloperidol or olanzapine) is added only as an adjunct for severe agitation or hallucinations that persist despite adequate benzodiazepine, never as monotherapy, and with care because antipsychotics lower the seizure threshold (BAP 2026; WHO: do not use antipsychotics as stand-alone treatment for alcohol withdrawal).

STEP	ACTION
Setting	**Medical emergency: admit to high-dependency/monitored bed; consider ICU**
Mainstay	**Parenteral benzodiazepine (IV lorazepam or diazepam) titrated to light sedation**
Vitamin	Parenteral thiamine BEFORE any glucose (Wernicke prophylaxis and treatment)
Supportive	Correct fluids and electrolytes (K, Mg, phosphate); monitor pulse, BP, temperature
Exclude	Infection, head injury, hepatic encephalopathy, metabolic causes
Antipsychotic	Adjunct only (haloperidol/olanzapine) for refractory agitation, never as monotherapy

The management of delirium tremens: parenteral benzodiazepine plus a supportive, exclusionary package; the antipsychotic is an adjunct, never the mainstay (Maudsley Prescribing Guidelines; IPS guidelines; BAP 2026).

GOOD TO REMEMBER

- **Lorazepam (in delirium tremens):** the parenteral benzodiazepine of choice when the oral route is unreliable or the liver is compromised; glucuronidated with no active metabolite so it does not accumulate; give IV/IM, titrated to light arousable sedation (about 1 to 2 mg per dose repeated to effect); it controls the autonomic storm and prevents seizures.
- **Diazepam (in delirium tremens):** long-acting benzodiazepine used IV, titrated to light sedation; its long half-life self-tapers and smooths the course; front-loading (repeated doses until symptoms settle) is used under close inpatient monitoring; avoid where hepatic metabolism is significantly impaired (active metabolites accumulate).

10.5 Thiamine before glucose: the one supportive rule that cannot be skipped

The rule. Give parenteral thiamine *before* any intravenous glucose in a malnourished or actively withdrawing drinker (NICE; WHO mhGAP 2016; IPS guidelines). A carbohydrate load consumes the last of a depleted thiamine store and can precipitate acute Wernicke encephalopathy; the sequence is thiamine first, glucose second. For prophylaxis in withdrawal, parenteral thiamine 100 mg IM/IV daily for at least 3 to 5 days is standard; where any Wernicke feature is present, escalate to **500 mg IV three times daily** for 2 to 3 days (the emergency regimen; see 10.7).

TRAP **Never give IV glucose before thiamine in a drinker.** A glucose load in a thiamine-depleted patient can precipitate acute Wernicke encephalopathy; the order is thiamine first, always, and parenterally.

GOOD TO REMEMBER

- **Thiamine (vitamin B1):** give parenterally BEFORE any glucose in a malnourished or withdrawing drinker; withdrawal prophylaxis is 100 mg IM/IV daily for at least 3 to 5 days (then oral); suspected Wernicke encephalopathy is treated as an emergency with 500 mg IV three times daily for 2 to 3 days; oral thiamine has poor, saturable absorption, so the acute treatment must be parenteral.

10.6 The substance-emergency differential, one discriminator each

The five-way split. This is arc Step 5a: when a patient with a substance history is acutely disturbed, the emergency differential is delirium tremens against Wernicke encephalopathy, alcoholic hallucinosis, opioid overdose and sedative-hypnotic withdrawal. Each pair separates on a single high-yield discriminator, and holding those five discriminators is what lets you decide the treatment in one beat (Kaplan and Sadock 2024; New Oxford Textbook of Psychiatry; the substance-induced psychotic boundary sits in the Other psychotic disorders, delusional syndromes and catatonia notes).

EMERGENCY	CORE PICTURE	THE ONE DISCRIMINATOR	FIRST MOVE
Delirium tremens	Clouded consciousness, disorientation, autonomic storm, vivid visual/tactile hallucinations, 48 to 96 h after last drink	**Clouded sensorium PLUS autonomic storm (a delirium)**	Parenteral benzodiazepine, supportive care, thiamine
Wernicke encephalopathy	Confusion, ophthalmoplegia/nystagmus, ataxia (classic triad in only ~10%)	**Eye signs (ophthalmoplegia/nystagmus) and ataxia, no autonomic storm**	High-dose IV thiamine (500 mg TID) immediately
Alcoholic hallucinosis	Hallucinations (usually auditory) after regular use, ~2% of drinkers	**CLEAR consciousness, no disorientation**	Reassurance, observation; antipsychotic if distressing/persistent
Opioid overdose	Coma, respiratory depression, cyanosis	**PINPOINT (miotic) pupils + respiratory depression**	Naloxone plus airway/ventilation support
Sedative-hypnotic withdrawal	Tremor, autonomic overactivity, seizures, delirium; resembles alcohol withdrawal	**Timing keyed to the agent's half-life (short-acting 12 to 24 h; long-acting peaks at 5 to 8 days)**	Long-acting benzodiazepine or phenobarbital taper

The substance-emergency differential, keyed on one discriminator each; delirium tremens is the clouded-plus-autonomic delirium, Wernicke the eye-signs-and-ataxia state, hallucinosis the clear-sensorium exception, opioid overdose the pinpoint-pupil respiratory failure, sedative-hypnotic withdrawal the half-life-timed mimic (Kaplan and Sadock 2024; New Oxford Textbook of Psychiatry).

MNEMONIC

PUPILS tell the story

In the collapsed or confused substance patient, look at the **pupils** first: *pinpoint* pupils with slow respiration point to opioid overdose (give naloxone); ophthalmoplegia or nystagmus with ataxia point to Wernicke (give IV thiamine); a clouded, autonomically stormy delirium with normal-to-dilated pupils points to delirium tremens (give benzodiazepine). The eyes and the sensorium do most of the triage.

10.7 Delirium tremens versus Wernicke encephalopathy: the discriminator that changes the drug

The split that matters most. Both arise in the malnourished drinker and both can present with confusion, so they are the pair most often confused, yet the first drug differs. Wernicke encephalopathy is a thiamine-deficiency emergency whose classic triad is *confusion, ophthalmoplegia (or nystagmus) and ataxia*, and the exam trap is that the full triad appears in only about **10 per cent** of cases, so any one of the three in a malnourished or withdrawing patient should trigger empirical treatment (Kaplan and Sadock 2024; NICE). The discriminator from delirium tremens is the presence of *eye signs and ataxia without a florid autonomic storm*; delirium tremens clouds consciousness and drives the autonomic system, Wernicke gives ocular and cerebellar signs. Treat suspected Wernicke immediately with high-dose IV thiamine (500 mg three times daily for 2 to 3 days, then 250 mg daily for 5 days) before it progresses to the irreversible amnesia of Korsakoff syndrome (anterograde amnesia with confabulation).

GOOD TO REMEMBER

- **Wernicke encephalopathy (syndrome):** the criterion is the triad of confusion, ophthalmoplegia/nystagmus and ataxia, but the full triad is present in only about 10 per cent, so treat on any one feature; the discriminator from delirium tremens is eye signs and ataxia without the autonomic storm; the first step is high-dose IV thiamine (500 mg TID) at once, before it becomes irreversible Korsakoff.

10.8 Opioid overdose and naloxone: the emergency that is not withdrawal

The picture and the antidote. The far more urgent opioid emergency is *overdose*, not withdrawal. Opioid overdose is a triad of *coma, respiratory depression and pinpoint (miotic) pupils*, with cyanosis in severe cases (Kaplan and Sadock 2024). The antidote is naloxone, a competitive opioid antagonist: intramuscular 0.4 to 2 mg, repeated every 2 to 3 minutes up to about 10 mg, or intranasal 4 mg per spray repeated after 2 to 3 minutes, alongside airway and ventilatory support (BAP 2026; WHO). Because naloxone's half-life is shorter than that of many opioids, watch for re-narcotisation and re-dose as needed. Take-home naloxone (in India, the 0.4 mg/1 mL ampoule; the branded intranasal spray Nexnal where available) with family training in rescue breathing is recommended for anyone with current or recent opioid use, especially after a period of forced abstinence (post-detoxification, post-release from custody) when tolerance has fallen, the leading cause of death in opioid use disorder.

TRAP **Opioid withdrawal is not a medical emergency; opioid overdose is.** Opioid withdrawal is intensely unpleasant but rarely life-threatening; do not treat it as an emergency, and do not confuse it with overdose, which is the pinpoint-pupil respiratory failure that naloxone reverses.

GOOD TO REMEMBER

- **Naloxone:** competitive opioid antagonist and the antidote to opioid overdose (coma + respiratory depression + pinpoint pupils); give IM 0.4 to 2 mg, repeat every 2 to 3 minutes up to about 10 mg, or intranasal 4 mg per spray; short half-life means watch for re-narcotisation and re-dose; take-home naloxone is recommended for anyone with current or recent opioid use, especially in the fallen-tolerance windows after detoxification or custody.

10.9 Sedative-hypnotic withdrawal: the half-life-timed mimic

Why it hides. Withdrawal from benzodiazepines, barbiturates and other sedative-hypnotics closely resembles alcohol withdrawal, tremor, autonomic overactivity, seizures and its own delirium, and is genuinely life-threatening (Kaplan and Sadock 2024). The discriminator is *timing keyed to the agent's half-life*: short-acting agents (for example alprazolam, lorazepam) begin 12 to 24 hours after the last dose and peak at 24 to 72 hours, whereas long-acting agents (diazepam, clonazepam, phenobarbital) may not peak until **5 to 8 days** after the last dose. A patient who looks well for four days and then develops a withdrawal delirium is far more likely to be withdrawing from a long-acting sedative than from alcohol. Management is a controlled taper: substitute a long-acting benzodiazepine (or use a phenobarbital taper for mixed sedative dependence) and reduce slowly; abrupt cessation is the danger, and a too-fast benzodiazepine taper is itself a classic error.

INDIA

India carries a very large substance-use treatment gap: most people with alcohol or opioid dependence never reach formal care, and delirium tremens frequently presents to general and emergency wards after an unsupervised, abrupt stop rather than through a planned detoxification. Services concentrate in the government de-addiction centres and the Drug De-addiction Programme (DDAP) units, not in general practice, and the legal frame for the opioid emergencies here is the Narcotic Drugs and Psychotropic Substances (NDPS) Act, 1985 (the medico-legal detail is developed in the Mental health legislation and forensic psychiatry notes). Naloxone for overdose reversal is available as the 0.4 mg/1 mL ampoule and, increasingly, as take-home kits, and buprenorphine is the workhorse of Indian opioid-agonist treatment precisely because methadone is restricted to licensed OST clinics. The practical exam point: recognise delirium tremens early, because the Indian patient who self-detoxifies at home to save cost or avoid stigma is exactly the one who arrives at hour 60 in a full autonomic storm.

HOLD THIS

Delirium tremens is clouded consciousness plus disorientation plus an autonomic storm, 48 to 96 hours after the last drink, ~10 to 20 per cent mortality untreated; treat it as a medical emergency with parenteral benzodiazepine and supportive care, and give thiamine before glucose.

11 · Wernicke encephalopathy and Korsakoff syndrome

Chronic heavy drinking starves the brain of **thiamine** (vitamin B1), and thiamine is the cofactor two glucose-handling enzymes cannot work without. When it runs out, the diencephalon and brainstem fail acutely, producing **Wernicke encephalopathy**; if that acute failure is not reversed fast, the mammillary bodies and thalamus are permanently damaged and the patient is left with the chronic amnestic state called **Korsakoff syndrome**. Examiners treat this pair as a package because they are two ends of one thiamine-deficiency continuum, and because it carries the single most testable emergency rule in the whole substance-use block: **parenteral thiamine goes in before any glucose.**

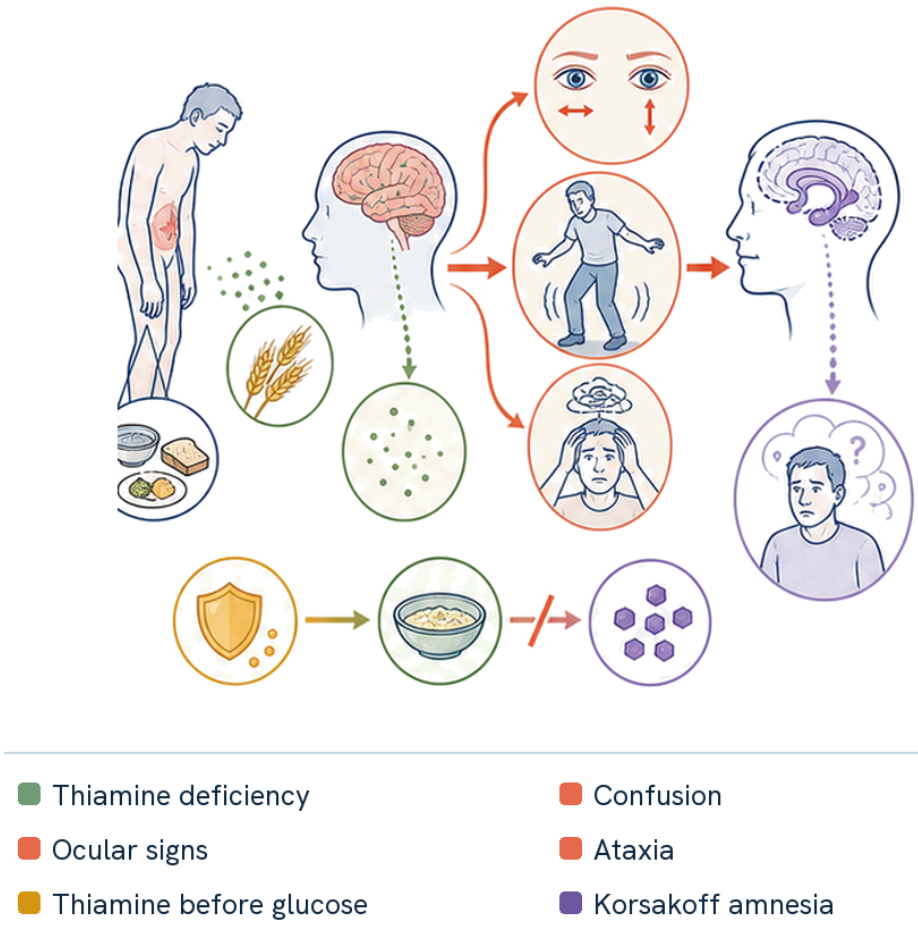


Fig 13.8 Thiamine deficiency can produce acute Wernicke encephalopathy with confusion, ocular abnormalities and ataxia. Immediate thiamine, before carbohydrate loading, reduces progression to persistent Korsakoff amnesia.

Why it matters clinically. Wernicke encephalopathy is an underdiagnosed medical emergency, the full triad is present in only about one patient in ten, and a single well-meant bag of intravenous dextrose given first can precipitate or worsen it. Get the two thiamine regimens (the small oral prophylaxis dose and the large parenteral treatment dose) and the glucose rule exact and you have the marks. The amnestic mechanism in the wider organic frame is developed in the Dementias and neurocognitive disorders notes and the Neuropsychiatry of systemic and neurological disease notes; here the task is to recognise the emergency and treat it by the number.

~10%	500	3 to 5	~50%
PRESENT WITH THE COMPLETE WERNICKE TRIAD	TREATMENT THIAMINE, IV MG, TWO TO THREE TIMES DAILY	DAYS OF PARENTERAL THIAMINE BEFORE SWITCHING TO ORAL	LEFT WITH PERMANENT KORSAKOFF AMNESIA

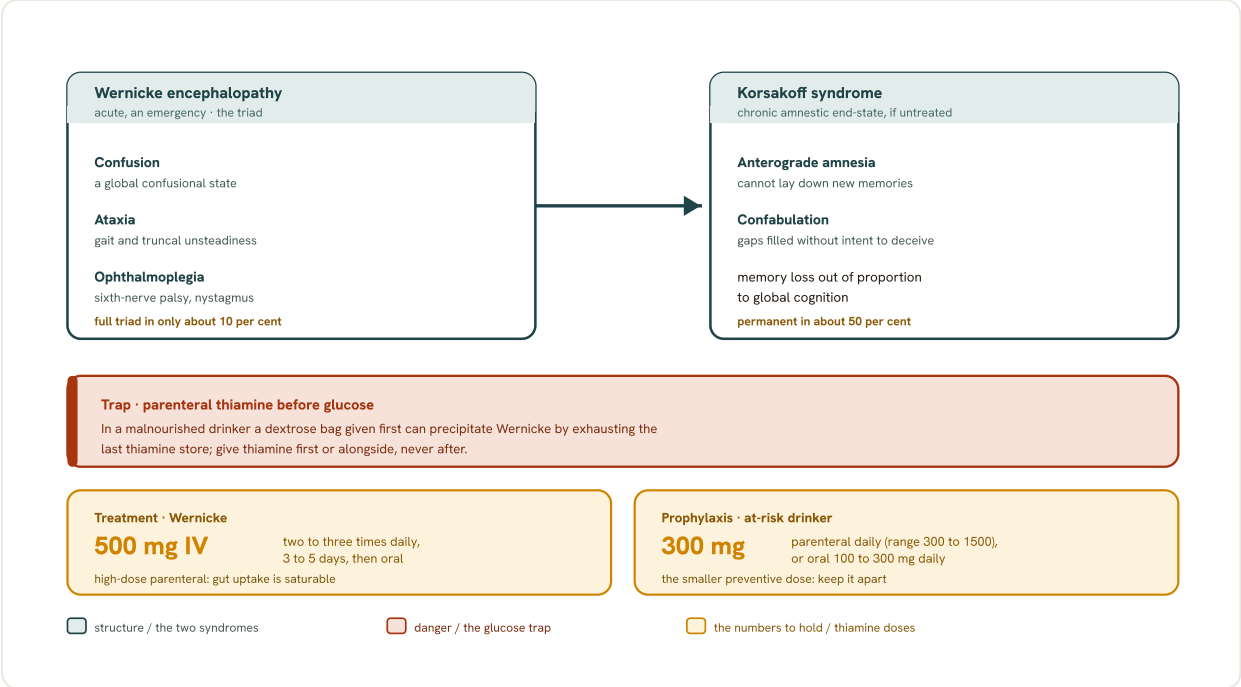


Fig 13.9 Wernicke encephalopathy to Korsakoff syndrome: the thiamine rule. The acute triad of confusion, ataxia and ophthalmoplegia is Wernicke, present in full in only about one patient in ten; untreated it fixes into Korsakoff, the chronic anterograde amnesia with confabulation. The non-negotiable rule is parenteral thiamine before any glucose in a malnourished drinker. Keep the two regimens apart: the large parenteral treatment dose (500 mg IV two to three times daily) versus the smaller preventive dose (300 mg parenteral, or 100 to 300 mg oral, daily).

11.1 The mechanism: why thiamine deficiency destroys the diencephalon

The cofactor that runs out. Thiamine (as thiamine pyrophosphate) is the essential cofactor for transketolase and for pyruvate and alpha-ketoglutarate dehydrogenase, so a deficient brain cannot run the pentose-phosphate shunt or oxidative glucose metabolism (Kaplan and Sadock 2024). The neurons that depend most heavily on this pathway, in the mammillary bodies, the medial thalamus, the periaqueductal grey and the cerebellar vermis, are the first to fail, which is exactly why the clinical picture is confusion, eye-movement palsy and ataxia rather than a diffuse global slowing.

Why some drinkers are more vulnerable. A genetically influenced **transketolase** abnormality lowers the enzyme's affinity for thiamine, so a subset of drinkers cross into deficiency at intakes others tolerate (Kaplan and Sadock 2024). Add the poor diet, malabsorption and vomiting of chronic alcohol use disorder and the marginal thiamine store empties quickly, especially under any metabolic stress.

11.2 Wernicke encephalopathy: the triad and why it is usually incomplete

The classic triad. Wernicke encephalopathy is defined by the triad of acute **confusion ataxia ophthalmoplegia**: a global confusional state, gait and truncal ataxia, and eye-movement signs, most characteristically a lateral rectus (sixth cranial nerve) palsy with nystagmus (Kaplan and Sadock 2024; Companion to Psychiatric Studies). The confusion tends to reverse fairly rapidly with vitamin supplementation, and the ophthalmoplegia is the sign that often responds first, sometimes within hours of parenteral thiamine.

Why waiting for the triad is a trap. The complete triad is present in only about **10 per cent** of cases (Indian Psychiatric Society CPG), so the diagnosis has to be made on any one of confusion, ophthalmoplegia or ataxia appearing in a malnourished or actively withdrawing drinker, not on the textbook three-together. This under-presentation is precisely why the condition is missed and why the treatment threshold is set so low.

RULE **Treat on suspicion, not on the full triad.** Any one of new confusion, ophthalmoplegia or ataxia in a malnourished or withdrawing drinker is enough to give parenteral thiamine immediately; the complete triad appears in only about one in ten.

GOOD TO REMEMBER

- **Wernicke encephalopathy:** the criterion picture is the triad of confusion, ataxia and ophthalmoplegia (a sixth-nerve palsy with nystagmus) driven by acute thiamine deficiency; the full triad is present in only about 10 per cent, so the discriminator is that any single element in a malnourished or withdrawing drinker is treated as the emergency; the first management step is immediate parenteral (not oral) thiamine, and it must precede any glucose.

11.3 Korsakoff syndrome: the chronic amnestic end-state

What it is. When Wernicke encephalopathy is untreated or undertreated, the acute lesion becomes fixed and the patient is left with Korsakoff syndrome, a chronic **amnestic** syndrome dominated by a dense *anterograde* amnesia (an inability to lay down new memories) with a variable retrograde component, in which the loss of recent memory is strikingly out of proportion to the overall level of cognitive impairment (Kaplan and Sadock 2024). Attention, procedural learning and general intellect can be relatively preserved, which is what makes the isolated memory failure so distinctive.

Confabulation, the signature sign. The classic accompaniment is **confabulation**: the patient fills the memory gap with fabricated or misplaced accounts, given without any intent to deceive and often without insight, so that a plausible but false narrative substitutes for the missing recollection. Confabulation is most prominent early and tends to fade as the syndrome settles, leaving the amnesia. Korsakoff syndrome is permanent, at least in partial form, in about **half** of those affected (Kaplan and Sadock 2024).

FEATURE	WERNICKE ENCEPHALOPATHY	KORSAKOFF SYNDROME
Tempo	**Acute, an emergency**	Chronic, an end-state
Core signs	Confusion, ataxia, ophthalmoplegia	**Anterograde amnesia with confabulation**
Lesion emphasis	Periaqueductal grey, medial thalamus, cerebellar vermis	Mammillary bodies, medial dorsal thalamus
Reversibility	**Often reversible with prompt parenteral thiamine**	Permanent in about 50 per cent
Management	High-dose parenteral thiamine as an emergency	Prolonged thiamine, supportive care, safeguarding

Wernicke and Korsakoff are two ends of one thiamine-deficiency continuum; the acute, treatable syndrome converts to the chronic amnestic one if thiamine is not replaced fast (Kaplan and Sadock 2024; Companion to Psychiatric Studies).

GOOD TO REMEMBER

- **Korsakoff syndrome:** the criterion feature is a chronic amnestic syndrome with dense anterograde amnesia and confabulation, the memory loss being out of proportion to global cognition; the discriminator from a global dementia is that recent memory fails selectively while other domains are relatively spared; it is the permanent sequel (in about 50 per cent) of untreated Wernicke encephalopathy, so the first step is prevention by treating Wernicke aggressively before the lesion fixes.

11.4 The glucose-first trap: the single most testable rule

The rule and its mechanism. In a malnourished or alcohol-dependent patient, **parenteral thiamine** must be given *before* any glucose load, because a carbohydrate load consumes the last of the marginal thiamine store as a cofactor and can precipitate or acutely worsen Wernicke encephalopathy (Indian Psychiatric Society CPG; Companion to Psychiatric Studies). The Companion frames it exactly this way: Wernicke can be precipitated on admission by the stress of withdrawal, an intercurrent illness, or *the first carbohydrate meal for some days*, which is why immediate parenteral thiamine is standard for any malnourished drinker.

Where it bites in practice. The trap is the collapsed or hypoglycaemic-looking drinker in whom the reflex is to hang intravenous dextrose. Give the thiamine first (or at least concurrently), never dextrose alone into an unreplenished drinker. This does not mean withholding glucose from a genuinely hypoglycaemic patient; it means the thiamine goes in alongside or ahead of it, not after.

TRAP **Never give glucose before thiamine in a malnourished drinker.** An intravenous dextrose bag given first can precipitate Wernicke encephalopathy by exhausting the residual thiamine; parenteral thiamine goes in first or alongside, never after.

11.5 Thiamine as treatment: the large parenteral emergency dose

The treatment regimen. Established or suspected Wernicke encephalopathy is a medical emergency treated with *high-dose parenteral* thiamine: about **500 mg** intravenously two to three times a day for 3 to 5 days, followed by a longer oral course (Kaplan and Sadock 2024; Indian Psychiatric Society CPG). The Indian CPG operationalises this as intravenous thiamine 500 mg three times daily for 2 to 3 days, then 250 mg daily intramuscularly or intravenously for a further 5 days. In UK practice the same is delivered as Pabrinex (a paired B-and-C ampoule preparation): two pairs of ampoules three times daily for 2 to 3 days, then one pair daily for a further 3 days, each ampoule diluted and infused over about 30 minutes with anaphylaxis facilities to hand (Companion to Psychiatric Studies).

Why parenteral and why high-dose. High-dose intravenous thiamine is superior to oral for both prevention and treatment because gut absorption of thiamine is limited and saturable, and high serum concentrations are needed to drive thiamine across the blood-brain barrier (Kaplan and Sadock 2024). Oral thiamine simply cannot achieve the brain levels an acute Wernicke lesion needs, which is the whole reason the emergency route is intravenous.

SETTING	ROUTE AND DOSE (THIAMINE)	DURATION
Established / suspected Wernicke (treatment)	**IV 500 mg two to three times daily**	3 to 5 days, then switch to oral
Indian CPG treatment schedule	IV 500 mg three times daily, then 250 mg daily IM/IV	2 to 3 days, then a further 5 days
Pabrinex treatment (UK)	2 pairs of ampoules three times daily, then 1 pair daily	2 to 3 days, then a further 3 days
At-risk drinker in withdrawal (prophylaxis)	Parenteral 300 mg daily (range 300 to 1500)	3 to 5 days, then oral
Low-risk ambulatory (prophylaxis)	Oral 100 to 300 mg daily	3 to 5 days; oral 100 mg daily to cover detoxification

The two thiamine regimens that must be kept apart: the large parenteral treatment dose for Wernicke, and the smaller prophylactic dose for the at-risk drinker (Kaplan and Sadock 2024; IPS CPG; BAP 2026; Companion to Psychiatric Studies). Units are in the header; cells carry bare numbers.

GOOD TO REMEMBER

- **Thiamine (treatment dose):** the cofactor whose deficiency causes the syndrome; for established or suspected Wernicke give it parenterally at about 500 mg IV two to three times daily for 3 to 5 days, then oral; parenteral and high-dose because gut absorption is saturable and high serum levels are needed to cross the blood-brain barrier; the one non-negotiable caution is to give it before any glucose.

11.6 Thiamine as prophylaxis: the smaller dose, and how it differs

The prophylaxis regimen. The dose given to *prevent* Wernicke in an at-risk but neurologically intact drinker is far smaller than the treatment dose. For a drinker in withdrawal with risk factors for Wernicke-Korsakoff, give parenteral thiamine (BAP quotes a wide 300 to 1500 mg/day band, in practice around 300 mg daily) for 3 to 5 days followed by oral thiamine; for those at very low risk in ambulatory settings, oral thiamine 100 to 300 mg daily for 3 to 5 days suffices (BAP 2026). The Indian CPG adds oral thiamine 100 mg daily continued for at least 3 months of any detoxification.

The examinable contrast. Keep the two doses and durations distinct: prophylaxis is a low dose (often oral, or modest parenteral) to stop the deficiency developing, whereas treatment is a large parenteral dose to reverse an established lesion. Confusing the two, giving a Wernicke patient only oral prophylactic thiamine, is a recognised cause of a preventable Korsakoff syndrome.

COMMON TRAP

Do not treat established Wernicke encephalopathy with the prophylactic dose. A confused, ataxic drinker needs the large parenteral treatment regimen (about 500 mg IV two to three times daily), not the 100 to 300 mg oral prophylaxis dose. Undertreating an acute lesion with a preventive dose lets it fix into a permanent Korsakoff amnesia.

11.7 Wernicke versus delirium tremens: the discrimination examiners love

Two confused drinkers, opposite treatments. Both Wernicke encephalopathy and delirium tremens present as an acutely confused drinker, but the discriminators and the treatments diverge. Delirium tremens is a hyperadrenergic withdrawal state (clouded consciousness, vivid visual and tactile hallucinations, coarse tremor and a gross autonomic storm) emerging 48 to 72 hours after the last drink, and its treatment is generously titrated benzodiazepine. Wernicke is a thiamine-deficiency state whose hallmark is the eye-movement palsy and ataxia rather than an autonomic storm, and its treatment is high-dose parenteral thiamine. The two frequently coexist, so the safe posture is to give thiamine to every confused or withdrawing drinker regardless, and to add benzodiazepine for the withdrawal component.

DISCRIMINATOR	WERNICKE ENCEPHALOPATHY	DELIRIUM TREMENS
Driver	Thiamine deficiency	Alcohol withdrawal (hyperadrenergic)
Timing	Any time in a malnourished drinker	**48 to 72 hours after the last drink**
Signature sign	**Ophthalmoplegia and ataxia**	Autonomic storm, vivid hallucinations
First treatment	**Parenteral thiamine**	**Titrated benzodiazepine**

Wernicke and delirium tremens can coexist; the safe rule is thiamine for every confused drinker plus benzodiazepine for the withdrawal (Kaplan and Sadock 2024; IPS CPG). The wider withdrawal spectrum sits in the alcohol-withdrawal topic.

WORKED EXAMPLE

A dishevelled man is brought to casualty drowsy and unsteady, smelling of alcohol, with a bruise over the occiput. The intern draws up intravenous dextrose for a presumed hypoglycaemia. The correct sequence is to give parenteral thiamine first (or alongside), because dextrose alone into a malnourished drinker can precipitate Wernicke encephalopathy; to examine the eyes for nystagmus and a lateral rectus palsy and the gait for ataxia; and, because of the head injury, to image the brain rather than attribute the confusion to alcohol alone. Confusion in a drinker is never assumed to be simple intoxication.

11.8 The Indian context: malnutrition, the treatment gap and where the vitamin gets missed

Why the syndrome is common and the diagnosis is missed. India carries a large burden of alcohol use disorder against a background of frequent baseline malnutrition, and the vast substance-use *treatment gap* means most dependent drinkers reach services late, malnourished, and often only when acutely unwell, exactly the profile in which Wernicke is precipitated. Detoxification happens across a patchwork of government de-addiction centres (the national Drug De-addiction Programme), the day care centre model, medical college psychiatry units and private facilities, and thiamine is the cheap, universally available intervention that most reliably prevents a lifelong Korsakoff disability.

The practical Indian rule. The Indian Psychiatric Society CPG makes parenteral thiamine standard for all suspected or high-risk Wernicke-Korsakoff cases and continues oral thiamine 100

to 200 mg for at least three months across all detoxification, with the same glucose-first caution. In a resource-limited casualty the highest-yield habit is simple: give thiamine before the dextrose, to every malnourished drinker, every time.

INDIA

Thiamine is one of the highest-value, lowest-cost interventions in Indian addiction practice: injectable and oral thiamine are inexpensive and universally stocked, whereas an established Korsakoff syndrome is an untreatable, lifelong disability. Against a wide treatment gap and a malnourished, late-presenting population, a standing casualty protocol of parenteral thiamine before glucose for every dependent drinker prevents far more disability than any anti-craving agent. The medico-legal and NDPS-Act frame for substance use sits in the Mental health legislation and forensic psychiatry notes.

HOLD THIS

In a malnourished drinker, parenteral thiamine goes in before any glucose; the acute triad of confusion, ataxia and ophthalmoplegia is Wernicke (full triad in only ~10 per cent, treat on any one sign with high-dose IV thiamine), and untreated it fixes into Korsakoff, the chronic anterograde amnesia with confabulation.

12 · Alcoholic hallucinosis and alcohol-induced psychosis

A chronic drinker who hears voices is one of the most misread presentations in the substance-use viva, because the same complaint sits astride three very different diagnoses. **Why it matters clinically.** The examiner wants you to separate **alcoholic hallucinosis** (persistent **auditory hallucinations** in a fully **clear sensorium**) from the clouded, autonomically stormy picture of delirium tremens, and to separate both from schizophrenia. Get that triangulation right and you have the highest-yield discrimination of the whole psychosis-substance interface; get it wrong and you either treat a self-limiting organic psychosis as schizophrenia for life, or miss a lethal delirium behind a "chronic drinker with voices".

This is a clinical (diagnosis and discrimination) topic. The wider substance-induced psychotic-disorder frame and the psychosis boundary are cross-referenced to the Other psychotic disorders, delusional syndromes and catatonia notes and are not re-derived here; the reward-pathway mechanics sit in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the amnestic Wernicke-Korsakoff mechanism sits in the Dementias and neurocognitive disorders notes and the Neuropsychiatry of systemic and neurological disease notes. Here the task is to define the two named syndromes precisely, place them against their look-alikes, and know the management principle.

12.1 Alcoholic hallucinosis: the criterion definition

The definition. Alcoholic hallucinosis is the occurrence of hallucinations, characteristically **auditory**, in a **clear sensorium** in a person with a history of heavy drinking and alcohol dependence, usually following a prolonged drinking bout, in partial or complete abstinence (Kaplan and Sadock 2024; Shorter Oxford Textbook of Psychiatry). The term was coined by

Eugene Bleuler. The three load-bearing words are *auditory*, *clear sensorium* and *abstinence-related*: the voices are typically third-person, accusatory or threatening, and the patient is distressed, anxious and restless but fully alert and oriented.

The signature. Unlike the transient perceptual disturbances of simple withdrawal, alcoholic hallucinosis persists after the acute withdrawal syndrome is over and can continue for weeks; classically recovery occurs within one month and it is very rarely prolonged beyond six months. It is uncommon, occurring in roughly 2 per cent of dependent drinkers, and in the modern nosologies it is subsumed under alcohol-induced psychotic disorder, coded F10.5 in ICD-10 and 6C40.60 (with hallucinations) in ICD-11.

GOOD TO REMEMBER

- **Alcoholic hallucinosis:** the criterion picture is persistent, usually third-person accusatory or threatening *auditory* hallucinations arising in a *clear sensorium* in a dependent drinker, typically during abstinence after a heavy bout; the discriminator from delirium tremens is the intact sensorium and the discriminator from schizophrenia is the clear temporal link to alcohol and the good prognosis on abstinence; the first management step is abstinence plus an antipsychotic (haloperidol) with a benzodiazepine, and it usually resolves within one month.

12.2 The three-way discrimination: hallucinosis vs delirium tremens vs schizophrenia

The core carrier. This table is the topic. The single axis that separates alcoholic hallucinosis from delirium tremens is the state of the **sensorium**: hallucinosis occurs in a clear sensorium, delirium tremens in a clouded one. The axis that separates hallucinosis from schizophrenia is the *course* and the *temporal relation to alcohol*: hallucinosis clears on abstinence and leaves no primary thought disorder or enduring negative symptoms.

FEATURE	ALCOHOLIC HALLUCINOSIS	DELIRIUM TREMENS	SCHIZOPHRENIA
Sensorium	**Clear, fully oriented**	**Clouded, disoriented**	Clear
Dominant hallucination	**Auditory (voices, third-person, accusatory)**	Visual and tactile, vivid, frightening	Auditory (often running commentary, thought echo)
Autonomic storm	Absent or mild	**Gross (tachycardia, fever, sweating, hypertension)**	Absent
Onset relative to alcohol	During or after abstinence; persists beyond withdrawal	48 to 72 hours after the last drink	No consistent temporal link to alcohol
Course	**Resolves on abstinence, usually within one month**	Short, 3 to 5 days; medical emergency	Chronic, over 6 months; enduring negative symptoms
First-rank / thought disorder	Usually absent; insight often partly retained	Not the picture (this is a delirium)	May be present; formal thought disorder

FEATURE	ALCOHOLIC HALLUCINOSIS	DELIRIUM TREMENS	SCHIZOPHRENIA
Mortality	Low	**1 to 5 per cent even treated; higher untreated**	Not directly lethal

The three-way discrimination; the sensorium separates hallucinosis from delirium tremens, and the course plus the temporal link to alcohol separates hallucinosis from schizophrenia (Kaplan and Sadock 2024; Shorter Oxford Textbook of Psychiatry; AIIMS Clinical Methods in Psychiatry 2024).

RULE **Check the sensorium first.** Voices plus a clear, oriented sensorium in a drinker points to alcoholic hallucinosis; voices plus clouding and an autonomic storm points to delirium tremens, a medical emergency, no matter how "psychotic" the surface looks.

2%	**1 month**	**3%**
OF DEPENDENT DRINKERS DEVELOP ALCOHOLIC HALLUCINOSIS	TYPICAL TIME TO RESOLUTION ON ABSTINENCE	OF AUD DEVELOP AN ALCOHOL-INDUCED PSYCHOTIC DISORDER

12.3 Alcohol-induced psychotic disorder: the modern umbrella diagnosis

What it is. The alcohol-induced psychotic disorder (ICD-11 6C40.6; DSM-5-TR substance/medication-induced psychotic disorder) is the umbrella under which alcoholic hallucinosis now sits. About 3 per cent of people with an alcohol use disorder experience it: auditory hallucinations and/or paranoid delusions arising in a clear sensorium in the context of heavy drinking or withdrawal (Kaplan and Sadock 2024). ICD-11 lets you specify the presentation: 6C40.60 with hallucinations (the classic hallucinosis), 6C40.61 with delusions, and 6C40.62 with mixed psychotic symptoms.

The essential features. The diagnosis requires that the psychotic symptoms develop during or soon after alcohol intoxication or withdrawal; that alcohol is capable of producing such symptoms; that the symptoms are not better explained by an independent psychotic disorder such as schizophrenia; and that they are not confined to a delirium (ICD-11 CDDR; DSM-5-TR). Symptoms occurring exclusively during a delirium are coded as alcohol-induced delirium (6C40.5), not as a psychotic disorder, which is exactly why the sensorium check in 12.2 is the pivot of the whole topic.

GOOD TO REMEMBER

- **Alcohol-induced psychotic disorder:** the criterion is hallucinations and/or delusions in a clear sensorium developing during or soon after heavy drinking or withdrawal, judged the direct consequence of alcohol and not better explained by a primary psychotic disorder or confined to a delirium (ICD-11 6C40.6; DSM-5-TR); the specifiers are with hallucinations, with delusions and mixed; the first step is to establish the temporal link to alcohol and to reassess longitudinally on abstinence.

12.4 Alcoholic paranoia (the alcohol-paranoid state): morbid jealousy

The delusional cousin. Alongside the hallucinatory picture sits the alcohol-paranoid state (alcoholic paranoia), classically dominated by **delusional jealousy**, the fixed false belief that the spouse is unfaithful (the Othello theme). It develops in chronic dependent drinkers, in a clear

sensorium, and maps onto the "with delusions" specifier (ICD-11 6C40.61). It matters out of proportion to its frequency because morbid jealousy is a recognised risk factor for serious partner violence and homicide, so its detection carries a real-world safety weight.

How to place it. Delusional jealousy is not specific to alcohol: it also occurs in schizophrenia, in affective psychosis and in organic states. The alcohol attribution rests on the temporal link to heavy drinking and, as with hallucinosis, on whether it clears with abstinence. The fuller frame for delusional jealousy as a delusional syndrome belongs to the Other psychotic disorders, delusional syndromes and catatonia notes.

COMMON TRAP

Do not diagnose schizophrenia at the first assessment of a drinker with a clear-sensorium psychosis. Substance-induced psychosis and a primary psychotic disorder are hard to separate cross-sectionally; the anchor is the longitudinal course. Psychotic symptoms that *preceded* the drinking, that recur off alcohol, or that persist for one month or longer after intoxication and withdrawal have resolved point to an independent primary psychotic disorder rather than an alcohol-induced one (ICD-11 CDDR; DSM-5-TR). In one first-episode cohort about a third (35.6 per cent) of substance-induced psychosis diagnoses were later revised to a primary schizophrenia-spectrum or bipolar disorder, so the initial label is provisional and demands review.

12.5 Prognosis, diagnostic instability and the schizophrenia boundary

The prognosis. The prognosis of a genuinely alcohol-induced psychosis is good if abstinence is achieved: the picture typically clears spontaneously within a few days to a month of abstinence, and it is estimated that fewer than 5 per cent of these psychoses occur in individuals who later develop schizophrenia (Kaplan and Sadock 2024). This is the reassuring counterweight to the trap above: most true alcoholic hallucinosis is not incipient schizophrenia.

The boundary in one line. Duration is the arbiter. Clearance on abstinence within a month supports the alcohol-induced diagnosis; persistence beyond a month off alcohol, or a positive history predating the drinking, moves the diagnosis toward a primary psychotic disorder. The wider schizophrenia and delusional-disorder frame is developed in the Other psychotic disorders, delusional syndromes and catatonia notes.

HOLD THIS

Auditory hallucinations in a clear sensorium in a dependent drinker = alcoholic hallucinosis; they clear on abstinence (usually within one month), and persistence beyond a month off alcohol re-opens the schizophrenia question.

12.6 Management: abstinence, an antipsychotic and a benzodiazepine

The management principle. The foundation is abstinence: because the disorder is alcohol-induced, removing the offending agent is itself the definitive treatment, and the psychosis typically remits after abstinence. Symptomatic control while it settles uses an antipsychotic, classically haloperidol, which reduces the intensity of the delusions and hallucinations, together with a benzodiazepine (for example chlordiazepoxide or diazepam) to cover any concurrent

withdrawal and agitation; admission is usually necessary, the environment should be safe, uncluttered and uniformly lit, and parenteral thiamine plus attention to electrolytes and glucose is given (Companion to Psychiatric Studies). Antipsychotic treatment is escalated where there is severe agitation or suicidal or homicidal ideation (Kaplan and Sadock 2024).

Dosing anchor. Haloperidol is the standard agent for the psychotic symptoms; the concurrent benzodiazepine is dosed and tapered exactly as for alcohol withdrawal (the Companion example commences chlordiazepoxide at 100 to 150 mg/day or diazepam at 50 to 80 mg/day, reducing after the second or third day and stopping within one to two weeks). The full withdrawal-dosing detail sits in the alcohol withdrawal topic and is not re-derived here.

GOOD TO REMEMBER

- **Haloperidol (in alcohol-induced psychosis):** high-potency dopamine antagonist used to reduce the intensity of the hallucinations and delusions while abstinence does the definitive work; give with a benzodiazepine to cover concurrent withdrawal, never a benzodiazepine or antipsychotic alone for the whole picture; escalate for severe agitation or suicidal or homicidal ideation.
- **Chlordiazepoxide / diazepam (adjunct here):** long-acting benzodiazepine covering concurrent withdrawal and agitation; representative start chlordiazepoxide 100 to 150 mg/day or diazepam 50 to 80 mg/day, reducing from the second or third day and stopping within one to two weeks (Companion to Psychiatric Studies).

INDIA

Alcohol-induced psychoses present overwhelmingly to India's de-addiction system, the network of de-addiction centres and the Drug De-addiction Programme (DDAP) that anchor tertiary substance-use care, yet the national treatment gap for alcohol use disorders is very large, so most drinkers with a psychosis reach services late, often through the general hospital or a family-brought emergency. The Indian Psychiatric Society substance-use CPGs frame both the acute management and the strategic shift toward community and home-based delivery using trained non-specialist health workers to close that gap. The de-addiction context also carries the medico-legal frame of the NDPS Act, 1985; the Act, capacity and medico-legal aspects belong to the Mental health legislation and forensic psychiatry notes.

WORKED EXAMPLE

A 46-year-old man with 20 years of daily heavy drinking is brought in five days after his last drink, having stopped because of gastritis. He is fully alert and oriented, knows the date and the ward, and there is no tremor or autonomic disturbance, but he reports two male voices discussing him in the third person and calling him a thief, which frighten him and have been present for four days. Sensorium clear, no clouding: this is alcoholic hallucinosis, not delirium tremens (which would show clouding and an autonomic storm and would have peaked at 48 to 72 hours, not persisted clear on day five). You maintain abstinence, start haloperidol for the voices with a benzodiazepine to cover any residual withdrawal, give parenteral thiamine, and plan longitudinal review, expecting resolution within a month; if the voices persist beyond a month off alcohol you reconsider a primary psychotic disorder.

13 · Medical complications of alcohol use

Chronic heavy drinking is a whole-body disease, not just a psychiatric one, and the **medical complications of alcohol** are what actually kill most dependent drinkers. Ethanol and its metabolite acetaldehyde injure the liver, the peripheral and central nervous system, the heart, the gut and the marrow, so a single patient can carry a fatty liver, a numb-footed neuropathy, an enlarged heart and a macrocytic anaemia at once. Examiners test this as a systems checklist: they want you to name the organ, name the lesion, and know which lesions reverse with abstinence and which are terminal.

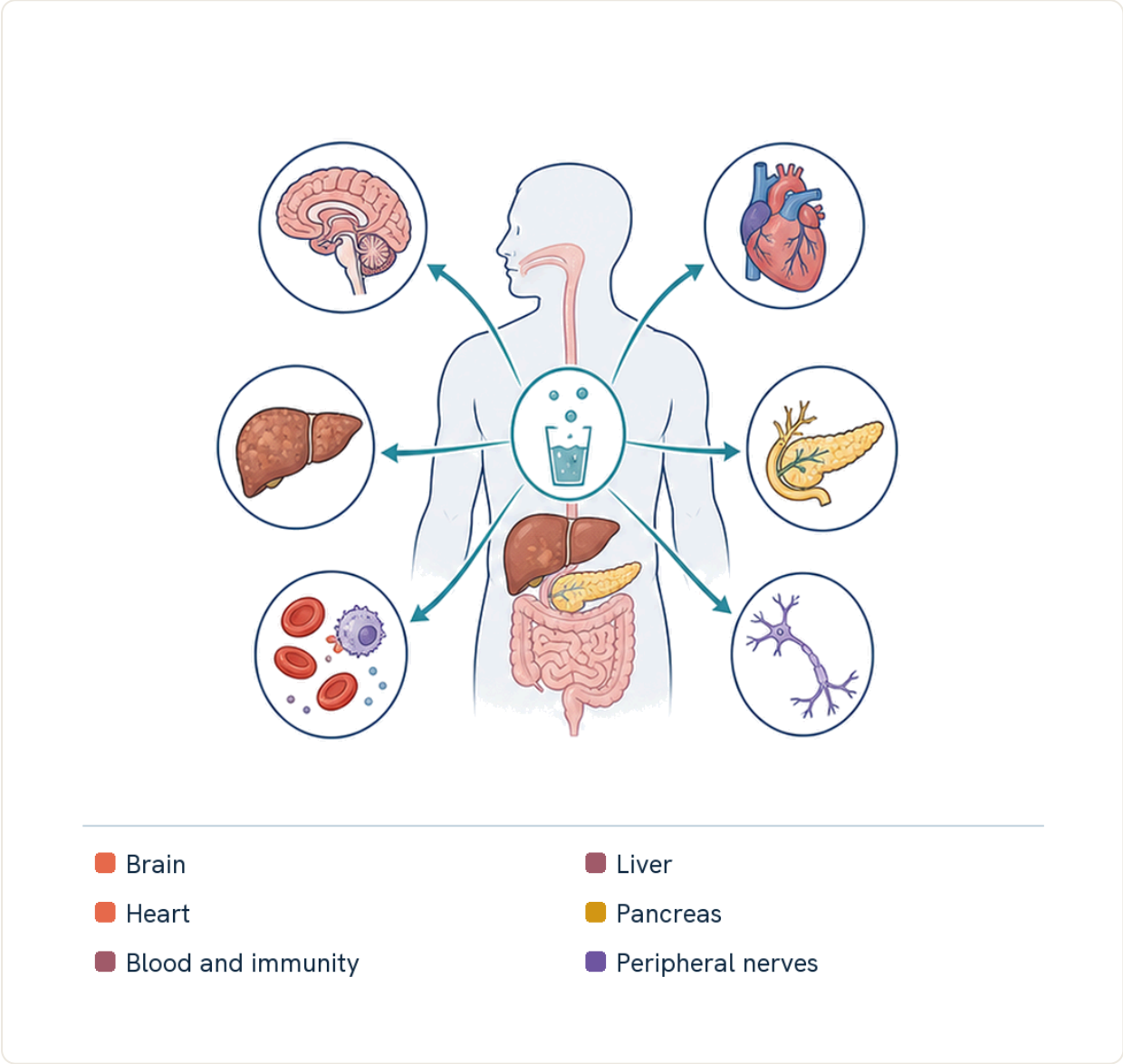


Fig 13.10 Alcohol-related harm is multisystemic, affecting the brain, liver, heart, pancreas, blood and immune function, and peripheral nerves in addition to its behavioural and social consequences.

Why it matters clinically. Recognising the physical sequelae changes management at the bedside, because the confused drinker may be encephalopathic rather than simply intoxicated, the anaemia may be a marrow effect rather than blood loss, and the raised **GGT** and **MCV** are the biochemical fingerprints that betray covert heavy drinking. The reward-pathway mechanics that drive the drinking sit in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic

Psychopharmacology notes; here the task is the somatic damage the drinking leaves behind, organ by organ.

>30	>100	~50%
ETHANOL G PER 24 HOURS IN MEN THAT RAISES HYPERTENSION RISK	MCV FEMTOLITRES DEFINING MACROCYTOSIS IN HEAVY DRINKERS	OF CHRONIC DRINKERS DEVELOP ALCOHOLIC MYOPATHY

13.1 The overall map: which organs, and what reverses

The systems affected. Cluster the complications by organ so the list is retrievable in an exam: *hepatic* (fatty liver, alcoholic hepatitis, cirrhosis), *neurological* (peripheral neuropathy, cerebellar degeneration, central pontine myelinolysis, Marchiafava-Bignami disease, and the Wernicke-Korsakoff pair), *cardiac* (dilated cardiomyopathy, atrial fibrillation, hypertension), *gastrointestinal* (gastritis, pancreatitis, variceal bleeding) and *haematological* (macrocytosis, thrombocytopenia) (Goodman and Gilman). The Wernicke-Korsakoff amnestic syndrome is the one neurological complication given its own topic, so it is only signposted here.

The reversibility rule that organises the whole list. Fatty liver and acute alcoholic hepatitis are usually reversible with abstinence, whereas cirrhosis is largely fixed and usually terminal without transplant (Goodman and Gilman). The same early-reversible, late-fixed logic runs through the other systems, which is why abstinence is itself the single most powerful treatment for almost every complication on the list.

RULE **Abstinence is the first-line treatment for the complication, not just the addiction.** Fatty liver, hepatitis, cardiomyopathy, neuropathy and marrow changes all improve or stabilise on stopping alcohol; the drug you reach for treats the organ, but the alcohol is the poison you must remove.

13.2 Hepatic complications: the fatty liver to cirrhosis sequence

The three stages. Alcohol perturbs hepatic lipid metabolism, and because ethanol and acetaldehyde metabolism generates excess NADH that inhibits fat oxidation, fat accumulates in the liver within a few days as fatty liver (steatosis) (Goodman and Gilman). A subset progress to alcoholic hepatitis, an inflammatory injury with hepatocyte necrosis, and repeated necrosis with chronic inflammation drives the fibrosis that becomes cirrhosis. Only a minority of drinkers with fatty liver ever reach cirrhosis, but cirrhosis is the end-stage that defines **alcohol-related liver disease**.

The sequelae of cirrhosis. Once the liver is cirrhotic, portal hypertension produces oesophageal **varices** that can bleed catastrophically, ascites, splenomegaly with hypersplenism, and hepatic encephalopathy; synthetic failure gives coagulopathy and hypoalbuminaemia, and there is a raised risk of hepatocellular carcinoma. Testicular atrophy and gynaecomastia follow from disordered sex-steroid handling. Cirrhosis is largely irreversible and usually terminal without a liver transplant (Goodman and Gilman).

GOOD TO REMEMBER

- **Alcoholic cirrhosis:** the criterion lesion is diffuse hepatic fibrosis with regenerative nodules ending the fatty-liver to hepatitis to cirrhosis sequence; the discriminator from the earlier stages is that fatty liver and hepatitis reverse with abstinence while cirrhosis does not; its high-yield sequelae are portal hypertension with bleeding varices, ascites, encephalopathy and hepatocellular carcinoma, and the first management step is complete abstinence, with transplant assessment for end-stage disease.

TRAP **A cirrhotic drinker cannot metabolise the usual detox drugs.** In hepatic impairment switch from long-acting chlordiazepoxide to a benzodiazepine needing minimal hepatic metabolism such as lorazepam, and prefer acamprosate or baclofen over naltrexone for relapse prevention (NICE 2011; IPS 2014).

13.3 Neurological complications: neuropathy and cerebellar degeneration

Peripheral neuropathy. A symmetrical, length-dependent sensorimotor peripheral neuropathy is one of the commonest neurological complications of chronic drinking, driven by direct ethanol toxicity compounded by thiamine and other B-vitamin deficiency. It presents with distal, glove-and-stocking numbness, burning dysaesthesia and reduced ankle reflexes, worst in the feet, and it is a mixed toxic-nutritional picture rather than a pure deficiency state, which is why B-vitamin replacement helps but abstinence matters most.

Cerebellar degeneration. Cerebellar degeneration from chronic alcohol targets the anterior superior vermis, producing a broad-based, unsteady gait and truncal ataxia with the legs affected far more than the arms or speech (Shorter Oxford). It is distinct from the acute cerebellar signs of Wernicke encephalopathy: this is a slowly evolving, largely fixed atrophy rather than an acute, thiamine-responsive lesion, though the two share a nutritional contribution.

GOOD TO REMEMBER

- **Alcoholic cerebellar degeneration:** the criterion feature is a chronic, broad-based gait ataxia with the legs affected out of proportion to arms and speech, from anterior-vermis atrophy; the discriminator from Wernicke is that it is slow-onset and largely fixed rather than acute and thiamine-responsive; the first step is abstinence plus B-vitamin replacement, with no dramatic reversal expected.

13.4 Neurological complications: the two demyelinating eponyms

Central pontine myelinolysis. Central pontine myelinolysis is a demyelinating lesion of the central pons that classically follows the *too-rapid correction of hyponatraemia* in a malnourished drinker, producing a rapidly evolving quadriparesis, pseudobulbar palsy, dysarthria and, in severe cases, a locked-in state (Shorter Oxford; Kaplan and Sadock 2024). The high-yield point is preventive: correct sodium slowly in the alcohol-dependent, chronically hyponatraemic patient, because it is the speed of correction, not the alcohol alone, that triggers the lesion.

Marchiafava-Bignami disease. Marchiafava-Bignami disease is a rare disorder of widespread demyelination and necrosis of the *corpus callosum* (with optic tracts and cerebellar peduncles), presenting with disorientation, seizures, ataxia, dysarthria, hallucinations, spastic limb paralysis

and a progressive dementia with personality change, and is attributed to alcohol-related nutritional deficiency (Shorter Oxford). The callosal signature is what makes it examinable, even though it is genuinely uncommon.

SYNDROME	LESION SITE	SIGNATURE CLUE
Peripheral neuropathy	Distal peripheral nerves	Glove-and-stocking sensory loss, absent ankle jerks
Cerebellar degeneration	**Anterior superior vermis**	Gait ataxia, legs > arms and speech
Central pontine myelinolysis	**Central pons**	Follows rapid correction of hyponatraemia; quadriparesis
Marchiafava-Bignami disease	**Corpus callosum**	Callosal demyelination, dementia with seizures
Wernicke-Korsakoff	Mammillary bodies, medial thalamus	Confusion, ophthalmoplegia, ataxia; then amnesia (own topic)

The neurological complications sorted by lesion site; matching the eponym to the site is the classic exam manoeuvre (Shorter Oxford; Kaplan and Sadock 2024).

GOOD TO REMEMBER

- **Marchiafava-Bignami disease:** the criterion lesion is demyelination and necrosis of the corpus callosum in a chronic malnourished drinker; the discriminator is the callosal signature with disconnection features, seizures and progressive dementia; management is nutritional replacement and abstinence, with a variable and often poor outcome.

13.5 Cardiac complications: cardiomyopathy, arrhythmia and hypertension

Dilated cardiomyopathy. Alcoholic cardiomyopathy is an acquired form of dilated cardiomyopathy from long-term heavy drinking, with a dilated left ventricle, increased mass, thin or normal wall, and a reduced ejection fraction in advanced disease, driven by oxidative stress, mitochondrial dysfunction and impaired contractile-protein handling (Goodman and Gilman). It presents as heart failure, and early disease can improve with sustained abstinence.

Arrhythmia and hypertension. Atrial fibrillation is the commonest alcohol-related **arrhythmia** and is characteristically precipitated by binge drinking, the pattern clinicians label holiday-heart syndrome, and it carries a stroke risk (Goodman and Gilman). Chronic heavy intake also raises blood pressure: risk climbs above roughly **30 g ethanol per day** in men and **20 g per day** in women, so alcohol is a genuinely reversible cause of hypertension worth asking about in any hypertensive patient (Goodman and Gilman).

GOOD TO REMEMBER

- **Alcoholic cardiomyopathy:** the criterion picture is an acquired dilated cardiomyopathy with a dilated, poorly contracting left ventricle and reduced ejection fraction from chronic heavy drinking; the discriminator is the alcohol history in a dilated heart with no other cause; binge-related atrial fibrillation (holiday heart) and reversible hypertension complete the cardiac triad, and the first management step is abstinence, which can reverse early disease.

13.6 Gastrointestinal complications: gastritis, pancreatitis and variceal bleeding

Upper-gut mucosal injury. Ethanol directly damages the oesophageal and gastric mucosa, lowers oesophageal sphincter pressure and alters acid secretion, producing reflux, peptic ulceration and acute or chronic **gastritis** (Goodman and Gilman). In an established cirrhotic the more dangerous upper-gut event is variceal bleeding from portal hypertension, a life-threatening haematemesis that is a downstream sequela of the liver disease rather than a primary mucosal lesion.

Pancreatitis. Heavy alcohol use is the commonest cause of both acute and chronic pancreatitis (Goodman and Gilman). Acute alcoholic pancreatitis presents with abrupt severe abdominal pain, vomiting and raised serum or urine pancreatic enzymes and is managed with fluids, analgesia and supportive care; recurrent attacks drive the progressive acinar destruction and fibrosis of chronic pancreatitis, mirroring the cirrhotic sequence in the liver and leaving exocrine and endocrine (diabetic) failure.

GOOD TO REMEMBER

- **Alcoholic pancreatitis:** the criterion picture is acute severe epigastric pain with vomiting and raised amylase or lipase, alcohol being the commonest cause of both acute and chronic disease; the discriminator for the chronic form is the recurrent-attacks-to-fibrosis course leaving exocrine insufficiency and secondary diabetes; management is supportive for the acute attack and abstinence to halt progression.

13.7 Haematological complications and the biochemical fingerprints of heavy drinking

The marrow effects. The two **haematological** hallmarks are macrocytosis (a raised MCV above about **100 fL**) and thrombocytopenia. Macrocytosis arises from a direct toxic effect of alcohol on developing red cells, compounded by folate deficiency, and it is a slow-turnover marker that stays raised for weeks after drinking stops. Alcohol-induced thrombocytopenia reflects direct marrow suppression plus, in cirrhotics, splenic sequestration, and it typically recovers within days to a couple of weeks of abstinence (Goodman and Gilman; Silczuk and Habrat 2020).

The biomarkers examiners want. A raised GGT (gamma-glutamyl transferase) and a raised MCV are the two classic laboratory pointers to covert heavy drinking, and combining them, ideally with carbohydrate-deficient transferrin where available, raises sensitivity (IPS 2014). The Indian CPG operationalises monitoring as baseline and three-monthly AST, ALT, GGT, MCV and full blood count, so GGT and MCV double as screening flags and as relapse-monitoring tools across treatment.

HOLD THIS

Fatty liver and alcoholic hepatitis reverse with abstinence; cirrhosis does not and is usually terminal without transplant. That single reversibility line organises the entire complication list.

INDIA

India carries a heavy and rising alcohol burden against a background of frequent baseline malnutrition, so complicated presentations (advanced cirrhosis, florid neuropathy, Wernicke) reach services late because of the large substance-use *treatment gap*. Care is delivered across government de-addiction centres under the national Drug De-addiction Programme, medical-college psychiatry units, the day care centre model and private facilities, framed by the NDPS Act and the Mental Healthcare Act. In this resource-limited setting GGT and MCV are cheap, widely available biomarkers, and universal thiamine plus abstinence-oriented care are the highest-yield, lowest-cost interventions; the NDPS and medico-legal frame is developed in the Mental health legislation and forensic psychiatry notes.

PEARL

Use the labs as a lie-detector for covert drinking: a macrocytosis with a raised GGT, in the absence of another cause, points to sustained heavy alcohol use even when the patient minimises intake. MCV falls slowly (weeks) and GGT faster (days to weeks) with abstinence, so tracking both across follow-up distinguishes genuine abstinence from ongoing relapse.

WORKED EXAMPLE

A 45-year-old man presents with ankle swelling, breathlessness and a distended abdomen. Examination shows spider naevi, gynaecomastia, ascites and pitting oedema; bloods show a macrocytosis, thrombocytopenia and a raised GGT with a low albumin. The picture is decompensated alcoholic cirrhosis with portal hypertension, and the immediate risks are variceal bleeding and hepatic encephalopathy. Management is complete abstinence, cautious use of hepatically-cleared drugs (lorazepam rather than chlordiazepoxide for any withdrawal, acamprosate or baclofen rather than naltrexone for relapse prevention), parenteral thiamine, and referral for transplant assessment, because the cirrhosis itself will not reverse.

14 · Fetal alcohol spectrum disorder

Alcohol is the commonest human teratogen, and the injury it does to the developing brain is entirely preventable, which is exactly why the **fetal alcohol** question recurs in the substance-use viva. **Why it matters clinically.** The examiner is not asking you to run a dysmorphology clinic; the point is that a drinker in front of you may be pregnant, that there is *no* established safe threshold of maternal alcohol, and that the classic phenotype is a triad you must be able to recite. Get the three cardinal facial features, the growth deficiency and the neurodevelopmental core right and you have the whole low-tier topic.

This is a clinical (recognition and definition) topic, kept deliberately brief. **Fetal alcohol spectrum disorder** (**fasd**) is the umbrella term; **fetal alcohol** syndrome is its most severe, fully expressed form. The wider perinatal frame, alcohol screening in the antenatal clinic, the management of maternal withdrawal in pregnancy and substance use in pregnancy generally are cross-referenced to the Perinatal/women's mental health and emergency psychiatry notes and are

not re-derived here; the Wernicke amnestic mechanism sits in the Dementias and neurocognitive disorders notes and the Neuropsychiatry of systemic and neurological disease notes.

14.1 The spectrum and the classic triad

The umbrella. Fetal alcohol spectrum disorder (FASD) is the collective term for the physical, behavioural and cognitive effects of prenatal alcohol exposure; the reported United States prevalence is between **1.1 and 5.0 per cent** (Kaplan and Sadock 2024). The full-blown severe end is fetal alcohol syndrome (FAS), first delineated by Jones and Smith in 1973. The mnemonic anchor for FAS is the *triad*: a characteristic pattern of **facial dysmorphism**, pre- or postnatal **growth deficiency**, and central-nervous-system involvement (deficient brain growth with neurodevelopmental impairment), on a background of prenatal ethanol exposure (Goodman and Gilman; Companion to Psychiatric Studies).

The subdiagnoses. Under the FASD umbrella sit five conditions (Hoyme criteria): FAS, partial FAS (PFAS), alcohol-related neurodevelopmental disorder (ARND), alcohol-related birth defects (ARBD, primarily physical), and neurobehavioral disorder associated with prenatal alcohol exposure (ND-PAE). ND-PAE is the DSM-5-TR construct that captures the neurobehavioural picture *without* the facial and growth findings, and it sits in the DSM appendix as a condition for further study (Kaplan and Sadock 2024). For the exam you need FAS cold; the others you name.

14.2 The facial dysmorphism: the three cardinal features

The load-bearing three. The **facial dysmorphism** of FAS is a specific pattern of minor anomalies, and three features do the diagnostic work: **short palpebral fissures** (at or below the 10th centile), a **smooth philtrum** (loss of the vertical ridges between nose and upper lip), and a **thin vermilion border** of the upper lip. The philtrum and lip are ranked 4 or 5 on a racially normed lip-philtrum guide (Kaplan and Sadock 2024). Two or more of these are required to satisfy the facial domain. Because this triad of facial features is so specific to heavy prenatal alcohol exposure, a diagnosis of FAS can be made even without documented confirmation of maternal drinking.

DOMAIN	CARDINAL FEATURE	THRESHOLD
Face	**Short (small) palpebral fissures**	≤ 10th centile
Face	**Smooth philtrum**	Rank 4 or 5 on lip-philtrum guide
Face	**Thin vermilion border (upper lip)**	Rank 4 or 5 on lip-philtrum guide
Growth	Pre- or postnatal growth deficiency (height or weight)	≤ 10th centile
Brain	Deficient brain growth / abnormal morphogenesis	Head circumference ≤ 10th centile or structural abnormality

The FAS diagnostic domains: two or more facial features plus growth and brain involvement carry the full syndrome (Hoyme criteria, per Kaplan and Sadock 2024).

MNEMONIC

Small eyes, Smooth philtrum, thin Lip

The three cardinal facial features of FAS: *short palpebral fissures*, a *smooth philtrum* and a *thin vermilion border* of the upper lip. Add growth deficiency and the CNS impairment and you have the syndrome.

14.3 Growth restriction and the neurodevelopmental core

Growth. Prenatal alcohol produces intrauterine growth retardation that persists postnatally; height or weight at or below the 10th centile satisfies the growth domain (Companion to Psychiatric Studies; Kaplan and Sadock 2024). Microcephaly (head circumference at or below the 10th centile) reflects the deficient brain growth that underlies the whole picture.

The neurobehavioural core is the clinically important part. The average IQ in FAS is around **72**, though most affected children do *not* score below 70; the signature deficits are in executive function, attention, verbal learning and memory, and visual-spatial processing (Kaplan and Sadock 2024). The single commonest comorbid psychiatric diagnosis is ADHD, present in **44 to 96 per cent** across studies, but FASD-attention is not identical to idiopathic ADHD: FASD children show more trouble *shifting* attentional sets and encoding, and generally perform worse than children with idiopathic ADHD on IQ and adaptive behaviour. This neurodevelopmental impairment, not the face, is what drives lifelong disability, school failure, and elevated rates of later substance use and suicide.

RULE **No safe amount, so counsel abstinence.** There is no established safe quantity or trimester of maternal alcohol; the only evidence-based advice to a pregnant woman is complete abstinence, and FASD is 100 per cent preventable by not drinking in pregnancy.

TRAP **The face is neither necessary nor the point.** Most alcohol-exposed children have *no* dysmorphism (ARND / ND-PAE); waiting for the classic facies means missing the majority of affected children, whose harm is the invisible neurodevelopmental one.

3	10th	72
CARDINAL FAS FACIAL FEATURES (SHORT FISSURES, SMOOTH PHILTRUM, THIN LIP)	CENTILE CUT-OFF FOR THE GROWTH AND PALPEBRAL-FISSURE CRITERIA	APPROXIMATE AVERAGE IQ IN FETAL ALCOHOL SYNDROME

14.4 The India frame: an under-recognised diagnosis

Why it is missed here. Alcohol use in Indian women of reproductive age is lower than in the West but is rising and is heavily under-reported because of stigma, so a maternal drinking history is rarely volunteered and rarely asked. FASD is correspondingly under-diagnosed: there is no systematic antenatal alcohol screening in most Indian obstetric settings, the racially normed lip-philtrum guides are Western-derived, and the neurodevelopmental presentation is easily filed under generic intellectual disability or idiopathic ADHD (Companion to Psychiatric Studies). The de-addiction and antenatal services rarely connect, so the pregnant drinker who could be counselled is often not identified.

The prevention message. The high-yield India point is upstream: systematic screening for maternal drinking at the first antenatal visit and clear abstinence advice, which is squarely within the reach of primary antenatal care. The screening instruments and their cut-offs are taught in the screening-instruments topic and the scales gallery; the antenatal-clinic and pregnancy-withdrawal detail sits in the Perinatal/women's mental health and emergency psychiatry notes.

INDIA

FASD is almost certainly under-diagnosed in India: female drinking is stigmatised and under-reported, antenatal alcohol screening is not routine, and the phenotype is misattributed to intellectual disability or ADHD. The actionable step is to *ask* every antenatal patient about alcohol and to advise abstinence, since the syndrome is wholly preventable and there is no pharmacological treatment once the damage is done.

HOLD THIS

FAS = facial dysmorphism (short palpebral fissures, smooth philtrum, thin vermilion border) + growth deficiency + CNS/neurodevelopmental impairment, on prenatal alcohol exposure; there is no safe amount, and abstinence is the only prevention.

GOOD TO REMEMBER

- **Fetal alcohol syndrome:** the criterion picture is the triad of characteristic facial dysmorphism (two or more of short palpebral fissures at or below the 10th centile, a smooth philtrum, and a thin vermilion border), pre- or postnatal growth deficiency (height or weight at or below the 10th centile), and deficient brain growth with neurodevelopmental impairment, on a background of prenatal alcohol exposure; the neurodevelopmental core (average IQ around 72, ADHD in up to 96 per cent) is what drives lifelong disability, the discriminator from ARND/ND-PAE is the presence of the face and growth findings, and the first and only effective step is prevention through maternal abstinence, since alcohol is the commonest human teratogen and there is no safe threshold.

15 · Assessment and laboratory markers of alcohol use

People with an alcohol problem *underreport*, and they do it reliably, so the clinical assessment of drinking cannot lean on the patient's own account alone. It has to triangulate: a structured history and a validated screen, a focused examination for end-organ damage, and a small panel of **laboratory markers** that betray heavy drinking the patient will not admit. This topic is the **assessment and markers** pair, and the exam mines it for two things: the logic of a good alcohol assessment, and the relative sensitivity and specificity of the four state markers, gamma-glutamyl transferase (GGT), carbohydrate-deficient transferrin (CDT), the mean corpuscular volume (MCV) and the AST to ALT ratio. Get the one discriminator right (CDT is the most specific) and you own the topic.

Why it matters clinically. A biomarker does three jobs a questionnaire cannot: it detects the drinker who denies, it corroborates a suspected history, and it monitors abstinence objectively over follow-up (a rising GGT or CDT after a fall is the fingerprint of relapse). None of these markers diagnoses alcohol use disorder, which is a criterion-based clinical diagnosis; they are

biomarkers of recent heavy consumption that support the picture. The screening instruments themselves (AUDIT, CAGE) are developed in the screening-instruments topic and the actual forms sit in the scales gallery; here the focus is the assessment as a whole and the laboratory markers of chronic use.

15.1 The structure of an alcohol assessment: history, examination, corroboration

The three legs. A complete alcohol assessment rests on a detailed drinking history (quantity in units, frequency, pattern, the timeline of dependence features and withdrawal), a physical examination directed at the systems alcohol damages first (cardiovascular, gastrointestinal, and the central and peripheral nervous systems), and objective corroboration from a screen plus laboratory markers (Companion 2009; Tasman). The history quantifies; the examination stages the end-organ harm; the markers catch what the patient minimises.

Quantify in units and map the timeline. Convert intake to standard units (roughly **8 g** of ethanol per UK unit) and build a timeline of tolerance, withdrawal, salience and loss of control, because the *severity* of dependence, not just its presence, drives the withdrawal risk and the management plan. Ask every newly admitted and referred patient, not only the obvious cases (Companion 2009).

RULE **Corroborate, do not interrogate.** Because self-report underestimates intake, a good alcohol assessment always pairs the history with an objective marker; the markers are there to detect and monitor, never to accuse.

15.2 State versus trait, and what a biomarker can and cannot do

State markers. GGT, CDT, MCV and the transaminases are **state markers**: they rise with recent heavy drinking and fall with abstinence, which is exactly what makes them useful for detection and for monitoring recovery. A positive marker means "has been drinking heavily", not "has an alcohol use disorder"; the diagnosis is still made against the ICD-11 or DSM-5-TR criterion set (developed in the dependence-syndrome topic).

The monitoring trick. Because both GGT and CDT normalise within days to weeks of stopping, serial values track abstinence. The clinically telling event is a marker that *rises* again after falling, which indicates a return to heavy drinking (Kaplan & Sadock 2024; DSM-5-TR). Present the trend to the patient graphically to reinforce motivation (Tasman).

15.3 Gamma-glutamyl transferase (GGT): the sensitive, early, non-specific workhorse

What it is. GGT is a hepatic enzyme induced by alcohol, and its rise is one of the *earliest* laboratory signs of heavy drinking, often before any clinical evidence of liver disease (Tasman; Companion 2009). It is cheap, widely available and the routine first-line marker. GGT and other liver enzymes are elevated in roughly **60 to 75%** of heavy drinkers, and a raised GGT may be the *only* laboratory finding (DSM-5-TR; Tasman). DSM-5-TR frames the sensitive indicator as a modest elevation or high-normal level (over **35 units**), and notes that at least 70% of people with a high GGT are persistent heavy drinkers consuming eight or more drinks daily.

Its limitation. GGT is *sensitive but not specific*. It also rises with non-alcoholic liver disease, biliary obstruction, obesity, and enzyme-inducing drugs, so a raised GGT never stands alone as proof of drinking. It reflects consumption over the preceding three to five weeks and returns toward normal after roughly four to five weeks of abstinence (Companion 2009; Tasman), which is what makes it a serviceable, if blunt, monitoring tool.

GOOD TO REMEMBER

- **GGT:** hepatic enzyme, the **earliest and most widely used** alcohol marker; elevated in ~60 to 75% of heavy drinkers (DSM cut ~>35 units); **sensitive but NOT specific** (rises in liver disease, obesity, enzyme-inducing drugs); reflects the last 3 to 5 weeks of drinking; normalises after ~4 to 5 weeks of abstinence, so useful for monitoring relapse.

15.4 Carbohydrate-deficient transferrin (CDT): the most specific marker

What it is. CDT (carbohydrate-deficient transferrin) is the transferrin isoform that accumulates with sustained heavy alcohol intake, and it is the **most specific** of the routine laboratory markers for heavy drinking (Tasman; Companion 2009). DSM-5-TR treats it as a marker of comparable or even higher sensitivity *and* specificity than GGT, with a level of **20 units** or higher identifying people who regularly consume eight or more drinks daily; the Companion, more conservatively, calls it more specific but *not* more sensitive than GGT. The safe exam line is that CDT is the *most specific* marker, and that its specificity, not extra sensitivity, is its selling point.

Why it is prized. CDT is little affected by the non-alcoholic liver disease that confounds GGT, so a raised CDT points more confidently at alcohol, and it detects relapse to heavy drinking more accurately than other laboratory tests (Tasman). Like GGT it returns toward normal within days to weeks of abstinence, so it also serves monitoring. Its practical weakness is availability and cost: it is not widely available in routine Indian (or UK) laboratories, so GGT and MCV remain the everyday panel.

PEARL

Combining CDT with GGT gives higher sensitivity and specificity than either test alone (DSM-5-TR). In practice the standard alcohol laboratory panel is GGT plus MCV plus the transaminases (with their ratio), and CDT is added where it is available and specificity is at a premium, for example to settle a diagnostic dilemma or to confirm suspected relapse.

GOOD TO REMEMBER

- **CDT:** the **most specific** laboratory marker of chronic heavy drinking (level >=20 units ~ 8+ drinks/day, DSM-5-TR); relatively unaffected by non-alcoholic liver disease; best single marker for detecting relapse; normalises in days to weeks; limited by cost and availability. CDT + GGT combined beats either alone.

15.5 Mean corpuscular volume (MCV): the slow, insensitive macrocytosis marker

What it is. The MCV (mean corpuscular volume) rises to high-normal or frankly macrocytic values in heavy drinkers through a *direct toxic effect of alcohol on erythropoiesis* (bone marrow), and characteristically the macrocytosis appears *without anaemia* (DSM-5-TR; Companion 2009). It is

raised in roughly **30 to 50%** of dependent drinkers and is a cheap, ubiquitous part of the full blood count.

Its two limitations. First, low sensitivity: it misses more than half of heavy drinkers. Second, and more examinable, it is a *poor marker for monitoring abstinence* because red cells have a long lifespan (about 120 days), so the MCV lags weeks to months behind a change in drinking. Macrocytosis is also non-specific, seen with folate and B12 deficiency, hypothyroidism and some drugs, so the alcohol interpretation needs the clinical context.

GOOD TO REMEMBER

- **MCV:** macrocytosis **without anaemia** from direct marrow toxicity; raised in ~30 to 50% of heavy drinkers; **insensitive** and **poor for monitoring abstinence** (RBC lifespan ~120 days, so it lags); non-specific (also folate/B12 deficiency, hypothyroidism).

15.6 The AST to ALT ratio and the transaminases

What it is. The transaminases AST (aspartate aminotransferase, formerly SGOT) and ALT (alanine aminotransferase, formerly SGPT) rise with alcohol-related liver injury but are *less sensitive* markers of heavy drinking than GGT (Tasman). Their diagnostic value lies less in the absolute values than in the **ratio**: an **AST to ALT ratio greater than 2** favours alcoholic liver injury, whereas a ratio at or below 1 points to a non-alcoholic cause (Tasman; standard hepatology). The mechanism worth knowing is that alcohol-associated pyridoxine (vitamin B6) deficiency depresses ALT synthesis more than AST, tipping the ratio upward.

How to use it. AST and ALT are part of the standard liver panel; read them alongside GGT rather than instead of it, and use the ratio, not the raw numbers, as the alcohol pointer. A markedly raised GGT with an AST:ALT over 2 and a high-normal MCV is a classic biochemical triad of chronic heavy drinking.

MARKER	WHAT IT REFLECTS	SENSITIVITY	SPECIFICITY	WINDOW / MONITORING NOTE
GGT	Hepatic enzyme induction / injury	**Good (earliest sign)**	Low (many confounders)	Last 3 to 5 weeks; normalises ~4 to 5 weeks abstinent
CDT	Transferrin glycosylation with sustained intake	Comparable (not more, per Companion)	**Highest of the routine markers**	Days to weeks; best single relapse marker; limited availability
MCV	Direct marrow toxicity (macrocytosis, no anaemia)	**Low (~30 to 50%)**	Low (folate/B12, thyroid)	Lags weeks to months; poor for monitoring (RBC ~120 days)
AST:ALT ratio	Pattern of hepatocellular injury	Low (transaminases less sensitive than GGT)	Moderate when ratio >2	Ratio >2 favours alcohol; <=1 suggests other cause

MARKER	WHAT IT REFLECTS	SENSITIVITY	SPECIFICITY	WINDOW / MONITORING NOTE
EtG / PEth (direct)	Direct alcohol metabolites	High (recent use)	High (alcohol-specific)	Urine EtG up to ~4 days; newer, less routine

The state markers of chronic alcohol use ranked by their examinable property: GGT is the sensitive workhorse, CDT the most specific, MCV the insensitive laggard, the AST:ALT ratio the pattern pointer (DSM-5-TR; Tasman; Companion 2009).

15.7 Direct biomarkers and blood alcohol as a tolerance gauge

Direct metabolites. Beyond the indirect state markers, direct alcohol biomarkers detect ethanol metabolites themselves: urinary **ethyl glucuronide** (EtG) evidences alcohol use for up to about **4 days** (Tasman), and phosphatidylethanol (PEth) in blood extends the window further; both are alcohol-specific and increasingly used to verify abstinence, though not yet routine in Indian practice.

Blood alcohol reads tolerance. The most direct cross-sectional test is the blood alcohol concentration, which doubles as a tolerance gauge. A person at **150 mg/dL** with no signs of intoxication has acquired tolerance; someone who appears sober at **200 mg/dL** or above is highly tolerant and will almost certainly withdraw on abrupt cessation (DSM-5-TR; Companion 2009). Concentrations around 300 mg/dL indicate a need for emergency care and levels over 400 mg/dL can be fatal (Tasman).

TRAP **Treating a normal GGT as a clean bill.** GGT is insensitive to lighter drinking and CDT is often unavailable, so normal markers never exclude an alcohol problem; the history and screen still stand. Equally, do not read a raised GGT alone as proof of drinking, since it is non-specific.

20	35	120	4
CDT UNITS FLAGGING ~8+ DRINKS DAILY (DSM-5-TR)	GGT UNITS, HIGH-NORMAL SENSITIVE CUT (DSM-5-TR)	RBC LIFESPAN IN DAYS, WHY MCV LAGS	DAYS URINE ETG DETECTS RECENT USE

INDIA

In the Indian de-addiction context the everyday alcohol laboratory panel is deliberately lean: baseline and three-monthly liver function tests (AST, ALT, GGT), MCV and a full blood count, with GGT and MCV as the workhorse biomarkers of recent heavy drinking and their combination raising sensitivity (IPS 2014). Carbohydrate-deficient transferrin, though the most specific marker, is used only "where available", which in most government de-addiction centres and Drug De-addiction Programme (DDAP) units means rarely, so GGT and MCV carry the load. This is the same treatment-gap logic that pushes Indian services toward brief, motivation-based assessment delivered by trained non-specialists: a validated screen plus a cheap GGT and full blood count are within reach of a district hospital in a way that CDT and PEth are not. The wider Narcotic Drugs and Psychotropic Substances (NDPS) Act frame and capacity issues around assessment are developed in the Mental health legislation and forensic psychiatry notes.

WORKED EXAMPLE

A 46-year-old man is admitted with dyspepsia and denies problem drinking. His GGT is three times the upper limit, AST:ALT is 2.4, and the MCV is high-normal at the top of the reference range, but he has no anaemia. The biochemical triad (raised GGT, AST:ALT over 2, macrocytosis without anaemia) corroborates heavy drinking despite the denial, and the AUDIT, administered next, scores 22, in the probable-dependence band. CDT is unavailable locally, so it is not sent. Two weeks into a supervised admission the GGT has fallen by half; a subsequent rise on follow-up would flag relapse. No single number diagnosed him; the pattern plus the screen did, and the diagnosis was then confirmed against the criteria.

HOLD THIS

Four markers, four properties: GGT is the sensitive-but-not-specific early workhorse, CDT is the most specific, MCV is the insensitive macrocytosis-without-anaemia laggard that is useless for monitoring (RBC lifespan ~120 days), and an AST:ALT ratio over 2 favours alcohol; every marker detects and monitors heavy drinking but none makes the diagnosis.

Opioid use disorder

16 · Opioid intoxication, overdose and naloxone

Of every acute presentation on this block, opioid overdose is the one where a single correct decision reverses death within minutes. The examiner wants three things off the top: the recognisable picture of **opioid intoxication**, the lethal **triad** that defines **opioid overdose**, and the antidote given by the number. Get the antidote and its titration right and you are competent at the bedside; get the dose or the re-dosing wrong and the patient dies after a false recovery.

Why it matters clinically. Opioids kill by suppressing the brainstem respiratory drive. Overdose is the leading cause of death in opioid use disorder, and much of that mortality clusters in a predictable window: the period after forced abstinence (post-detoxification, post-release from custody, after disengaging from opioid substitution treatment) when tolerance has fallen but the person returns to a previously tolerated dose. The reward-pathway mechanics that drive the use sit in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the NDPS Act frame around possession and mandated treatment sits in the Mental health legislation and forensic psychiatry notes. Here the task is to recognise the state, reverse it safely, and understand why the reversal can wear off before the poison does.

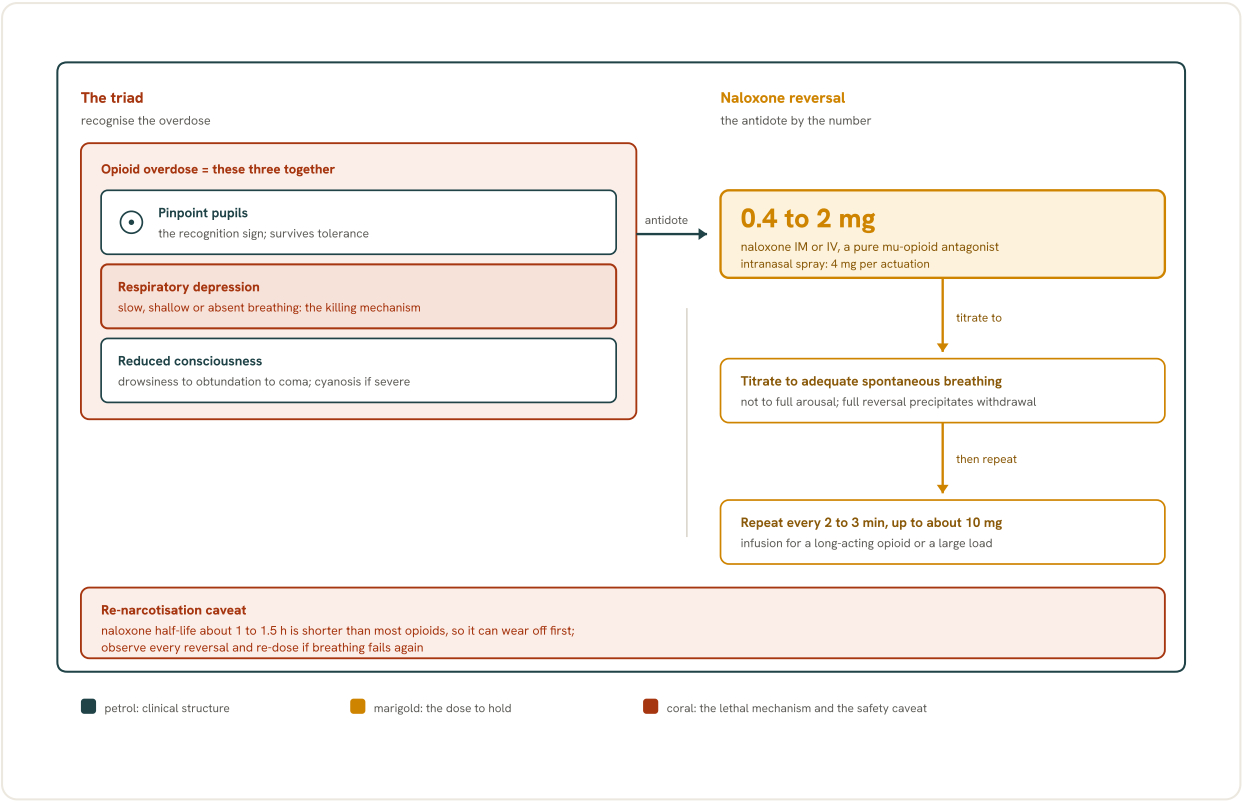


Fig 13.11 Opioid overdose: the triad and naloxone reversal. The overdose is the triad of pinpoint pupils, respiratory depression (the lethal component) and reduced consciousness taken together; the antidote is naloxone 0.4 to 2 mg IM or IV (intranasal 4 mg), titrated to adequate spontaneous breathing rather than full arousal and repeated every 2 to 3 minutes up to about 10 mg. Because naloxone's half-life of about 1 to 1.5 hours is shorter than most opioids', an apparently recovered patient must be observed and re-dosed for re-narcotisation.

16.1 Opioid intoxication: the recognisable clinical state

The picture. Opioid intoxication is a state of euphoria or apathy with psychomotor slowing, drowsiness or obtundation, slurred speech, impaired attention and memory, and pupillary constriction (Kaplan and Sadock 2024; Tasman). On examination the signs cluster as **miosis** (constricted pupils), a drowsy or obtunded sensorium, dry mouth and nose, and slowed gastrointestinal activity with constipation. It is a clinical diagnosis: the combination of a depressed, apathetic, drowsy patient with small pupils in the right context is opioid intoxication until proven otherwise.

The tolerance point that anchors the exam. Tolerance develops to the euphoric, analgesic, sedative and respiratory-depressant effects of opioids, but *not* to **miosis** and constipation (New Oxford Textbook of Psychiatry). That single fact is why constricted pupils remain a reliable sign even in a heavily tolerant chronic user, and why the pupil is the physical sign to look for first.

RULE **Small pupils survive tolerance.** Tolerance blunts euphoria and even respiratory depression, but never miosis, so pinpoint pupils remain a dependable pointer to opioids however chronic the user.

GOOD TO REMEMBER

- **Opioid intoxication (syndrome):** euphoria or apathy with psychomotor slowing, drowsiness or obtundation, slurred speech and impaired attention, plus the signature sign of **miosis**; the discriminator is that tolerance never develops to pupillary constriction, so small pupils persist even in a chronic user; the first management step is to assess airway, breathing and conscious level, because the danger is not the intoxication itself but its progression to respiratory depression.

16.2 Opioid overdose: the classic triad

The triad to say first. Opioid overdose is a clinical **triad** of *pinpoint (miotic) pupils*, *respiratory depression*, and *reduced consciousness* progressing to coma, with cyanosis in severe cases (Kaplan and Sadock 2024; Tasman; New Oxford Textbook of Psychiatry). This is the highest-yield line in the topic: severe intoxication tips into coma, slowed or absent respiration, and death. The **respiratory depression** is the killing mechanism; the **pinpoint pupils** are the recognition sign; the reduced conscious level is what brings the patient to attention.

TRIAD COMPONENT	WHAT YOU SEE
Pinpoint pupils	**Bilateral miosis (constricted, "pinpoint"); persists despite tolerance, so a reliable sign**
Respiratory depression	**Slow, shallow or absent breathing (brainstem respiratory-drive suppression); the killing mechanism**
Reduced consciousness	Drowsiness to obtundation to coma; cyanosis and pulmonary oedema in severe overdose

The classic triad of opioid overdose: pinpoint pupils, respiratory depression and reduced consciousness; respiratory depression is the lethal component (Kaplan and Sadock 2024; Tasman; New Oxford Textbook of Psychiatry).

The pupil caveat. Pupils may paradoxically *dilate* once hypoxia and cerebral anoxia are advanced, or when a mixed overdose (co-ingested stimulant or a hypoxic terminal state) is present, so a normal or dilated pupil does not exclude opioid overdose in an apnoeic patient. Treat the breathing, not the pupil, when respiration is failing.

WORKED EXAMPLE

A man in his twenties is found unresponsive at home shortly after release from custody. Respiratory rate 4, oxygen saturation 78 per cent, pupils pinpoint, GCS 5. This is the triad, in the classic high-risk window: tolerance fell during enforced abstinence, and a previously tolerated dose is now an overdose. Support ventilation with bag-valve-mask, give **naloxone**, and titrate to a return of adequate spontaneous breathing rather than to full wakefulness.

GOOD TO REMEMBER

- **Opioid overdose (emergency):** the criterion picture is the triad of pinpoint pupils, respiratory depression and reduced consciousness or coma; the discriminator from simple intoxication is failing respiration and a fall in conscious level; the antidote is **naloxone**; the first management step is airway and ventilatory support alongside naloxone, and the highest-risk window is the return to use after a period of lost tolerance.

16.3 Naloxone: the antidote and its verified dose

What it is. Naloxone (in India the 0.4 mg per 1 mL injectable ampoule; the intranasal spray branded Nexnal where available; internationally sold as **Narcan**) is a pure competitive mu-opioid receptor **antagonist** that displaces the opioid from the receptor and reverses **respiratory depression**, sedation and analgesia within minutes. It has essentially no effect in the absence of opioids, which makes empirical use in an undifferentiated coma with respiratory depression safe.

The dose, verified. Give naloxone **0.4 to 2 mg** intramuscularly (or intravenously), repeated every **2 to 3 minutes** up to a total of about **10 mg**; the intranasal preparation is **4 mg** per spray, repeated after 2 to 3 minutes if there is no response (BAP 2026; WHO; Maudsley Prescribing Guidelines). If there is no response by roughly 10 mg cumulative, reconsider the diagnosis (non-opioid cause, or a co-ingestant). Buprenorphine overdose is the exception: its high receptor affinity means *higher* naloxone doses, of the order of 2 to 4 mg with diminishing return beyond about 5 mg, and often ventilatory support are needed to reverse it (Maudsley Prescribing Guidelines).

TRAP **Titrate to breathing, not to full arousal.** Reversing a dependent patient all the way to wakefulness precipitates a violent, distressing acute withdrawal; the goal is adequate spontaneous respiration and airway protection, not a bright-eyed, agitated patient.

GOOD TO REMEMBER

- **Naloxone (mu-opioid antagonist):** competitive antagonist that reverses opioid respiratory depression within minutes; dose **0.4 to 2 mg** IM/IV repeated every 2 to 3 minutes up to about **10 mg**, or intranasal **4 mg** per spray; titrate to adequate respiration, not full arousal; short half-life (about 1 to 1.5 hours) means re-narcotisation risk; buprenorphine overdose needs higher doses (2 to 4 mg). Provide take-home naloxone with family rescue-breathing training for anyone with current or recent opioid use.

16.4 Titration and repeat dosing: adequate respiration is the endpoint

The endpoint that defines good practice. The management principle in overdose is to titrate naloxone *to restore adequate spontaneous respiration and airway protection*, not to full consciousness (BAP 2026; WHO). In an opioid-dependent patient, a large single bolus that fully reverses the receptor triggers a sudden, severe **precipitated withdrawal**: agitation, vomiting (with aspiration risk), pain, tachycardia and, occasionally, flash pulmonary oedema. Small, repeated increments titrated to breathing avoid this while still saving life.

Repeat dosing and the infusion. Because a single dose is short-acting, doses are repeated every 2 to 3 minutes until respiration is adequate, and where a long-acting opioid (methadone, slow-release morphine) or a large ingested load is involved, a continuous naloxone infusion is often required to hold the reversal (Maudsley Prescribing Guidelines). Every reversed overdose needs a period of observation, because the naloxone can wear off first (16.5).

16.5 Re-narcotisation: why naloxone can wear off before the opioid does

The pharmacokinetic mismatch. Naloxone has a short elimination half-life of about **1 to 1.5 hours**, which is shorter than that of most opioids it is used to reverse (heroin and its active

metabolites, and especially long-acting agents such as methadone with a half-life measured in tens of hours, or slow-release oral morphine) (New Oxford Textbook of Psychiatry; Maudsley Prescribing Guidelines). As the naloxone is cleared, unbound opioid still circulating re-occupies the receptor and the patient *re-narcotises*: respiratory depression and coma recur after an apparent recovery.

The practical consequence. A reversed patient is never simply discharged. They are observed (a minimum of several hours, longer after a long-acting opioid), re-dosed or placed on an infusion if respiration falls again, and in methadone or extended-release overdose admitted for prolonged monitoring, because a single reversal buys time, not cure.

RULE **Observe every reversal.** Naloxone outlives few opioids; the shorter-acting antidote can fade before the longer-acting poison, so an apparently recovered patient must be watched and re-dosed for re-narcotisation.

HOLD THIS

Opioid overdose is the triad of pinpoint pupils, respiratory depression and reduced consciousness; give naloxone 0.4 to 2 mg IM (intranasal 4 mg), titrated to adequate breathing not full arousal, repeated every 2 to 3 minutes, and observe for re-narcotisation because naloxone's half-life (about 1 to 1.5 hours) is shorter than most opioids'.

0.4 to 2 mg	4 mg	1 to 1.5 h	10 mg
NALOXONE IM/IV STARTING DOSE (REPEAT EVERY 2 TO 3 MIN)	NALOXONE INTRANASAL SPRAY DOSE PER ACTUATION	NALOXONE HALF-LIFE, SHORTER THAN MOST OPIOIDS (RE-NARCOTISATION)	CUMULATIVE NALOXONE BY WHICH A RESPONSE SHOULD HAVE APPEARED

16.6 The naltrexone contrast: an antagonist you must never give to a current user

Same class, opposite timing. Naloxone is the emergency reversal; naltrexone (in India Naltima or Nodict) is the long-acting oral or depot mu-antagonist for relapse *prevention* after detoxification, dosed at **50 mg/day** orally (Kaplan and Sadock 2024; Maudsley Prescribing Guidelines). The examiners pair them precisely to test one discrimination: naltrexone given to a patient with opioid still on board precipitates a severe, prolonged withdrawal, because unlike naloxone its long half-life means the withdrawal it triggers cannot be quickly outlasted.

The opioid-free window. Naltrexone is started only after a documented opioid-free interval (at least **7 to 10 days**, longer after methadone) confirmed by a negative urine opioid screen, and often after a small naloxone challenge (0.2 to 0.8 mg) to expose residual dependence safely with the short-acting drug before committing to the long-acting one (Maudsley Prescribing Guidelines; IPS 2014).

COMMON TRAP

Giving naltrexone to a current opioid user precipitates withdrawal. Naltrexone is a relapse-prevention agent for the abstinent patient, not a reversal agent and not something to start until the opioid-free window has passed and, where there is doubt, a naloxone challenge is clean. Confusing the emergency reversal (naloxone) with the maintenance antagonist (naltrexone) is a classic and dangerous error.

GOOD TO REMEMBER

- **Naltrexone (long-acting mu-antagonist):** for relapse prevention after detoxification, not for overdose reversal; oral dose **50 mg/day**; contraindicated in current opioid use and started only after a documented opioid-free interval (7 to 10 days, longer for methadone) with a negative urine screen and, if in doubt, a naloxone challenge; its long half-life is exactly why a precipitated withdrawal from it cannot be quickly reversed.

16.7 The Indian frame: treatment gap, NDPS and take-home naloxone

The gap and the epidemiology. India carries a large opioid burden (heroin, raw and processed opium, and pharmaceutical opioids), concentrated in the north-west and north-east, and a wide **treatment gap**: only a small fraction of people with opioid dependence reach any evidence-based care, and de-addiction services are unevenly distributed (IPS 2014). Opioid substitution treatment is delivered through the government **OST** programme and de-addiction centres, with buprenorphine the workhorse of accessible maintenance.

Access and the legal frame. Sublingual buprenorphine-naloxone in a 4:1 ratio (buprenorphine with a naloxone component that deters injection; branded Suboxone or Bunorph, buprenorphine alone as Tidigesic) is the first-line agonist maintenance option in Indian outpatient practice, inducted at **4 mg/1 mg** once the patient is in objective withdrawal (COWS at least 8 to 12) and titrated to a usual 8 to 16 mg/day (IPS 2014). Methadone remains restricted to licensed government OST clinics. All of this operates within the **NDPS Act 1985**, which frames possession offences, prescriber compliance and court-mandated treatment in lieu of conviction, and is developed in the Mental health legislation and forensic psychiatry notes. Take-home **naloxone** with family rescue-breathing training, long standard in high-income systems, is expanding in India as the single most cost-effective intervention against overdose death, particularly for patients leaving detoxification or custody with lowered tolerance.

INDIA

Buprenorphine, usually as the buprenorphine-naloxone 4:1 combination, is the accessible backbone of Indian opioid maintenance, inducted only in objective withdrawal to avoid precipitating it; methadone is confined to licensed government OST clinics. Against a heavy opioid burden and a wide treatment gap, and within the NDPS Act 1985 frame, take-home naloxone with family training is the highest-value overdose intervention, especially at the post-detoxification and post-release points where tolerance has fallen.

MNEMONIC

PPR then N

Pinpoint pupils, respiratory depression, reduced consciousness are the triad; then Naloxone, titrated to breathing. PPR flags the diagnosis, N is the antidote.

17 · Opioid withdrawal, COWS and its management

Stopping opioids in a physically dependent user unmasks a brain whose locus coeruleus has spent months suppressed by exogenous agonist, and the result is a florid, time-ordered but rarely lethal **noradrenergic storm**. The single most examinable contrast on this topic is with alcohol: **opioid withdrawal** is intensely uncomfortable but, in an otherwise healthy adult, not life-threatening, whereas alcohol and benzodiazepine withdrawal can kill. Examiners want the withdrawal features and their time-course by the clock (and the rule that onset and peak track the parent opioid's half-life), the **Clinical Opiate Withdrawal Scale** with its exact severity bands, and the management: buprenorphine-assisted withdrawal, the alpha-2 agonists, and the symptomatic agents. Get the COWS bands and the induction threshold exact and most of the viva follows.

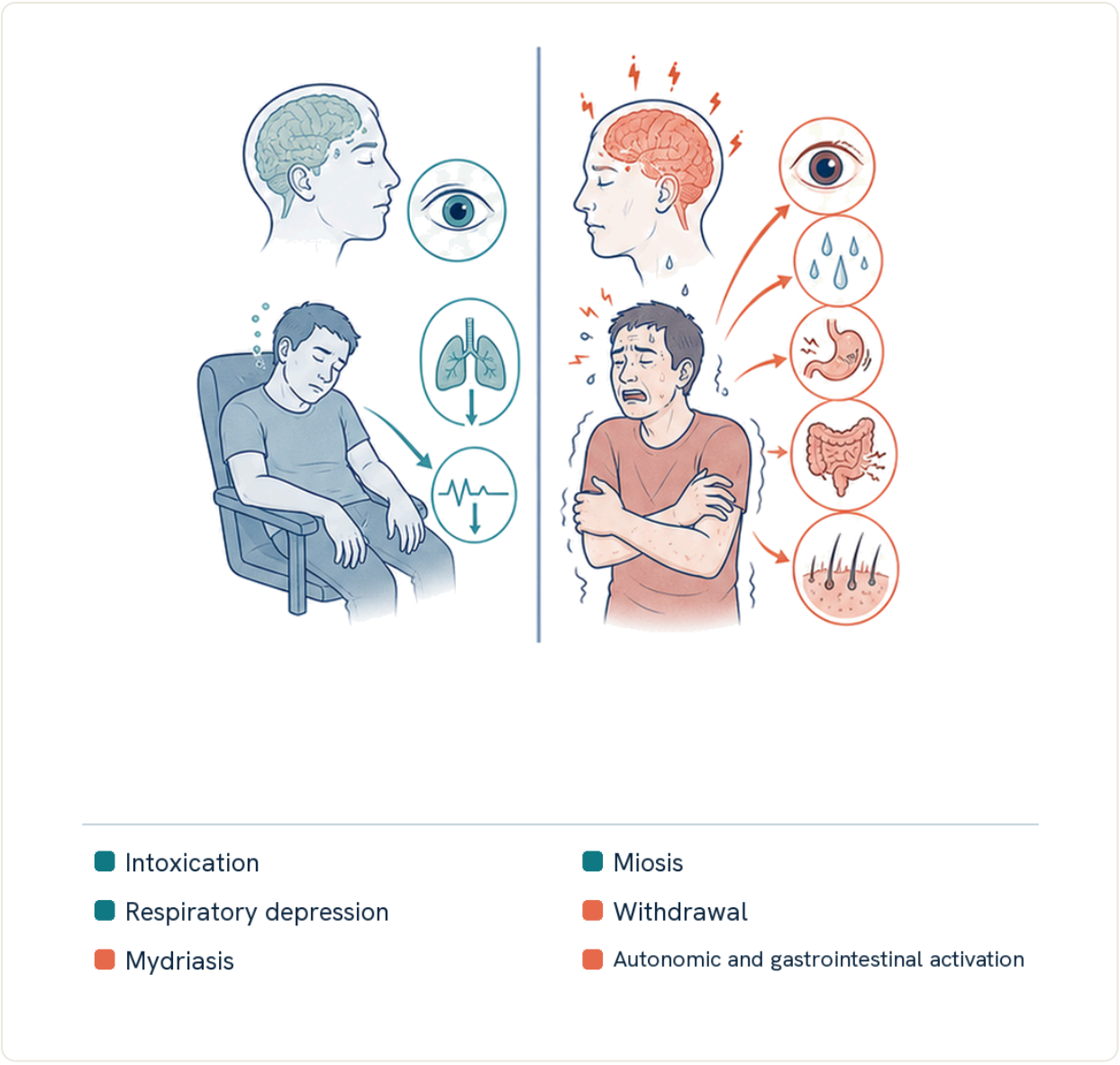
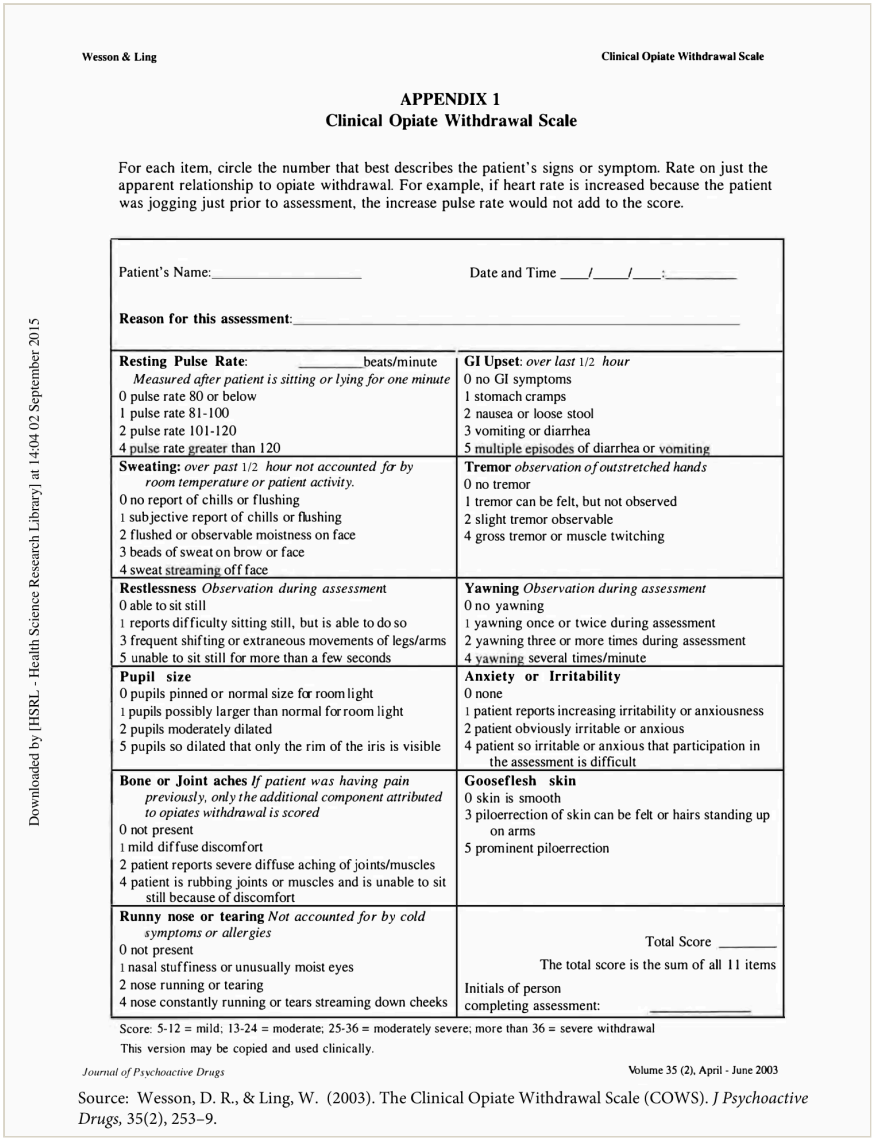


Fig 13.12 Opioid intoxication and withdrawal have opposing patterns: intoxication produces reduced consciousness, miosis and respiratory suppression, whereas withdrawal produces mydriasis, autonomic activation, piloerection, gastrointestinal distress and agitation.

Why it matters clinically. The **management of opioid withdrawal** is never an end in itself: withdrawal management alone, without ongoing opioid substitution or relapse-prevention pharmacotherapy, produces high relapse, morbidity and mortality (BAP 2026; NICE 2011; VA/DoD 2021). The two lethal windows are not the withdrawal itself but its aftermath, overdose after tolerance has fallen (post-detoxification, post-incarceration, post-disengagement) and withdrawal-induced suicidality (Indian Psychiatric Society). The reward-pathway and locus-coeruleus mechanics are developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and are not re-derived here; the NDPS Act frame sits in the Mental health legislation and forensic psychiatry notes. Here the task is to read the syndrome off the clock, stage it with the COWS, and manage it by the number.



Wesson & Ling — Clinical Opiate Withdrawal Scale

APPENDIX 1
Clinical Opiate Withdrawal Scale

For each item, circle the number that best describes the patient's signs or symptom. Rate on just the apparent relationship to opiate withdrawal. For example, if heart rate is increased because the patient was jogging just prior to assessment, the increase pulse rate would not add to the score.

Patient's Name:_____ Date and Time ____/____/____:_____

Reason for this assessment:_____

Resting Pulse Rate: _____beats/minute *Measured after patient is sitting or lying for one minute* 0 pulse rate 80 or below 1 pulse rate 81-100 2 pulse rate 101-120 4 pulse rate greater than 120	**GI Upset**: *over last 1/2 hour* 0 no GI symptoms 1 stomach cramps 2 nausea or loose stool 3 vomiting or diarrhea 5 multiple episodes of diarrhea or vomiting
Sweating: *over past 1/2 hour not accounted for by room temperature or patient activity.* 0 no report of chills or flushing 1 subjective report of chills or flushing 2 flushed or observable moistness on face 3 beads of sweat on brow or face 4 sweat streaming off face	**Tremor** *observation of outstretched hands* 0 no tremor 1 tremor can be felt, but not observed 2 slight tremor observable 4 gross tremor or muscle twitching
Restlessness *Observation during assessment* 0 able to sit still 1 reports difficulty sitting still, but is able to do so 3 frequent shifting or extraneous movements of legs/arms 5 unable to sit still for more than a few seconds	**Yawning** *Observation during assessment* 0 no yawning 1 yawning once or twice during assessment 2 yawning three or more times during assessment 4 yawning several times/minute
Pupil size 0 pupils pinned or normal size for room light 1 pupils possibly larger than normal for room light 2 pupils moderately dilated 5 pupils so dilated that only the rim of the iris is visible	**Anxiety or Irritability** 0 none 1 patient reports increasing irritability or anxiousness 2 patient obviously irritable or anxious 4 patient so irritable or anxious that participation in the assessment is difficult
Bone or Joint aches *If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored* 0 not present 1 mild diffuse discomfort 2 patient reports severe diffuse aching of joints/muscles 4 patient is rubbing joints or muscles and is unable to sit still because of discomfort	**Gooseflesh skin** 0 skin is smooth 3 piloerrection of skin can be felt or hairs standing up on arms 5 prominent piloerrection
Runny nose or tearing *Not accounted for by cold symptoms or allergies* 0 not present 1 nasal stuffiness or unusually moist eyes 2 nose running or tearing 4 nose constantly running or tears streaming down cheeks	Total Score _____ The total score is the sum of all 11 items Initials of person completing assessment: _____

Score: 5-12 = mild; 13-24 = moderate; 25-36 = moderately severe; more than 36 = severe withdrawal

This version may be copied and used clinically.

Journal of Psychoactive Drugs Volume 35 (2), April - June 2003

Source: Wesson, D. R., & Ling, W. (2003). The Clinical Opiate Withdrawal Scale (COWS). *J Psychoactive Drugs*, 35(2), 253–9.

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COWS (Wesson and Ling, 2003); reproduced from the NIDA/SAMHSA form, freely reproducible with acknowledgement.

Fig 13.13 The Clinical Opiate Withdrawal Scale (COWS), the 11-item clinician-rated instrument that quantifies opioid withdrawal severity so that treatment, above all the timing of buprenorphine induction, is driven by a number rather than by impression. Each item is scored on the form and the total is read against four verified severity bands printed at the foot: 5 to 12 is mild, 13 to 24 moderate, 25 to 36 moderately severe, and above 36 severe withdrawal. The examinable threshold sits inside the mild band: buprenorphine is withheld until objective withdrawal is established at a COWS of about 8 to 12, because a partial agonist given too early precipitates withdrawal.

17.1 The withdrawal syndrome: the noradrenergic features

The clinical picture. Opioid withdrawal is a syndrome of autonomic and noradrenergic overactivity that is, in essence, the mirror image of intoxication. The frequently occurring signs and symptoms are sweating, **piloerection** (gooseflesh, the "cold turkey"), yawning, **rhinorrhoea**, sneezing, **lacrimation**, pupillary dilatation (mydriasis), nausea, vomiting, abdominal cramps, diarrhoea, tremor, muscle and bone aches, agitation, dysphoric mood, fever, piloerection and sleep disturbance (Kaplan and Sadock 2024; Stahl Substance Use; ICD-11 CDDR). None of these is dangerous in isolation; taken together they are so aversive that the person uses again simply to stop them, which is the engine of continued dependence.

Objective versus subjective signs. A useful examination distinction: the *objective* signs (mydriasis, lacrimation, rhinorrhoea, piloerection, yawning, sweating, tremor, raised pulse) can be observed and are what a withdrawal scale rates, whereas the *subjective* symptoms (anxiety, bone and muscle ache, restlessness, dysphoria, drug craving) are reported. Buprenorphine induction is timed to *objective* withdrawal precisely because subjective distress alone is unreliable.

GOOD TO REMEMBER

- **Opioid withdrawal syndrome:** the criterion picture is autonomic and noradrenergic overactivity, the mirror of intoxication, mydriasis, lacrimation, rhinorrhoea, sneezing, yawning, piloerection, sweating, nausea, vomiting, diarrhoea, muscle and bone aches, and dysphoria; the discriminator from alcohol and sedative withdrawal is that it is intensely uncomfortable but *not* life-threatening in the otherwise healthy; the first management step is to confirm objective withdrawal (a scale such as the COWS) before any opioid agonist is given.

17.2 The time-course by the clock: onset and peak track the half-life

The governing principle. The onset, peak and duration of opioid withdrawal are set by the pharmacokinetics of the parent opioid: withdrawal follows the rate at which the drug clears from its receptors, so the shorter the half-life, the sooner and sharper the syndrome (Tasman; Kaplan and Sadock 2024). This single rule lets you predict the course from the drug alone.

Short-acting opioids. For a short-acting opioid such as heroin (diamorphine), withdrawal begins about **6 to 8 hours** after the last dose (the wider range across opioids is 4 to 24 hours), peaks at roughly **36 to 48 hours**, and largely resolves by **5 to 7 days** (Tasman; Maudsley Prescribing Guidelines). This is the acute, dramatic "cold turkey" course.

Long-acting opioids. For a long-acting opioid such as methadone (half-life of the order of **24 to 36 hours** in maintenance), onset is delayed to **24 to 48 hours**, the peak comes later, and the syndrome is more protracted (often 10 to 14 days or more) but less intense. A protracted, low-grade phase (dysphoria, insomnia, craving, autonomic instability) can persist for weeks after either.

OPIOID	ONSET AFTER LAST DOSE	PEAK	BROAD DURATION
Heroin / short-acting	**6 to 8 hours**	**36 to 48 hours**	5 to 7 days
Methadone / long-acting	**24 to 48 hours**	4 to 6 days	10 to 14 days or more
Protracted phase (either)	days to weeks	-	weeks (dysphoria, insomnia, craving)

Opioid withdrawal time-course; onset and peak track the parent opioid's half-life, so heroin withdrawal is early and sharp while methadone withdrawal is delayed and protracted (Tasman; Kaplan and Sadock 2024; Maudsley Prescribing Guidelines).

RULE **Read the drug, then read the clock.** The half-life sets everything, short-acting opioids withdraw early, sharp and brief; long-acting opioids withdraw late, milder and protracted, so you time induction and taper to the parent drug, not to a fixed schedule.

17.3 The COWS: what it is and what it measures

What it is. The Clinical Opiate Withdrawal Scale (COWS, Wesson and Ling 2003) is the most commonly used clinician-rated instrument for quantifying the severity of opioid withdrawal, so that treatment (above all the timing of buprenorphine induction) can be driven by a number rather than by impression (Kaplan and Sadock 2024; Maudsley Prescribing Guidelines). It is an 11-item observer-rated scale scoring resting **pulse rate**, sweating, restlessness, pupil size, bone or joint aches, **rhinorrhoea or lacrimation**, gastrointestinal upset, tremor, yawning, anxiety or irritability, and **piloerection** (gooseflesh). The full instrument is reproduced in the scales gallery.

Why it is preferred. The COWS rates *objective* withdrawal, which is exactly what makes it the tool for timing agonist induction: because buprenorphine is a partial agonist that will displace a full agonist from the receptor, giving it too early precipitates withdrawal, so a scale that confirms the patient is already in objective withdrawal (rather than merely subjectively distressed) is the safeguard. The related Objective Opiate Withdrawal Scale (OOWS) rates observable signs only; the COWS is the default in most protocols.

17.4 The COWS severity bands: the numbers that drive treatment

The bands to memorise. The COWS total maps to four verified severity bands: **5 to 12** is mild withdrawal, **13 to 24** is moderate, **25 to 36** is moderately severe, and a score **above 36** is severe withdrawal (Wesson and Ling 2003; Kaplan and Sadock 2024; Maudsley Prescribing Guidelines). A score under 5 indicates little or no withdrawal. These bands are the anchor for the induction decision in the next subtopic.

COWS TOTAL SCORE	SEVERITY BAND	INTERPRETATION
5 to 12	Mild	Objective withdrawal present but mild; the usual minimum threshold to begin buprenorphine induction.
13 to 24	Moderate	Clearly established withdrawal; a comfortable window for buprenorphine first dose.
25 to 36	Moderately severe	Marked distress; symptomatic cover needed alongside agonist induction.
above 36	Severe	Severe withdrawal; intensive symptomatic management.

COWS severity bands (5 to 12 mild, 13 to 24 moderate, 25 to 36 moderately severe, above 36 severe); verified against two independent sources (Wesson and Ling 2003; Kaplan and Sadock 2024; Maudsley Prescribing Guidelines).

COMMON TRAP

The COWS band and the induction threshold are not the same number, and confusing them is the classic error. The mild band *starts* at a score of 5, but the accepted threshold to give the first dose of buprenorphine is higher, a COWS of about **8 to 12** (Indian Psychiatric Society; APA targets above 10). Inducting on a COWS of 5 to 7 risks precipitated withdrawal because the patient is not yet in sufficiently established withdrawal for the partial agonist to be a net improvement.

17.5 Management overview: withdrawal management is never a stand-alone

The overarching rule. Across every guideline, the first principle of the **management of opioid withdrawal** is that it must not be done in isolation. BAP, NICE, WHO mhGAP, VA/DoD and CANMAT are unanimous: do not undertake opioid withdrawal management without planned ongoing pharmacotherapy (agonist maintenance or naltrexone) and psychosocial support, because withdrawal alone carries a high risk of relapse and, through lost tolerance, of fatal overdose (BAP 2026; NICE 2011; WHO mhGAP 2016; VA/DoD 2021). Two approaches are legitimate: a supervised agonist taper (buprenorphine or methadone) for those choosing to detoxify, and, more often, continued opioid substitution therapy (OST). Ultra-rapid detoxification under anaesthesia or heavy sedation is contraindicated, it confers no benefit and carries life-threatening risk (BAP 2026; NICE 2011; WHO 2009).

The guideline positions, in order. BAP directs that for medically assisted withdrawal an agonist taper is used, delaying the first buprenorphine dose until objective withdrawal, and names lofexidine or clonidine as adjunctive or monotherapy where an agonist is not used, preferring lofexidine (BAP 2026). The **Indian Psychiatric Society** makes a buprenorphine taper the preferred medically assisted withdrawal regimen and buprenorphine-naloxone the first-line agonist maintenance option in Indian outpatient practice (IPS guidelines). NICE offers methadone or buprenorphine as first-line for detoxification, with lofexidine for those who decline them or have mild or uncertain dependence (NICE 2011). WHO mhGAP recommends tapered opioid agonists, with alpha-2 agonists as an alternative (WHO mhGAP 2016). None of these is contradicted here; the agonist-taper-first and continued-OST positions are verified across all four.

17.6 Buprenorphine-assisted withdrawal: the partial agonist and its induction rule

Why buprenorphine. Buprenorphine (Indian brand Tidigesic; as buprenorphine-naloxone, Suboxone or Bunorph) is a high-affinity *partial* mu-receptor agonist. Its ceiling effect on respiratory depression makes it substantially safer in overdose than methadone, and its high receptor affinity means it both relieves withdrawal and blocks the effect of further illicit opioid, which is why it is the workhorse of ambulatory Indian de-addiction practice. In India it is most often prescribed as the buprenorphine-naloxone sublingual combination (a 4:1 ratio), where the poorly absorbed naloxone deters injection misuse, the buprenorphine-naloxone combination (IPS guidelines).

The induction rule. The one non-negotiable is timing. Because buprenorphine will displace a full agonist from the receptor while only partially activating it, giving it while a full agonist is still on board *precipitates* withdrawal. The first dose is therefore delayed until the patient is in objective

withdrawal, operationally a COWS of about **8 to 12** and typically **12 to 24 hours** after the last short-acting opioid (IPS guidelines; BAP 2026; APA). The IPS induction is buprenorphine-naloxone 4 mg / 1 mg at that point, titrated by 2 to 4 mg/day to a usual maintenance of 8 to 16 mg/day, some patients needing up to 24 mg/day (IPS guidelines). For a supervised buprenorphine *taper* the IPS uses reductions of 2 to 4 mg/day over 7 to 14 days from the stabilisation dose (IPS guidelines).

WORKED EXAMPLE

A man dependent on injected heroin last used ten hours ago and is subjectively distressed but has a COWS of 6 (mild band): mild anxiety, a few yawns, faint sweating. The wrong move is to induct now, at a COWS of 6, with a full agonist likely still partly on the receptor, buprenorphine can precipitate an abrupt worsening. The correct move is to wait, giving symptomatic cover (an alpha-2 agonist, an antiemetic, loperamide), and to re-score; once the COWS reaches about 8 to 12 (usually by 12 to 24 hours after the last heroin dose), give buprenorphine-naloxone 4 mg / 1 mg and titrate.

GOOD TO REMEMBER

- **Buprenorphine (Tidigesic; buprenorphine-naloxone as Suboxone or Bunorph):** high-affinity *partial* mu-agonist with a ceiling on respiratory depression (safer in overdose than methadone); the signature caution is precipitated withdrawal, so delay the first dose until objective withdrawal (COWS about 8 to 12, roughly 12 to 24 hours after a short-acting opioid); IPS induction is buprenorphine-naloxone 4 mg / 1 mg titrated by 2 to 4 mg/day to a usual maintenance of 8 to 16 mg/day.

17.7 Methadone: the long-acting full agonist and its induction ceiling

Where it fits. Methadone is a long-acting *full* mu-agonist, an alternative first-line agent for both detoxification and maintenance (NICE 2011; WHO mhGAP 2016). It does not precipitate withdrawal, so it can be started without waiting for a high COWS, but as a full agonist it has no ceiling on respiratory depression and the first two weeks of treatment are a high-risk overdose window because of methadone's long half-life and accumulation (BAP 2026). Its half-life of roughly 24 hours or more is what makes it once-daily and smooth, but also what makes early induction dangerous.

The induction ceiling. The verified safety rule is a cautious start: WHO and WHO mhGAP set the initial daily dose by neuroadaptation, generally **not more than 20 mg** and certainly not more than 30 mg, increasing by no more than about 10 mg every few days (WHO 2009; WHO mhGAP 2016). Effective maintenance is usually **60 to 120 mg/day**, since doses below 60 mg/day carry a two- to three-fold higher risk of dropout (BAP 2026; WHO mhGAP 2016). Monitor the QT interval. In India, methadone maintenance is restricted to government OST clinics under the National AIDS Control Organisation (NACO) and select institutions, so the private psychiatrist refers rather than prescribes it (IPS guidelines).

FEATURE	BUPRENORPHINE (PARTIAL AGONIST)	METHADONE (FULL AGONIST)
Overdose safety	**Ceiling on respiratory depression; safer**	No ceiling; high-risk first 2 weeks
Induction timing	**Must wait for objective withdrawal (COWS about 8 to 12)**	No wait; can precipitate none, but start low
Initial dose	Buprenorphine-naloxone 4 mg / 1 mg	**20 mg/day or less (max 30)**
Usual maintenance	8 to 16 mg/day (up to 24)	**60 to 120 mg/day**
India access	Outpatient de-addiction first-line (as bup-naloxone)	Restricted to NACO OST clinics

Buprenorphine versus methadone for opioid withdrawal and substitution; buprenorphine is safer and India's outpatient first-line but must await objective withdrawal, methadone needs no wait but a low, cautious induction (IPS guidelines; NICE 2011; WHO mhGAP 2016; BAP 2026).

GOOD TO REMEMBER

- **Methadone:** long-acting *full* mu-agonist with no ceiling on respiratory depression, so the signature caution is overdose during the first two weeks of induction; start low (20 mg/day or less, never above 30 mg), increase by about 10 mg every few days, maintain at 60 to 120 mg/day, and monitor the QT interval; in India it is confined to NACO-licensed OST clinics.

17.8 Clonidine and lofexidine: the alpha-2 agonists

How they work. The alpha-2 adrenergic agonists clonidine and lofexidine suppress the noradrenergic hyperactivity that drives opioid withdrawal by reducing central sympathetic outflow at the locus coeruleus. They are non-opioid, so they neither substitute at the mu-receptor nor risk diversion, and they treat the autonomic features (sweating, tachycardia, lacrimation, rhinorrhoea, gastrointestinal upset) but not the craving or the aches as completely as an agonist taper (Kaplan and Sadock 2024; BAP 2026). They are second-line to agonists, used where methadone and buprenorphine are declined, contraindicated or unavailable, or where a shorter non-opioid detoxification is wanted (NICE 2011; VA/DoD 2021).

Lofexidine versus clonidine. The examinable discriminator: both work, but **lofexidine** is preferred over **clonidine** because clonidine's hypotension and sedation are dose-limiting, whereas lofexidine causes less postural hypotension (BAP 2026; WHO 2009; NICE 2011). NICE will consider lofexidine for people who decline methadone or buprenorphine, want a short detoxification, or have mild or uncertain dependence, but advises against using clonidine routinely. The clinical caution for both is blood pressure: check it before dosing and hold for hypotension. Lofexidine is not widely available in India, so clonidine (0.1 to 0.3 mg three times daily, titrated to blood pressure) is the practical alpha-2 agent here (IPS guidelines).

TRAP **Do not read opioid withdrawal as the medical emergency alcohol withdrawal is.** In an otherwise healthy adult opioid withdrawal is not life-threatening; the danger is the aftermath, overdose on lost tolerance and withdrawal-driven suicidality, so the emergency planning is take-home naloxone and suicide-risk assessment, not intensive medical rescue of the withdrawal itself.

GOOD TO REMEMBER

- **Clonidine and lofexidine (alpha-2 agonists):** non-opioid agents that damp the locus-coeruleus noradrenergic storm and treat the autonomic features of withdrawal; second-line to agonists; the signature caution is hypotension (check blood pressure before each dose); lofexidine is preferred (less postural hypotension) but clonidine 0.1 to 0.3 mg three times daily is the practical Indian choice; neither adequately covers craving, so pair with relapse-prevention planning.

17.9 Symptomatic agents and the buprenorphine taper regimen

The adjuncts. Whichever backbone is chosen, targeted symptomatic agents make withdrawal tolerable: **loperamide** for diarrhoea, an antiemetic (ondansetron or prochlorperazine) for nausea and vomiting, paracetamol or an NSAID for the muscle and bone aches, an antispasmodic (dicyclomine) for cramps, and hydroxyzine or a short course of a low-dose benzodiazepine or a sedative for insomnia (IPS guidelines; Kaplan and Sadock 2024). These target the individual features and are used alongside, not instead of, the agonist or alpha-2 backbone.

The IPS taper. The Indian Psychiatric Society's preferred medically assisted withdrawal is a buprenorphine taper, reductions of 2 to 4 mg/day over 7 to 14 days from the stabilisation dose, with clonidine 0.1 to 0.3 mg three times daily, loperamide as needed for diarrhoea, paracetamol or NSAIDs for myalgia, ondansetron as needed for nausea, and hydroxyzine or a short benzodiazepine course for insomnia (IPS guidelines).

WITHDRAWAL FEATURE	SYMPTOMATIC AGENT	NOTE
Autonomic overactivity (sweating, tachycardia, rhinorrhoea)	**Clonidine or lofexidine**	Alpha-2 backbone; monitor blood pressure.
Diarrhoea	Loperamide as needed	Peripheral opioid; does not cross into the CNS.
Nausea and vomiting	Ondansetron or prochlorperazine	As needed.
Muscle and bone aches	**Paracetamol or NSAID**	Regular dosing during the peak.
Abdominal cramps	Dicyclomine (antispasmodic)	As needed.
Insomnia	Hydroxyzine; short low-dose benzodiazepine or sedative	Short course only; avoid dependence-swapping.

Symptomatic agents for opioid withdrawal, matched to the feature; these are adjuncts to the agonist taper or alpha-2 backbone, never the whole treatment (IPS guidelines; Kaplan and Sadock 2024).

17.10 After withdrawal: naltrexone, the opioid-free window and take-home naloxone

Naltrexone for relapse prevention. Once withdrawal is complete, naltrexone (an oral mu-antagonist; Indian brands Nodict, Naltima, unconfirmed in this corpus) can be offered for relapse prevention to those wanting abstinence, at 50 mg/day orally (BAP 2026; IPS guidelines; WHO 2009). The absolute rule, and a favourite emergency-avoidance question: naltrexone must never be given to a current opioid user, because as an antagonist it precipitates immediate, severe withdrawal. It is started only after a documented **opioid-free window** of at least **7 to 10 days** (longer after methadone), confirmed by a negative urine opioid screen and, where uncertain, a naloxone challenge (IPS guidelines; Kaplan and Sadock 2024). A signature caution is that naltrexone strips tolerance, so relapse on stopping it carries a high overdose risk.

Naloxone for overdose. Naloxone is the rescue antagonist for opioid overdose. The IPS dosing is intramuscular 0.4 to 2 mg, repeated every 2 to 3 minutes up to 10 mg, or intranasal 4 mg per spray repeated after 2 to 3 minutes (IPS guidelines; WHO 2009). Every guideline recommends *take-home* naloxone with paired family training in rescue breathing and the recovery position for anyone with current or recent opioid use, especially in the high-overdose windows after detoxification or release from custody (BAP 2026; IPS guidelines; WHO 2009).

GOOD TO REMEMBER

- **Naltrexone (oral mu-antagonist, 50 mg/day; Nodict, Naltima):** for relapse prevention after abstinence only; the criterion contraindication is any current opioid use (it precipitates severe withdrawal), so start only after a documented opioid-free window of 7 to 10 days (longer post-methadone) with a negative urine screen; caution, it removes tolerance, so relapse afterwards risks fatal overdose.
- **Naloxone (mu-antagonist, overdose rescue; e.g. Nexnal, brand unconfirmed here):** IM 0.4 to 2 mg repeated every 2 to 3 minutes up to 10 mg, or intranasal 4 mg per spray; the dose-anchored action is take-home naloxone plus family rescue-breathing training for anyone with current or recent opioid use, especially post-detoxification or post-release.

17.11 The India frame: the treatment gap, NDPS and OST access

The clinical reality. India carries a very large opioid-use treatment gap, with most dependent users never reaching formal care, and opioid dependence (heroin in the north, and pharmaceutical opioids and, historically, natural-opium use in agrarian belts) concentrated in government de-addiction centres, the Drug De-addiction Programme, and the day care centre model rather than in general practice (IPS guidelines). The practical consequence is that buprenorphine-naloxone, inducted on a COWS of about 8 to 12, is the outpatient backbone the psychiatrist actually uses, while methadone maintenance is confined to NACO-licensed OST clinics and select institutions, so private practice refers for methadone rather than prescribing it.

Access and law. Buprenorphine and the other opioid agents are controlled under the Narcotic Drugs and Psychotropic Substances (NDPS) Act, 1985, whose scheduling and prescriber requirements shape access; the medico-legal detail, including treatment in lieu of conviction, sits in the Mental health legislation and forensic psychiatry notes. Harm-reduction services, needle and syringe programmes, safer-injecting education and take-home naloxone, are offered in addition to (not instead of) agonist maintenance for any current injector, alongside baseline and

annual screening for HIV, HBV, HCV, syphilis and tuberculosis (IPS guidelines). The wider CBT and motivational-interviewing technique that anchors the psychosocial arm is developed in the Psychotherapies, clinical assessment, MSE and nosology notes.

INDIA

Three India-specific points recur in the viva. First, buprenorphine-naloxone (the 4:1 sublingual combination) is the outpatient first-line agonist, inducted at 4 mg / 1 mg once the COWS reaches about 8 to 12 (roughly 12 to 24 hours after a short-acting opioid), because it is accessible, ambulatory and diversion-deterrent. Second, methadone is *not* a private-practice option, it is restricted to NACO OST clinics, so the correct answer to "how would you start methadone" often includes "refer to the nearest licensed OST centre". Third, lofexidine is largely unavailable, so clonidine is the practical alpha-2 agent despite its dose-limiting hypotension. Naltrexone (Nodict, Naltima) remains widely used for relapse prevention in supervised, family-monitored programmes, but only after a confirmed 7-to-10-day opioid-free window.

8 to 12 COWS THRESHOLD TO BEGIN BUPRENORPHINE INDUCTION (OBJECTIVE WITHDRAWAL)	**above 36** COWS SCORE DEFINING SEVERE OPIOID WITHDRAWAL	**6 to 12 h** ONSET OF HEROIN (SHORT-ACTING OPIOID) WITHDRAWAL AFTER THE LAST DOSE	**7 to 10 days** OPIOID-FREE WINDOW REQUIRED BEFORE STARTING NALTREXONE

HOLD THIS

Opioid withdrawal is a noradrenergic storm (mydriasis, lacrimation, rhinorrhoea, piloerection, aches) that is intensely uncomfortable but not life-threatening, with onset and peak tracking the parent opioid's half-life (heroin 6 to 8 hours, methadone 24 to 48 hours); stage it with the COWS (5 to 12 mild, 13 to 24 moderate, 25 to 36 moderately severe, above 36 severe), induct buprenorphine only once objective withdrawal is established (COWS about 8 to 12), use clonidine or lofexidine plus symptomatic agents where an agonist is declined, never give naltrexone to a current user (precipitated withdrawal; needs a 7 to 10 day opioid-free window), and give take-home naloxone for the post-detoxification overdose window.

18 · Opioid substitution therapy

Of all the management topics in this block, **opioid substitution therapy** is the one where a wrong number is dangerous, so examiners test it with confidence. The whole logic is simple: opioid dependence is a relapsing brain disorder, forced abstinence is followed by falling tolerance and a high risk of fatal overdose, and the single intervention that reliably keeps people alive and in care is a long-acting oral opioid agonist given daily under supervision. That is what **substitution therapy** means. The two agents to know cold are **buprenorphine**, a partial mu agonist with a ceiling on respiratory depression, and **methadone**, a full agonist with a slow titration and a QTc caution. Get their mechanisms, their **induction** doses and their **maintenance** targets exact, and the rest, from precipitated withdrawal to the Indian access story, follows.

Why it matters clinically. This is agonist maintenance, not a cure and not a detox: the goal is retention, blockade of illicit opioids and a fall in death risk, so the commonest exam error is to frame it as "getting the patient off drugs". The reward and mesolimbic-dopamine anatomy on

which the opioid pull is built is developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and is not re-derived here. The medico-legal frame, the NDPS Act and OST prescriber licensing, is developed in the Mental health legislation and forensic psychiatry notes; here the concern is the drug, the dose, the line and the monitoring. One figure carries this topic: Fig 13.14, the buprenorphine induction and precipitated-withdrawal timeline.

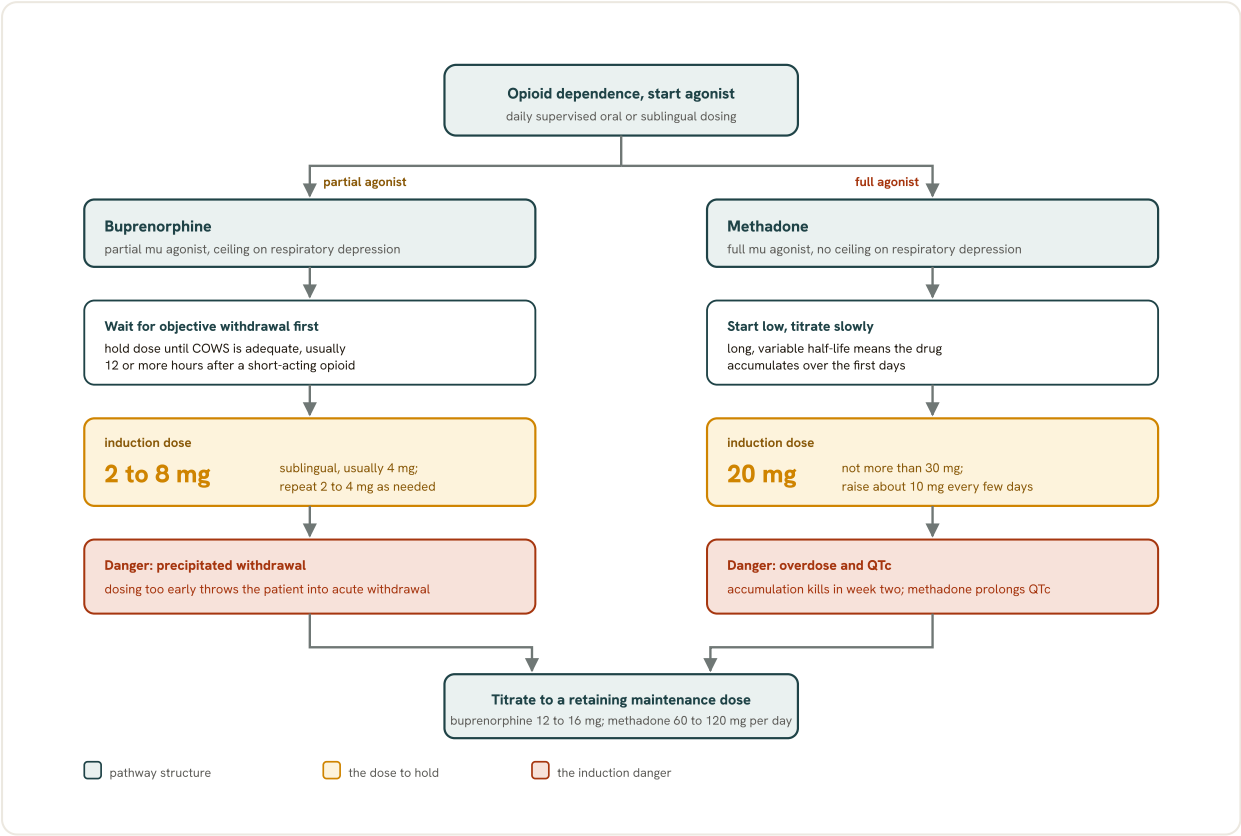


Fig 13.14 Opioid substitution: buprenorphine versus methadone induction. Buprenorphine is a partial mu agonist with a ceiling on respiratory depression: hold the first dose until objective withdrawal (an adequate COWS, usually 12 or more hours after a short-acting opioid), then induct at 2 to 8 mg sublingually, because dosing too early precipitates withdrawal. Methadone is a full agonist with no respiratory ceiling: start low at 20 mg (not more than 30) and titrate slowly by about 10 mg every few days, because its long half-life lets the drug accumulate into a fatal overdose in the second week, and it prolongs the QTc. Both then titrate to a retaining maintenance dose.

18.1 The principle: agonist maintenance keeps people alive and in care

What OST is for. Opioid agonist maintenance treatment (OATM, often just **OST**) substitutes a long-acting, orally or transmucosally delivered opioid for the short-acting injected drug, occupying the mu receptor steadily so that withdrawal and craving are suppressed and the "rush" of additional illicit opioid is blunted by tolerance and receptor occupancy (Kaplan and Sadock 2024). The evidence-based aims are retention in treatment, reduction of non-prescribed opioid use, and a fall in all-cause and overdose mortality; abstinence is a possible later goal, not the entry criterion.

The first-line position. The British Association for Psychopharmacology (BAP) recommends offering opioid substitution therapy, methadone or transmucosal buprenorphine or long-acting injectable buprenorphine, as the initial approach for opioid dependence, chosen with the patient,

because it delivers stabilisation, retention and reduced death risk (BAP 2026). This is a verified first-line and must anchor any answer.

RULE **Maintain, do not just detox.** Withdrawal management alone increases relapse and overdose death; every guideline (BAP, NICE, WHO, VA/DoD, CANMAT) says do not offer detoxification without planned ongoing agonist maintenance or naltrexone.

18.2 Buprenorphine: a partial mu agonist with a ceiling on respiratory depression

Mechanism and the ceiling. Buprenorphine is a high-affinity *partial* agonist at the mu-opioid receptor (and a kappa antagonist). Because it is a partial agonist, its effect on respiratory depression plateaus, a **ceiling effect**, so escalating the dose does not keep depressing respiration the way a full agonist does; this makes it markedly safer in overdose than methadone (Kaplan and Sadock 2024; Maudsley 2021). Its very high receptor affinity also means it displaces and blocks other opioids, which is why extra heroin "does nothing" on an adequate dose, but is exactly why it can trigger precipitated withdrawal.

Why it precipitates withdrawal. If buprenorphine is given while a full agonist still occupies the receptors, its high affinity knocks the full agonist off but replaces it with only a partial signal, so net opioid effect falls abruptly and the patient is thrown into acute withdrawal within minutes to an hour. The mandatory safeguard is to wait for objective withdrawal, an adequate COWS (Clinical Opiate Withdrawal Scale), before the first dose.

WORKED EXAMPLE

A man who last injected heroin 14 hours ago arrives sweating, with dilated pupils, yawning, gooseflesh and a runny nose; his COWS is 14. This is objective moderate withdrawal, so it is safe to induct: give buprenorphine **4 mg** sublingually, observe for an hour, and repeat 2 to 4 mg if withdrawal persists (APA 2021; IPS 2014). Had you dosed him at hour 4 with a COWS of 3, you would have precipitated severe withdrawal.

GOOD TO REMEMBER

- **Buprenorphine (Indian brand Tidigesic; buprenorphine-naloxone as Suboxone or Bunorph):** a high-affinity *partial* mu agonist / kappa antagonist with a ceiling on respiratory depression (safer in overdose than methadone); the signature caution is precipitated withdrawal, so the first dose waits for objective withdrawal (COWS at least 8 to 12, usually 12 or more hours after a short-acting opioid); induct at 2 to 4 mg (up to 8 mg), maintenance usually 12 to 16 mg/day (BAP target at or above 16 mg/day).

18.3 Buprenorphine induction: wait for withdrawal, then escalate fast

The induction protocol. Withhold the first dose until the patient is in objective opioid withdrawal, typically a COWS of at least 8 to 12 and roughly 12 to 24 hours after the last short-acting opioid (longer for methadone). Then give an initial dose of **2 to 8 mg** sublingually, most commonly 4 mg, observe, and repeat 2 to 4 mg every few hours as withdrawal allows on day one (WHO 2016; APA 2021; IPS 2014). Buprenorphine can reach a therapeutic dose of 12 to 16 mg within 2 to 3 days, far faster than methadone (Maudsley 2021).

The buprenorphine-naloxone combination. The combination product (buprenorphine with naloxone in a 4:1 ratio) is designed to deter injection: taken sublingually the naloxone is poorly absorbed and inert, but if the tablet is crushed and injected the naloxone becomes bioavailable and precipitates withdrawal, removing the incentive to divert. This is the first-line agonist maintenance option in Indian outpatient practice (IPS 2014).

OPIOID LAST USED	SPONTANEOUS WITHDRAWAL ONSET	SAFE TO START BUPRENORPHINE
Short-acting (heroin, morphine)	6 to 8 hours after last use	at COWS >= 8 to 12, usually 12 or more hours
Long-acting (methadone)	24 or more hours after last use	after taper to 30 mg/day or less, 24 to 36 hours, COWS 8 to 12
Long-acting (buprenorphine itself)	24 or more hours, milder syndrome	not applicable (already the agent)

Withdrawal-onset windows that set the mandatory wait before the first buprenorphine dose; starting too early precipitates withdrawal (Kaplan and Sadock 2024; BAP 2026).

18.4 Methadone: a full agonist needing slow titration and a QTc caution

Mechanism and the risk. Methadone is a long-acting *full* mu-opioid receptor agonist. Because it is a full agonist it has no ceiling on respiratory depression, so overdose in the induction fortnight is the principal danger, compounded by its long and variable half-life, which lets the drug accumulate over the first days even at a fixed dose (BAP 2026; Maudsley 2021). It is largely metabolised by CYP3A4, so inhibitors and inducers shift its level, and it prolongs the QT interval, so a baseline and monitoring ECG is prudent, especially above 100 mg/day or with other QT-prolonging drugs.

Slow titration, high maintenance. Methadone is started low and raised slowly: WHO advises an initial daily dose set by neuroadaptation, generally not more than **20 mg** and certainly not more than 30 mg, with increases of no more than about 10 mg every few days (WHO 2016). The therapeutic maintenance range is high, typically **60 to 120 mg/day**, because doses under 60 mg/day carry a two- to three-fold higher dropout (BAP 2026; WHO 2016).

COMMON TRAP

Do not titrate methadone quickly to "get on top of" withdrawal. Its long half-life means the drug keeps accumulating for days after a dose change, so a rapid rise stacks up into a fatal overdose in the second week, the highest-risk window. The rule is low start (20 to 30 mg), small increments (about 10 mg every few days), and supervised dosing during induction.

GOOD TO REMEMBER

- **Methadone:** a long-acting *full* mu agonist with no respiratory ceiling; the signature cautions are overdose during the first two weeks (long, variable half-life, accumulation) and QTc prolongation (CYP3A4-metabolised); induct at 20 mg (not more than 30 mg), raise by about 10 mg every few days, maintenance 60 to 120 mg/day; in India it is restricted to licensed government OST/NACO clinics, not private prescription.

18.5 Buprenorphine versus methadone: the head-to-head examiners want

How to choose. Both are first-line agonist maintenance (BAP, NICE, WHO, WFSBP, CANMAT all list both); the choice is by safety profile, patient preference and setting. Buprenorphine is safer in overdose and in cardiorespiratory comorbidity, has a milder withdrawal on cessation, and reaches a therapeutic dose within days; methadone gives greater treatment retention and suits patients at high diversion risk or those who destabilise on a partial agonist (Maudsley 2021; BAP 2026). WHO, weighing population-level retention, advises most patients use methadone in adequate doses; NICE treats the two as equivalent first-line choices.

FEATURE	BUPRENORPHINE (PARTIAL AGONIST)	METHADONE (FULL AGONIST)
Respiratory depression	ceiling effect, safer in overdose	no ceiling, overdose risk in induction
Start-of-treatment risk	precipitated withdrawal if started too early	accumulation and overdose in first 2 weeks
Time to therapeutic dose	2 to 3 days (fast)	several weeks (slow titration)
Initial (induction) dose	2 to 8 mg after COWS >= 8 to 12	20 mg (not more than 30 mg)
Usual maintenance dose	12 to 16 mg/day (BAP >= 16 mg/day)	60 to 120 mg/day
Cardiac	little QT effect	QTc prolongation, ECG monitoring
Retention vs the other	slightly lower retention	greater retention
Cessation withdrawal	milder, more delayed	more marked and prolonged

Buprenorphine versus methadone: the discriminators that decide agonist choice (Maudsley 2021; BAP 2026; WHO 2016).

18.6 Maintenance, monitoring and the exit routes

Maintenance targets. Optimise the dose to the level that retains the person in treatment and stops non-prescribed opioid use: buprenorphine typically at or above 16 mg/day (range 12 to 24 mg), methadone typically above 60 mg/day (60 to 120 mg/day), individualised and titrated to clinical response rather than a blood level (BAP 2026; WHO 2016). Continue for at least 12 months; open-ended long-term maintenance is appropriate and is not "failure" (IPS 2014).

What to monitor. Directly supervise dosing in the early phase (diversion and overdose risk), use random urine drug screens during induction and stabilisation, and screen for blood-borne viruses (HIV, HBV, HCV), syphilis and tuberculosis at baseline and annually in anyone with injecting use; check LFTs and, for methadone, the QTc (IPS 2014; BAP 2026). Provide take-home naloxone and overdose-reversal training to the patient and family, especially around the high-risk windows of post-detox, post-release and post-disengagement, when tolerance has fallen.

PEARL

Naltrexone is the opposite of substitution: a pure opioid antagonist (oral 50 mg/day) for relapse prevention in a patient who *wants* to be abstinent, started only after a documented opioid-free interval of at least 7 to 10 days (longer after methadone) confirmed by negative urine screen. Given to a current opioid user it precipitates severe withdrawal, and after any lapse the lost tolerance makes overdose more likely, so it is a different pathway from OST, not a maintenance agent.

18.7 The Indian OST context: the de-addiction programme, the DDAP model and buprenorphine access

The treatment gap and the setting. India carries a large opioid-use burden, much of it untreated, and services are concentrated in government de-addiction centres and Drug De-addiction Programme (DDAP) units rather than general practice; the apex training and treatment node is the National Drug Dependence Treatment Centre (NDDTC) at AIIMS, with NIMHANS and state centres alongside (IPS 2014). This is the **indian access** reality behind every prescribing choice.

Which agent, and the NDPS frame. In Indian outpatient practice the first-line agonist is *sublingual buprenorphine-naloxone* (4:1), inducted at 4 mg/1 mg once the patient shows objective withdrawal (COWS at least 8 to 12) and titrated to a usual 8 to 16 mg/day (IPS 2014). Methadone is available but restricted to licensed government OST clinics run under the National AIDS Control Organisation (NACO) and select institutions, so the private psychiatrist refers to the nearest licensed OST centre rather than prescribing it. The controlling statute throughout is the Narcotic Drugs and Psychotropic Substances (NDPS) Act, 1985, which governs scheduling, prescriber licensing and the treatment-in-lieu-of-conviction route; its detail sits in the Mental health legislation and forensic psychiatry notes.

INDIA

For an Indian exam, the clean line is: *buprenorphine-naloxone is the workhorse of Indian OST, methadone is largely confined to government OST/NACO clinics*. Buprenorphine's better safety, its take-home suitability in the 4:1 combination that deters injection, and the ease of dispensing it in outpatient de-addiction settings all fit a system with a large treatment gap and limited supervised-dosing capacity. Pair the medication with a needle and syringe programme referral and structured psychosocial treatment for any patient still injecting; harm reduction is offered *in addition to*, never instead of, agonist maintenance (IPS 2014). The whole framework operates under the NDPS Act, 1985.

MNEMONIC

"START LOW, WAIT for the COWS"

Methadone: START LOW (20 mg, not more than 30) and titrate slowly, because a full agonist accumulates and overdose lurks in week two. Buprenorphine: WAIT for the COWS (objective withdrawal, COWS at least 8 to 12) before the first dose, because a high-affinity partial agonist given too early precipitates withdrawal.

8 to 12	2 to 8 mg	20 mg	60 to 120 mg
COWS SCORE OF OBJECTIVE WITHDRAWAL NEEDED BEFORE THE FIRST BUPRENORPHINE DOSE	BUPRENORPHINE INDUCTION DOSE (USUALLY 4 MG)	METHADONE STARTING DOSE (NOT MORE THAN 30)	METHADONE MAINTENANCE RANGE PER DAY

TRAP **Never buprenorphine into a full agonist.** Dosing buprenorphine while a short-acting opioid still occupies the receptor precipitates acute withdrawal within the hour; wait for an objective COWS, do not dose on the clock or on the patient's word alone.

HOLD THIS

Opioid substitution therapy is agonist maintenance to retain people and cut overdose death: buprenorphine is a partial mu agonist with a respiratory ceiling, inducted at 2 to 8 mg only once objective withdrawal (COWS at least 8 to 12) appears and maintained at 12 to 16 mg/day; methadone is a full agonist started low at 20 mg (not more than 30) and titrated slowly to 60 to 120 mg/day with a QTc caution; in India buprenorphine-naloxone (4:1) is the outpatient first-line while methadone is restricted to government OST/NACO clinics, all under the NDPS Act.

19 · Naltrexone and antagonist relapse prevention

Substitution therapy keeps an opioid receptor *occupied*; antagonist therapy keeps it *blocked*. **Naltrexone** is the mirror image of an agonist maintenance drug: instead of giving a long-acting opioid to suppress craving, you give a pure **opioid antagonist** that sits on the mu receptor and makes any opioid the patient takes do nothing. That is the whole appeal for a highly motivated, abstinence-seeking patient, and it is the whole danger too, because putting an antagonist onto a receptor a full agonist still occupies rips the agonist off and throws the patient into acute withdrawal. This topic is examined on exactly two things: the mechanism (a competitive mu-opioid antagonist, oral and long-acting injectable) and the one rule that a wrong answer fails, the mandatory **opioid-free** window before you ever start it.

Why it matters clinically. Naltrexone is a management/drug topic, so the marks are in the drug, the dose, the line and the monitoring, not in a description of addiction. The single most tested, and most dangerous, error in the whole substance block is starting naltrexone in a current opioid user: it causes severe **precipitated withdrawal**. The mesolimbic-dopamine and opioid reward anatomy that antagonism interrupts is developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and is not re-derived here; the NDPS Act frame behind Indian de-addiction prescribing sits in the Mental health legislation and forensic psychiatry notes.

19.1 The mechanism: a pure competitive mu-opioid antagonist

What it does. Naltrexone is a competitive, essentially pure opioid antagonist at the mu-opioid receptor (with weaker kappa and delta antagonism); it binds the receptor and initiates no signal, so it selectively competes with any exogenous opioid for central and peripheral opioid receptors and blocks their activity (Kaplan and Sadock 2024). It has no agonist action, so the patient gets no "high" from naltrexone itself, there is no reinforcement, no meaningful withdrawal on

stopping, and no diversion value. After an oral dose the opioid blockade lasts up to **72 hours**, which is why once-daily (or even alternate-day) dosing is feasible.

Antagonist versus agonist, the exam contrast. This is the conceptual opposite of opioid substitution therapy, developed in the Opioid substitution therapy notes: substitution occupies the receptor with a long-acting agonist (buprenorphine, methadone) so withdrawal and craving are suppressed; antagonism *blocks* the receptor so a lapse of heroin produces no reward, extinguishing the drug-taking behaviour over time. Naltrexone is therefore a **relapse prevention** agent for a patient who has already detoxified and *wants* to stay abstinent, not a maintenance agent for a patient still using.

PEARL

The three "nal-" opioid antagonists are worth separating: *naloxone* is the short-acting parenteral antidote for overdose reversal (minutes); *naltrexone* is the long-acting oral/injectable antagonist for relapse prevention (days); *nalmefene* is an as-needed antagonist licensed to reduce heavy drinking in alcohol dependence. All three precipitate withdrawal in a current opioid user, because all three are antagonists.

19.2 The oral form: 50 mg a day for relapse prevention

The dose and the two indications. Oral naltrexone is given at **50 mg/day** (available as 25 mg and 50 mg tablets), often started at 25 mg to check tolerability then raised to 50 mg (WHO 2016; NICE 2011). It has two licensed relapse-prevention roles: in *opioid* use disorder, to maintain the receptor blockade in an abstinent, motivated patient; and in *alcohol* use disorder, where it reduces craving and the return to heavy drinking by blunting the opioid-mediated reward of alcohol (Kaplan and Sadock 2024; Maudsley 2021). Oral bioavailability is about 60%, and the active metabolite 6-beta-naltrexol prolongs its action.

The adherence problem. Oral naltrexone's Achilles heel is adherence: a patient who wants to lapse simply stops the tablet a few days beforehand, and a Cochrane review found oral naltrexone no better than placebo for opioid relapse prevention largely because of poor retention (Kaplan and Sadock 2024). This is the entire rationale for the long-acting forms.

GOOD TO REMEMBER

- **Naltrexone (Indian brand Nodict or Naltima; oral):** a competitive pure mu-opioid antagonist (no agonist effect, non-scheduled, no diversion) for relapse prevention in opioid and alcohol use disorder; oral dose **50 mg/day** (start 25 mg), blockade lasts about 72 hours; the signature caution is precipitated withdrawal if given to a current opioid user, so it demands an opioid-free interval first; monitor LFTs (dose-related hepatotoxicity).

19.3 The long-acting injectable and implant: the answer to non-adherence

Extended-release naltrexone. The extended-release injectable form (XR-NTX, brand Vivitrol) delivers **380 mg** intramuscularly once every 4 weeks, giving total naltrexone exposure three- to fourfold higher than daily oral dosing, with an elimination half-life of 5 to 10 days (Kaplan and Sadock 2024). Because a single injection covers a month, it removes the daily decision to take the

tablet, and retention on XR-NTX is at least twice that on oral naltrexone. A subcutaneous naltrexone *implant* lasting about 6 months exists but is investigational, its safety and efficacy not yet established.

What the guidelines say about the forms. The British Association for Psychopharmacology (BAP) recommends, for relapse prevention after opioid withdrawal, *preferring* long-acting injectable naltrexone (monthly) or a naltrexone implant (6-monthly) over oral naltrexone, because the long-acting forms improve treatment retention; naltrexone as a whole is offered to people who wish to be abstinent, in preference to withdrawal management alone (BAP 2026). This is the verified first-line antagonist position and must anchor any answer.

FORM	ROUTE AND SCHEDULE	DOSE (MG)	NOTE
Oral naltrexone	tablet, once daily	50 (start 25)	adherence-limited; blockade ~72 h
XR-NTX injectable (Vivitrol)	deep IM, every 4 weeks	380	BAP-preferred; retention 2x oral
Naltrexone implant	subcutaneous, ~6-monthly	surgical insert	investigational, not established

The three naltrexone formulations and their dosing; the long-acting forms exist to solve the adherence failure of the daily tablet (Kaplan and Sadock 2024; BAP 2026).

INDIA

In India the daily *oral* tablet (naltrexone, marketed as Nodict or Naltima) is the practical option: it is non-scheduled, cheap, and prescribable in any clinical setting without the OST licensing that agonist maintenance requires under the Narcotic Drugs and Psychotropic Substances (NDPS) Act, 1985. The long-acting depot and implant forms are *not yet routinely available* in Indian practice (IPS 2014), so the adherence problem is real and the fix is a co-resident family supervisor who observes the dose, exactly the family-supervised model already used for disulfiram in Indian de-addiction settings. This is a genuine access gap: the form that works best (depot) is the one an Indian patient usually cannot get.

19.4 The critical contraindication: never start naltrexone in a current opioid user

Why it precipitates withdrawal. If naltrexone is given while opioids still occupy the mu receptors, its competitive antagonism displaces the agonist and abruptly strips away all opioid tone, plunging a physiologically dependent patient into acute, severe **precipitated withdrawal** within minutes, far more violent than the gradual spontaneous syndrome (Kaplan and Sadock 2024; Tasman 2024). This is the same mechanism by which naloxone reverses overdose, only here it is unwanted. It is the single most dangerous prescribing error in the substance block, and it is the one the examiner is testing.

The mandatory opioid-free window. Naltrexone can be started only after a documented period of complete opioid abstinence: about **7 to 10 days** opioid-free for short-acting opioids and heroin, and longer after a long-acting opioid such as methadone (Kaplan and Sadock 2024; IPS 2014). The Indian Psychiatric Society is explicit: naltrexone 50 mg/day PO for relapse prevention

only after a documented opioid-free interval of at least 7 to 10 days, confirmed by a negative urine opioid screen and a naloxone challenge, because premature initiation precipitates severe withdrawal (IPS 2014).

WORKED EXAMPLE

A man completed a buprenorphine taper and his last opioid was 4 days ago; he is keen to start naltrexone to "block" any lapse. You do *not* start it. Four days is inside the danger window: residual receptor occupancy means a 50 mg dose now would precipitate acute withdrawal. You wait until he is at least 7 to 10 days opioid-free, confirm a negative urine opioid screen, and, if occult use is a question, do a naloxone challenge, a subcutaneous injection of up to 0.8 mg naloxone with 20 minutes of observation for emergent withdrawal, before the first naltrexone dose (Kaplan and Sadock 2024; IPS 2014).

TRAP **Naltrexone into a current opioid user precipitates withdrawal.** An antagonist onto occupied mu receptors strips the agonist off and causes acute severe withdrawal; confirm an opioid-free interval of about 7 to 10 days (longer after methadone) with a negative urine screen, and never start it "to be safe" while opioids may still be on board.

19.5 Confirming the window: urine screen and the naloxone challenge

Two checks before the first dose. The opioid-free interval is verified objectively, never on the patient's word alone. First, a negative urine opioid screen. Second, where occult use is possible, a naloxone challenge test: give an SC injection of up to 0.8 mg naloxone and observe for 20 minutes; if no withdrawal emerges, the patient is opioid-free and naltrexone can be started (Kaplan and Sadock 2024). Naloxone is used for the challenge precisely because it is short-acting, so any precipitated withdrawal it uncovers is brief.

The rapid-detox alternative. Newer protocols compress the unprotected wait: a rapid or antagonist-assisted detoxification uses ascending low-dose oral naltrexone (starting 0.25 mg) with clonidine and other symptomatic cover over about a week, allowing XR-NTX induction on day eight after a negative naloxone challenge, so the patient is opioid-free from the outset and the vulnerable 7-to-10-day gap is removed (Kaplan and Sadock 2024). Note the guideline caution alongside this: WHO and NICE both warn against *ultra-rapid* antagonist-induced detoxification under heavy sedation or general anaesthesia, which adds risk without benefit (WHO 2016; NICE 2011).

19.6 Monitoring, cautions and the overdose paradox on stopping

What to monitor. Naltrexone is dose-relatedly hepatotoxic, so baseline and periodic liver function tests are required; before starting it in opioid use disorder, VA/DoD advise baseline transaminases and bilirubin repeated at 6 and 12 months, and it is avoided in acute hepatitis or hepatic failure (VA/DoD; BAP 2026). It is generally well tolerated otherwise, with nausea, headache and dysphoria the common complaints.

The lost-tolerance overdose risk. A crucial safety point: because naltrexone maintains a blockade and abstinence, opioid tolerance falls while the patient is on it. If the patient stops

naltrexone (or a depot dose wears off) and then lapses to their old opioid dose, that dose is now potentially fatal, the lost-tolerance overdose paradox (Kaplan and Sadock 2024; BAP 2026). Retention is therefore not just about efficacy but about survival, and the analgesia problem is the same in reverse: an emergency opioid analgesic will not work through the blockade.

COMMON TRAP

Do not read a stable, adherent patient's *falling* opioid tolerance as a good thing to relax about. The most dangerous moment on naltrexone is *stopping* it: a patient who lapses to their previous "usual" heroin dose after the blockade lifts can die, because tolerance is gone. Counsel this explicitly, pair the patient with a take-home naloxone kit, and prefer the long-acting depot to avoid gaps in cover.

GOOD TO REMEMBER

- **XR-NTX (long-acting injectable naltrexone, Vivitrol):** 380 mg deep IM every 4 weeks; BAP-preferred over oral for opioid relapse prevention because it roughly doubles retention; same absolute contraindication (must be opioid-free 7 to 10 days first, or the depot precipitates a month-long withdrawal); monitor LFTs; warn about lost-tolerance overdose if the injection lapses.

19.7 Where naltrexone sits against agonist maintenance, and the guideline lines

Antagonist or agonist? For most patients guidelines still favour *agonist* maintenance (buprenorphine, methadone) over antagonist therapy, because agonists retain more people in treatment and cut death more reliably; WHO advises offering withdrawal management, agonist maintenance *and* naltrexone, but tells most patients to choose agonist maintenance (WHO 2016). Naltrexone earns its place in the specific, highly motivated, abstinence-committed patient, or where external contingency exists (probation, professional monitoring), or where the patient refuses an agonist. The Australian coronial data are sobering: patients on oral naltrexone were several times more likely to overdose than those on agonist maintenance, driven by the lost-tolerance mechanism (Kaplan and Sadock 2024).

The four-guideline map. BAP: offer naltrexone to those wishing to be abstinent, preferring the long-acting injectable or implant over oral. The Indian Psychiatric Society (IPS guidelines): naltrexone 50 mg/day PO only after a documented 7-to-10-day opioid-free interval confirmed by negative urine screen and naloxone challenge, with adherence the main limitation and depot forms not yet routine in India (IPS 2014). NICE: use oral naltrexone for relapse prevention after alcohol withdrawal (start 25 mg, aim 50 mg/day) and, for opioids, do not offer rapid antagonist detoxification under sedation. WHO: oral naltrexone 50 mg/day after withdrawal is an option, monitored for delirium, vomiting and diarrhoea during induction, but agonist maintenance is preferred for most (WHO mhGAP 2016).

GUIDELINE	NALTREXONE POSITION (OPIOID RELAPSE PREVENTION)
BAP (2026)	Offer to abstinence-seeking patients; prefer long-acting injectable or implant over oral
Indian Psychiatric Society (2014)	50 mg/day PO only after 7 to 10 days opioid-free, confirmed by urine screen and naloxone challenge; depot not yet routine
NICE (2011)	Oral for alcohol relapse prevention (25 then 50 mg/day); avoid ultra-rapid antagonist detox under sedation
WHO mhGAP (2016)	Oral 50 mg/day an option after withdrawal; agonist maintenance preferred for most patients

The antagonist relapse-prevention position across the four guidelines; BAP leads with the long-acting form, all agree on the mandatory opioid-free start.

RULE **Block only an empty receptor.** Naltrexone is started only in a patient who is already fully detoxified and abstinent (about 7 to 10 days opioid-free, verified), never as a way to *achieve* abstinence in someone still using.

MNEMONIC

"7 to 10 CLEAN before you BLOCK"

Before you start the antagonist (BLOCK), the patient must be 7 to 10 days CLEAN (opioid-free), proven by a negative urine screen and, if in doubt, a naloxone challenge. Skip the CLEAN window and you precipitate withdrawal.

7 to 10 days OPIOID-FREE INTERVAL REQUIRED BEFORE STARTING NALTREXONE (LONGER AFTER METHADONE)	**50 mg** ORAL NALTREXONE DAILY RELAPSE-PREVENTION DOSE	**380 mg** XR-NTX DEPOT INJECTION, EVERY 4 WEEKS	**0.8 mg** SC NALOXONE CHALLENGE DOSE, OBSERVE 20 MINUTES

HOLD THIS

Naltrexone is a pure competitive mu-opioid antagonist for relapse prevention (oral 50 mg/day, or the BAP-preferred long-acting injectable XR-NTX 380 mg IM every 4 weeks) in a motivated, already-detoxified patient; it blocks opioid reward but never suppresses withdrawal, so starting it in a current opioid user precipitates severe withdrawal, and it may be started only after a documented opioid-free interval of about 7 to 10 days (longer after methadone) confirmed by a negative urine screen and, if needed, a naloxone challenge.

20 · Opioid detoxification and the rapid-detox controversy

Detoxification is the medically supervised process of taking a physically dependent person off opioids while covering the withdrawal, and it is examined less for its mechanics than for two things: the menu of legitimate **detox approaches** (an agonist taper with buprenorphine or methadone, and alpha-2-agonist-assisted withdrawal) and the hard line every guideline draws against detoxification carried out at speed under sedation or anaesthesia. The examinable spine is

a single sentence: **detoxification** is never the treatment, it is a gateway to ongoing agonist maintenance or to naltrexone, and the faster and more heroic the method, the worse and more dangerous it tends to be.

Why it matters clinically. A viva that opens "how would you detoxify this heroin user" is testing whether you know that withdrawal management alone produces high relapse and, through lost tolerance, fatal overdose (BAP 2026; NICE 2011; VA/DoD 2021), and whether you can name the two safe backbones and reject the two unsafe short-cuts. The withdrawal syndrome itself, its noradrenergic time-course, the COWS bands, and the buprenorphine and methadone induction and maintenance numbers are developed in the opioid-withdrawal and opioid-substitution material and are not re-derived here; this topic is about the *choice of detoxification method* and the **rapid detox** and **ultra-rapid detox** controversy that examiners love because it has a clean, evidence-anchored answer. The reward-pathway and locus-coeruleus mechanics sit in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the NDPS Act frame sits in the Mental health legislation and forensic psychiatry notes.

20.1 What detoxification is (and what it is not)

The definition. Detoxification (increasingly called *medically assisted withdrawal*) is the supervised, symptom-covered removal of an opioid from a dependent person, achieved either by substituting a controlled agonist and tapering it, or by suppressing the withdrawal pharmacologically with a non-opioid while the illicit opioid clears (Tasman; Kaplan and Sadock 2024; Maudsley Prescribing Guidelines). It is a discrete, time-limited procedure, not a treatment for the disorder.

The governing rule. Every guideline is unanimous that detoxification must not be a stand-alone: do not undertake opioid withdrawal management without planned ongoing pharmacotherapy (agonist maintenance or naltrexone) and psychosocial support, because withdrawal alone carries a high risk of relapse and, through lost tolerance, of fatal overdose (BAP 2026; VA/DoD 2021; NICE 2011; CANMAT). The most serious drawback of detoxification, Tasman states plainly, is that the risk of relapse after completion is very high, so a strong aftercare plan (residential care, a solid outpatient programme, or pharmacological maintenance) is mandatory (Tasman; Kaplan and Sadock 2024).

RULE **Detoxify only into something.** Withdrawal management is a bridge, never a destination, so never detoxify without a planned onward arm (agonist maintenance or naltrexone) and take-home naloxone in place before you start.

20.2 The menu of legitimate detox approaches

The four modalities. Tasman frames the **detox approaches** as four: the alpha-2 agonists (clonidine, lofexidine); the long-acting full agonist methadone by taper; the partial agonist buprenorphine by taper; and rapid detoxification under general anaesthesia (Tasman). The first three are legitimate and guideline-endorsed; the fourth is the controversy this topic turns on. Methadone and buprenorphine double as the agents for post-detoxification agonist maintenance, which is why the "detoxify then maintain" and "just maintain" paths blur into one another.

The guideline default. NICE offers methadone or buprenorphine as the first-line treatment for opioid detoxification, with lofexidine reserved for those who decline them, want to detoxify within a short period, or have mild or uncertain dependence (NICE 2011). WHO mhGAP recommends tapered opioid agonists generally, with alpha-2 agonists as an alternative, and adds that agonist maintenance is usually more effective than detoxification at all (WHO mhGAP 2016). The Indian Psychiatric Society makes a buprenorphine taper the preferred medically assisted withdrawal regimen (IPS guidelines).

DETOX APPROACH	WHAT IT IS	GUIDELINE STANDING
Buprenorphine taper	**Stabilise on partial agonist, then reduce**	First-line (NICE; IPS preferred; BAP)
Methadone taper	Stabilise on long-acting full agonist, then reduce	First-line (NICE; WHO)
Alpha-2 agonist (lofexidine, clonidine)	Non-opioid suppression of noradrenergic storm	Second-line; lofexidine preferred
Rapid / ultra-rapid under sedation or anaesthesia	**Antagonist-precipitated withdrawal under sedation or general anaesthesia**	Not recommended (BAP; NICE; WHO)

The four opioid detox approaches; the first three are legitimate, the fourth is contraindicated across guidelines (Tasman; NICE 2011; WHO mhGAP 2016; BAP 2026).

20.3 The buprenorphine taper: the workhorse of tapering

Why it leads. A buprenorphine (Indian brand Tidigesic; as buprenorphine-naloxone, Suboxone or Bunorph) taper is the preferred medically assisted withdrawal because the partial agonist gives a ceiling on respiratory depression, blocks illicit top-ups, and tapers comfortably; it is the outpatient backbone of Indian de-addiction practice (IPS guidelines; BAP 2026). The one non-negotiable inherited from induction is timing: the first dose is delayed until objective withdrawal (COWS about **8 to 12**) because buprenorphine will precipitate withdrawal if a full agonist is still on the receptor.

The taper by the number. The IPS taper reduces buprenorphine by **2 to 4 mg/day** over **7 to 14 days** from the stabilisation dose, with symptomatic cover (IPS guidelines). NICE times buprenorphine detoxification over 14 days to a few weeks in the community and 7 to 14 days as an inpatient (NICE 2011; Maudsley Prescribing Guidelines). Maudsley graduates the reduction to the dose: above 16 mg by 4 mg every 1 to 2 weeks, 8 to 16 mg by 2 to 4 mg every 1 to 2 weeks, 2 to 8 mg by 2 mg per week or fortnight, and below 2 mg by 0.4 to 0.8 mg per week (Maudsley Prescribing Guidelines).

DAILY BUPRENORPHINE (MG)	REDUCTION STEP
Above 16	**4 mg every 1 to 2 weeks**
8 to 16	2 to 4 mg every 1 to 2 weeks
2 to 8	2 mg per week or fortnight
Below 2	**0.4 to 0.8 mg per week**

Maudsley buprenorphine reduction regime; the step shrinks as the dose falls, the final milligrams being the hardest (Maudsley Prescribing Guidelines).

GOOD TO REMEMBER

- **Buprenorphine (Tidigesic; buprenorphine-naloxone as Suboxone or Bunorph):** partial mu-agonist with a ceiling on respiratory depression, the preferred tapering agent for detoxification; the signature caution is precipitated withdrawal, so start only in objective withdrawal (COWS about 8 to 12); the IPS taper reduces by 2 to 4 mg/day over 7 to 14 days, and the final sub-2 mg steps (0.4 to 0.8 mg per week) are the hardest.

20.4 The methadone taper: the slow, long-acting backbone

Where it fits. A methadone taper is the alternative first-line detoxification, a long-acting full agonist that tapers slowly and smoothly (NICE 2011; WHO mhGAP 2016). Because it is a full agonist it needs no wait for a high COWS, but its long half-life makes the reduction protracted and the first two weeks of any methadone treatment a high-risk overdose window (BAP 2026).

The taper by the number. BAP tapers methadone at about **2 to 5 mg/day** every 1 to 2 weeks, switching to buprenorphine once the dose falls below 30 mg/day if the taper stalls (BAP 2026). Maudsley reduces methadone by 5 to 10 mg weekly or fortnightly, slowing to 1 to 2 mg/week near the end, and notes NICE guidance that methadone reduction is typically 14 to 21 days as an inpatient and up to about 3 months in the community (Maudsley Prescribing Guidelines; NICE 2011). WHO advises tapering opioid agonists over at least 3 days, roughly 5 days for buprenorphine and 10 days for methadone, to minimise rebound withdrawal (WHO 2009).

TRAP **Do not read a longer taper as a worse taper.** The evidence runs the other way, longer stabilisation and prolonged reduction schedules (up to a year) substantially improve the chances of sustained abstinence, so a slow methadone reduction is a feature, not a failure.

GOOD TO REMEMBER

- **Methadone (taper for detoxification):** long-acting full mu-agonist tapered slowly (BAP 2 to 5 mg/day every 1 to 2 weeks; Maudsley 5 to 10 mg weekly, slowing to 1 to 2 mg/week near the end); no wait for induction, but the signature caution is overdose in the first two weeks; switch to buprenorphine below 30 mg/day if the taper stalls, and in India refer to a NACO-licensed OST clinic rather than prescribing methadone in private practice.

20.5 Alpha-2-agonist-assisted withdrawal: the non-opioid route

How it works. The alpha-2 adrenergic agonists clonidine and lofexidine suppress the noradrenergic hyperactivity of withdrawal by reducing central sympathetic outflow at the locus coeruleus; they damp the autonomic features (insomnia, tachycardia, sweating, nausea) but not craving, muscle aches and pain as fully as an agonist taper (Tasman; Kaplan and Sadock 2024). Being non-opioid, they neither substitute at the mu-receptor nor risk diversion, which makes them the route for a shorter, opioid-free detoxification when an agonist is declined, contraindicated or unavailable (NICE 2011; VA/DoD 2021).

Lofexidine versus clonidine. The examinable discriminator: both work, but lofexidine is preferred because it causes less postural hypotension and sedation, effective at doses up to **2**

mg/day without the dose-limiting hypotension that caps clonidine (BAP 2026; WHO 2009; Tasman). NICE will consider lofexidine for a short detoxification but advises against using clonidine or dihydrocodeine routinely. The caution for both is blood pressure, checked before each dose. Lofexidine is not widely available in India, so clonidine **0.1 to 0.3 mg** three times daily, titrated to blood pressure, is the practical alpha-2 agent here (IPS guidelines).

GOOD TO REMEMBER

- **Clonidine and lofexidine (alpha-2 agonists for detoxification):** non-opioid agents that damp the locus-coeruleus noradrenergic storm; second-line to agonists and used for a shorter opioid-free detox; the signature caution is hypotension (check blood pressure before each dose); lofexidine is preferred (less postural hypotension, effective up to 2 mg/day) but clonidine 0.1 to 0.3 mg three times daily is the practical Indian choice, and neither adequately covers craving.

20.6 Rapid detox: antagonist-accelerated but not under anaesthesia

What "rapid detox" means. **Rapid detox** compresses the timeline by giving an opioid antagonist (naloxone or naltrexone) to precipitate and hasten withdrawal, so the person is opioid-free far sooner than a taper allows (Kaplan and Sadock 2024; Maudsley Prescribing Guidelines). The recognised outpatient protocol combines naltrexone with clonidine and adjuncts, allowing the patient to be opioid-free from the first day and to complete detoxification within **48 to 72 hours**, then to start naltrexone maintenance at once (Kaplan and Sadock 2024). Its appeal is that it removes the vulnerable, unprotected 7-to-10-day opioid-free window that ordinarily precedes naltrexone.

The catch. Precipitated withdrawal is abrupt and severe, so blood pressure must be watched for up to 8 hours on the first day and the method is best confined to patients with a *low* level of physiologic dependence, in settings with treatment rooms and adequate nursing (Kaplan and Sadock 2024). NICE is explicit: do not routinely offer rapid detoxification using precipitated withdrawal (NICE 2011). Rapid detox is thus a niche induction-into-naltrexone tool, not a routine detoxification.

COMMON TRAP

Do not conflate *rapid* detox with *ultra-rapid* detox. Rapid detox is antagonist-accelerated withdrawal (naltrexone plus clonidine) done *awake*, completing in 48 to 72 hours, and NICE merely advises against it routinely. Ultra-rapid detox adds general anaesthesia or heavy sedation with mechanical ventilation, and that is the one that is affirmatively contraindicated for causing life-threatening adverse events without any benefit. The word "anaesthesia" is the discriminator, and it is a favourite MCQ hinge.

20.7 Ultra-rapid detox under sedation or anaesthesia: the contraindicated procedure

What it is. **Ultra-rapid detox** (ultra-rapid opioid detoxification, UROD) places the opioid-dependent patient under light sedation or general anaesthesia, including mechanical ventilation, and then precipitates and completes withdrawal with full doses of an antagonist while the patient is unconscious (Kaplan and Sadock 2024; Tasman). The theory is to telescope the entire withdrawal into a few unconscious hours and induct naltrexone immediately.

Why it is condemned. The verdict is uniform. Kaplan and Sadock: ultra-rapid detoxification, although effective at reducing physiologic dependence, leads to a greater number of serious adverse events than the other approaches without superior outcomes, and is not recommended. Tasman: it was associated with more life-threatening adverse events and cannot be recommended. BAP (grade A): do not use ultra-rapid opioid detoxification under heavy sedation or anaesthesia, as it confers no benefit on withdrawal severity or naltrexone initiation and carries life-threatening risks; the named agents (propofol, midazolam, isoflurane) are not to be used for this purpose (BAP 2026). NICE: never offer ultra-rapid detoxification under general anaesthesia or heavy sedation (NICE 2011). WHO (strong): do not combine opioid antagonists with heavy sedation or anaesthesia for withdrawal, as this risks respiratory depression without superior benefit (WHO 2009; WHO mhGAP 2016). The documented harms include pulmonary and cardiac complications, aspiration, metabolic derangement and deaths, all incurred to shorten a syndrome that is uncomfortable but not itself life-threatening.

FEATURE	RAPID DETOX (AWAKE)	ULTRA-RAPID DETOX (UROD)
Method	Naltrexone plus clonidine and adjuncts, patient awake	**Antagonist under general anaesthesia or heavy sedation, ventilated**
Timeline	**Opioid-free from the outset; complete in 48 to 72 hours**	Hours, under anaesthesia
Guideline standing	Do not offer routinely (NICE)	**Contraindicated (BAP grade A; NICE; WHO strong)**
Main hazard	Precipitated withdrawal; hypotension (monitor 8 h)	**Life-threatening adverse events, no benefit**

Rapid versus ultra-rapid opioid detoxification; the anaesthesia step is what moves the method from "not routine" to "contraindicated" (Kaplan and Sadock 2024; Tasman; BAP 2026; NICE 2011; WHO 2009).

TRAP **The anaesthetic risk is not justified by the syndrome.** Opioid withdrawal is not life-threatening in an otherwise healthy adult, so subjecting a patient to general anaesthesia and ventilation to shorten it trades a non-lethal syndrome for a genuinely lethal procedure, the reason every guideline forbids it.

20.8 After detoxification: the two paths and the overdose window

Naltrexone or maintenance. Once detoxification is complete, the patient enters either agonist maintenance (methadone or buprenorphine, generally the more effective path) or antagonist relapse prevention with naltrexone (oral mu-antagonist, 50 mg/day; Indian brands Nodict, Naltima), offered to those who wish to be abstinent (BAP 2026; IPS guidelines; WHO 2009). The absolute rule: naltrexone must never be given to a current opioid user, because as an antagonist it precipitates immediate severe withdrawal, so it is started only after a documented **opioid-free window** of at least **7 to 10 days** (longer after methadone), confirmed by a negative urine screen and, where uncertain, a naloxone challenge (IPS guidelines; Kaplan and Sadock 2024). Rapid (antagonist-accelerated) detox exists precisely to shorten that unprotected window.

The lethal aftermath. Detoxification strips tolerance, so the deadliest period is *after* a completed detox: relapse onto a previously tolerated dose can be fatal. Take-home naloxone (IM 0.4 to 2 mg, repeated every 2 to 3 minutes up to 10 mg, or intranasal 4 mg per spray) with paired family rescue-breathing training is recommended for anyone with current or recent opioid use, especially in the high-overdose windows after detoxification or release from custody (IPS guidelines; WHO 2009; BAP 2026).

GOOD TO REMEMBER

- **Naltrexone (oral mu-antagonist, 50 mg/day; Nodict, Naltima):** relapse prevention after abstinence only; the criterion contraindication is any current opioid use (precipitated withdrawal), so start only after a documented 7-to-10-day opioid-free window (longer post-methadone) with a negative urine screen; it strips tolerance, so relapse afterwards risks fatal overdose, which is exactly why post-detox take-home naloxone is non-negotiable.

20.9 The India frame: the treatment gap, NDPS and the de-addiction model

The clinical reality. India carries a very large opioid-use treatment gap, with most dependent users never reaching formal care, and detoxification is delivered largely through government de-addiction centres, the Drug De-addiction Programme, and the day care centre model rather than general practice (IPS guidelines). The practical consequence is that a buprenorphine taper, inducted on a COWS of about 8 to 12, is the detoxification backbone the Indian psychiatrist actually uses; methadone tapering is confined to NACO-licensed OST clinics, so private practice refers rather than prescribes; and lofexidine being largely unavailable, clonidine is the practical alpha-2 agent despite its dose-limiting hypotension.

Access and law. Buprenorphine and the other opioid agents are controlled under the Narcotic Drugs and Psychotropic Substances (NDPS) Act, 1985, whose scheduling and prescriber requirements shape access; ultra-rapid anaesthesia-based detox has no place in Indian de-addiction practice, both because it is contraindicated and because it demands anaesthetic infrastructure the setting rarely has. The medico-legal detail, including treatment in lieu of conviction, sits in the Mental health legislation and forensic psychiatry notes, and the CBT and motivational-interviewing arm that must accompany any detoxification is developed in the Psychotherapies, clinical assessment, MSE and nosology notes.

INDIA

Three India-specific points recur. First, the practical detoxification is a buprenorphine-naloxone taper in a de-addiction centre or the day care centre, inducted at 4 mg / 1 mg once the COWS reaches about 8 to 12, then reduced by 2 to 4 mg/day over 7 to 14 days. Second, methadone tapering is *not* a private-practice option (NACO OST clinics only), so "refer to the nearest licensed OST centre" is often the correct answer. Third, ultra-rapid anaesthesia-based detox is both contraindicated and infrastructurally implausible here, so if a private "rapid detox under anaesthesia" clinic is described in a viva, the correct response is to name it as an unsafe, non-guideline practice.

48 to 72 h	7 to 10 days	2 to 4 mg/day
TIME TO COMPLETE AWAKE RAPID (ANTAGONIST-ACCELERATED) DETOX	OPIOID-FREE WINDOW BEFORE NALTREXONE (WHICH RAPID DETOX SHORTENS)	IPS BUPRENORPHINE TAPER REDUCTION STEP OVER 7 TO 14 DAYS

HOLD THIS

Opioid detoxification is a bridge, never a treatment: taper buprenorphine (IPS preferred, 2 to 4 mg/day over 7 to 14 days) or methadone (2 to 10 mg per step, slow), or use alpha-2 agonists (lofexidine preferred, clonidine the practical Indian choice) for a shorter opioid-free detox, always into planned maintenance or naltrexone with take-home naloxone for the post-detox lost-tolerance overdose window; awake rapid detox (naltrexone plus clonidine, opioid-free from the outset, complete in 48 to 72 hours) is not offered routinely, and ultra-rapid detox under sedation or general anaesthesia is contraindicated across BAP, NICE and WHO because it causes life-threatening adverse events with no benefit for a syndrome that is not itself lethal.

Other substances of misuse

21 · Cannabis

Cannabis is the most widely used illicit drug in the world and, in India, one that examiners return to because its clinical story is uniquely two-sided: an acute intoxication that is benign enough to look harmless, sitting on top of a dose-dependent link to **psychosis** and a genuine **cannabis withdrawal** syndrome that were both denied for decades. The high-yield task on this topic is to teach the acute effects and their receptor basis, to define **cannabis use disorder** against its criteria, to state the **psychosis link** as an odds ratio rather than a vague association, to settle the **amotivational** syndrome question honestly, and to give the withdrawal syndrome by its three signature symptoms and its clock.

Why it matters clinically. The plant *Cannabis sativa* yields over 100 **cannabinoid**s, of which delta-9-tetrahydrocannabinol (**THC**) is the one responsible for the psychoactive effect; cannabidiol (CBD) is only weakly active and may modulate THC. Because most young users perceive cannabis as safe, the disorder, the withdrawal, and the psychosis risk are all under-recognised, and a resident who can name the criteria and the dose-response numbers is doing real diagnostic work. The reward-pathway and dopamine mechanics that make THC reinforcing are developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and are not re-derived here; the boundary between a cannabis-induced psychotic disorder and a primary psychosis sits in the Other psychotic disorders, delusional syndromes and catatonia notes; the NDPS Act frame is in the Mental health legislation and forensic psychiatry notes.

21.1 THC, the cannabinoids and the receptor basis

The active molecule. THC (delta-9-tetrahydrocannabinol) is the principal psychoactive cannabinoid; it is fat-soluble, concentrated in the resin of the female plant's flowering tops, and produces its effects through an endogenous cannabinoid signalling system (Kaplan and Sadock 2024). There are two cannabinoid receptors: CB1, found primarily in the brain, mediates the

psychological and behavioural effects; CB2, mostly outside the central nervous system, is linked to the immune system. Both are G-protein-coupled receptors, and their natural ligands are anandamide and 2-arachidonyl-glycerol (2-AG).

Why the effects look the way they do. CB1 receptors are abundant in regions governing mood, motor control, memory, appetite, pain and sleep. Their density in the *hippocampus* is the neat explanation for cannabis's signature disruption of short-term memory (Kaplan and Sadock 2024). THC is highly fat-soluble, so it and its metabolites accumulate in fatty tissue and clear slowly, staying detectable in urine for weeks in frequent users; this slow, long half-life is precisely why the withdrawal syndrome is milder and more delayed than that of alcohol or opioids.

PEARL

The reason a urine cannabinoid screen (for 11-nor-9-carboxy-THC) can stay positive for weeks after last use in a daily user is the same reason cannabis withdrawal is slow to start and slow to clear: THC is fat-soluble and leaves the body's fat stores gradually. One fact explains both the lab result and the withdrawal time-course.

21.2 Acute intoxication: the criterion picture

The subjective high. Most users take cannabis for a "high" of mild euphoria, relaxation and perceptual alteration, with time distortion and intensification of ordinary experiences, often with talkativeness and infectious laughter in a social setting (Kaplan and Sadock 2024). Cognitively, short-term memory and attention are impaired and skilled psychomotor activity, reaction time and coordination degrade, which is what makes driving hazardous. When smoked, onset is within minutes and the effect lasts about 3 to 4 hours; when eaten, onset is delayed 1 to 3 hours and the effect is longer and harder to titrate (DSM-5-TR; Kaplan and Sadock 2024).

The examinable signs. DSM-5-TR anchors *cannabis intoxication* on clinically significant behavioural or psychological change plus two or more of four physical signs developing within **2 hours** of use: *conjunctival injection* (red eyes), *increased appetite*, *dry mouth*, and *tachycardia* (DSM-5-TR). Smoking cannabis produces a 20 to 50 per cent rise in heart rate within minutes, and a "with perceptual disturbances" specifier is added when hallucinations occur with intact reality testing (DSM-5-TR).

DOMAIN	ACUTE EFFECT OF CANNABIS INTOXICATION
Subjective	Euphoria, relaxation, time distortion, intensified perception; occasionally anxiety/panic in the naive user
Cognitive/motor	Impaired short-term memory and attention; impaired coordination, reaction time and psychomotor skill
Physical signs (DSM-5-TR)	**Conjunctival injection, increased appetite, dry mouth, tachycardia (two or more within 2 hours)**
Onset/duration	Smoked: minutes, lasts 3 to 4 h; oral: 1 to 3 h onset, longer and harder to titrate

Acute cannabis intoxication: the four DSM-5-TR physical signs (red eyes, increased appetite, dry mouth, tachycardia) are the criterion-level detail to name in a viva (DSM-5-TR; Kaplan and Sadock 2024).

GOOD TO REMEMBER

- **Cannabis intoxication (syndrome):** the criterion is significant behavioural or psychological change plus two or more of conjunctival injection, increased appetite, dry mouth, and tachycardia within 2 hours of use; onset is minutes when smoked (lasting 3 to 4 hours), delayed 1 to 3 hours when eaten; the acute toxicity is very low and there is no reliably lethal dose, so the first management step for a bad reaction is calm reassurance in a low-stimulus setting, not a drug.

21.3 Cannabis use disorder: definition and criteria

The construct. Cannabis use disorder is diagnosed on the same eleven criteria as the other substance use disorders, DSM-5-TR having merged the old abuse and dependence categories into a single severity-graded disorder (DSM-5-TR). The threshold is **2 or more** of the eleven criteria within a 12-month period, with severity graded mild (2 to 3), moderate (4 to 5) or severe (6 or more). The criteria cluster into impaired control (using more or longer than intended, unsuccessful efforts to cut down, craving, much time spent), social impairment (role failure, interpersonal problems, activities given up), risky use (hazardous use, use despite harm), and the pharmacological pair of tolerance and withdrawal (DSM-5-TR). ICD-11 frames the same territory as cannabis dependence, defined by impaired control, increasing priority of use, and physiological features, with a separate harmful-use category for problematic use that falls short of dependence.

Who develops it. Longitudinal data give roughly **1 in 10** of those who ever use cannabis developing dependence, rising to about **1 in 3** among regular users; the earlier the age of first use, and the heavier and longer the use, the higher the risk (Kaplan and Sadock 2024). There is no approved pharmacotherapy: management is psychosocial, chiefly cognitive behavioural therapy, motivational enhancement therapy and contingency management (Kaplan and Sadock 2024). The general MI technique is developed in the Psychotherapies, clinical assessment, MSE and nosology notes.

RULE **No drug is first-line for cannabis use disorder.** Unlike alcohol or opioids, there is no approved anti-craving or substitution agent; the evidence-based treatment is psychosocial (CBT, MET, contingency management), so the exam answer names a therapy, not a molecule.

GOOD TO REMEMBER

- **Cannabis use disorder (syndrome):** two or more of the eleven DSM-5-TR criteria within 12 months (mild 2 to 3, moderate 4 to 5, severe 6+); about 1 in 10 ever-users and 1 in 3 regular users become dependent; earlier onset and heavier use raise the risk; there is no approved pharmacotherapy, so the first management step is a psychosocial intervention (CBT, motivational enhancement therapy, contingency management).

21.4 The psychosis link: a dose-dependent association

Stating it as a number. The **psychosis link** is one of the most examined facts on this topic, and it must be given quantitatively. Meta-analyses of prospective studies show that people who have *ever* used cannabis carry about **1.4 times** higher odds of psychotic symptoms; the odds rise to

about **2.1 times** among regular users and to nearly **four times** in those using high-potency preparations (Kaplan and Sadock 2024). DSM-5-TR frames it as roughly a threefold increase in psychosis risk with cannabis use in critical developmental periods. The relationship is dose-dependent, is stronger with early-onset and high-THC use, and, in provocation studies, THC produces dose-related increases in psychotic symptoms in people with and without schizophrenia.

Contributory-cause, not the whole story. Young people with psychosis who use cannabis have a first episode on average about **2 years** earlier than non-users, and those who stop using after a first episode have better outcomes and fewer relapses (Kaplan and Sadock 2024). The careful reading is that cannabis is a *contributory* cause: it precipitates schizophreniform disorder in vulnerable individuals and worsens established illness, but only a small fraction of cases are attributable to it (in the Swedish conscript cohort, about 7 per cent). This is genuinely balanced against shared genetic vulnerability and reverse causation, and the substance-induced psychotic-disorder boundary is handled in the Other psychotic disorders, delusional syndromes and catatonia notes.

EXPOSURE	ODDS OF PSYCHOTIC SYMPTOMS (META-ANALYSIS)
Ever used cannabis	About 1.4 times
Regular use	**About 2.1 times**
High-potency preparations	**Nearly 4 times**
First episode in users	Onset about 2 years earlier than non-users

The dose-dependent cannabis-psychosis association: risk climbs from ever-use through regular use to high-potency use, and first-episode onset is earlier in users (Kaplan and Sadock 2024; DSM-5-TR gives a roughly threefold increase with use in critical periods).

INDIA

Cannabis psychosis is not a Western import into the Indian syllabus: "Indian hemp insanity" was first described by Dhunjibhoy in 1930 from Indian heavy users, characterised as an acute schizophreniform picture with disorientation and confusion and a good prognosis on abstinence. The traditional Indian preparations differ in potency, which matters for the dose-response above: bhang (dried leaves) is the weakest, ganja (cultivated flowering tops) intermediate, and charas or hashish (resin) the most potent plant form, with hash oil higher still.

21.5 The amotivational-syndrome question

The claim. The **amotivational** syndrome is the classic description, from case reports of chronic heavy users, of apathy, lethargy, loss of drive, blunted ambition and a narrowing of interest to little beyond using cannabis (Tasman). It is an attractive, tidy label, and DSM-5-TR still refers to cannabis-associated reduction in goal-directed activity and self-efficacy under that name.

The honest verdict. Controlled field and laboratory studies from the 1970s onward did not support a specific *amotivational* syndrome, and current empirical research does not either; the behaviour is better understood as the effect of *chronic daily intoxication* in a dependent user

rather than a distinct entity (Kaplan and Sadock 2024). The exam-safe position is to describe the phenomenon, name it, and then state that it is not established as a discrete syndrome and is best read as sustained intoxication plus, at times, cumulative cognitive impairment. That cognitive question is separate: long-term heavy use can produce deficits in memory and attention, clearest during intoxication, with incomplete evidence on full reversibility.

TRAP **Do not present the amotivational syndrome as an established diagnosis.** Controlled studies do not support a specific syndrome; describe it, then attribute the apathy to chronic daily intoxication, or you overstate the evidence.

21.6 Cannabis withdrawal: the syndrome and its clock

That it exists at all. For decades cannabis was thought to cause no withdrawal; the recognition of a genuine cannabis withdrawal syndrome is why DSM-5 added it as a diagnosis. The signature is that the symptoms are predominantly *behavioural and emotional* rather than physical, unlike alcohol or opioid withdrawal (DSM-5-TR). The three most examinable features to lead with are *irritability*, *sleep disturbance* (insomnia, disturbing dreams), and *appetite change* with weight loss.

The DSM-5-TR criteria. Criterion A requires cessation of heavy, prolonged use (usually daily or near-daily for at least a few months); Criterion B requires **3 or more** of seven signs within about a week: irritability/anger/aggression; nervousness or anxiety; sleep difficulty; decreased appetite or weight loss; restlessness; depressed mood; and at least one physical symptom causing significant discomfort (abdominal pain, tremor, sweating, fever, chills, or headache) (DSM-5-TR). Onset is within **24 to 48 hours** of cessation, symptoms peak at 2 to 5 days, and the syndrome resolves within 1 to 2 weeks, although sleep disturbance can outlast the rest (DSM-5-TR; Kaplan and Sadock 2024). It is not dangerous in an otherwise healthy person, and management is supportive; there is no licensed pharmacotherapy, although CB1 agonists such as nabiximols can attenuate symptoms in trials.

ELEMENT	DETAIL (DSM-5-TR)
Precondition (A)	Cessation of heavy, prolonged use (usually daily/near-daily for at least a few months)
Core requirement (B)	**Three or more of seven signs within about a week of stopping**
Signature three	**Irritability/anger; sleep disturbance (insomnia, vivid dreams); decreased appetite/weight loss**
Other emotional signs	Nervousness/anxiety, restlessness, depressed mood
Physical (at least one)	Abdominal pain, tremor, sweating, fever, chills, or headache causing discomfort
Onset	Within 24 to 48 hours of cessation
Peak	2 to 5 days
Resolution	Within 1 to 2 weeks (sleep disturbance may persist longer)

Cannabis withdrawal by DSM-5-TR: predominantly emotional and behavioural symptoms, onset 24 to 48 hours, peak 2 to 5 days, resolution within 1 to 2 weeks (DSM-5-TR; Kaplan and Sadock 2024).

2	24 to 48 h	1 to 2 wk	2.8
DSM-5-TR CRITERIA THRESHOLD FOR CANNABIS USE DISORDER IN 12 MONTHS	ONSET OF CANNABIS WITHDRAWAL AFTER CESSATION	TIME TO RESOLUTION OF CANNABIS WITHDRAWAL	PER CENT OF INDIANS AGED 10 TO 75 WHO USE CANNABIS (MAGNITUDE OF SUBSTANCE USE SURVEY)

GOOD TO REMEMBER

- **Cannabis withdrawal (syndrome):** three or more of seven signs within a week of stopping heavy, prolonged use; the discriminator from other withdrawals is that the picture is predominantly emotional and behavioural (irritability, sleep disturbance, appetite change) rather than physical; onset 24 to 48 hours, peak 2 to 5 days, resolution within 1 to 2 weeks; it is not dangerous in a healthy person, so the first management step is supportive care and sleep hygiene, with no licensed drug required.

21.7 The Indian frame: epidemiology, NDPS and the treatment gap

The numbers. The national Magnitude of Substance Use survey found that **2.8 per cent** of Indians aged 10 to 75 use cannabis, with about **72 lakh** people carrying a cannabis use disorder (AIIMS Clinical Methods in Psychiatry 2024). Cannabis is thus a mainstream Indian substance, not a fringe one, and traditional cultural use of bhang complicates both perception and detection.

The legal and service frame. Cannabis is controlled under the Narcotic Drugs and Psychotropic Substances (NDPS) Act, whose detailed medico-legal and capacity aspects are in the Mental health legislation and forensic psychiatry notes. The dominant service reality is the treatment gap: the treatment gap for substance use disorders in India runs at about **91 per cent** overall, and around 73 per cent specifically for the non-alcohol, non-tobacco substance use disorders that include cannabis, so the great majority of people with a cannabis use disorder never reach a de-addiction service (AIIMS Clinical Methods in Psychiatry 2024). Because there is no cannabis-specific medication, and because the buprenorphine-based substitution model that anchors opioid de-addiction has no cannabis equivalent, the Indian answer is squarely psychosocial and community-delivered, which fits the workforce constraint the treatment gap describes.

INDIA

Two India-specific facts to keep together: cannabis use disorder affects roughly 72 lakh Indians, yet the treatment gap for non-alcohol, non-tobacco substance use disorders is about 73 per cent, and the overall substance-use treatment gap is around 91 per cent. With no cannabis pharmacotherapy to offer and a de-addiction workforce spread thin, the realistic intervention is brief, motivation-based psychosocial work delivered close to the community rather than a specialist detoxification bed.

HOLD THIS

Cannabis withdrawal is real and predominantly emotional: three or more of irritability, sleep disturbance and appetite change within a week of stopping heavy use, onset 24 to 48 hours and resolving in 1 to 2 weeks; and the psychosis link is dose-dependent, rising from about 1.4 times odds for ever-use to nearly fourfold with high-potency cannabis.

22 · Stimulants: cocaine and amphetamine

Stimulants are the psychomotor accelerants of the drug world: **cocaine**, **amphetamine** and **methamphetamine** all drive dopamine, noradrenaline and serotonin into the synapse and produce a euphoriant, sympathomimetic high. DSM-5-TR and ICD-11 both fold amphetamine-type substances and cocaine into a single *stimulant* rubric because their psychoactive and sympathomimetic effects overlap almost completely; the pharmacology of that dopamine surge belongs to the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and is not re-derived here. The high-yield exam task is to name the **intoxication** picture and its physical signs, to recognise **stimulant psychosis** with its signature tactile hallucination of **formication**, to list the medical emergencies (cardiac, cerebrovascular, hyperthermic), to describe the withdrawal *crash*, and to state honestly that there is no approved anti-craving agent so management is psychosocial.

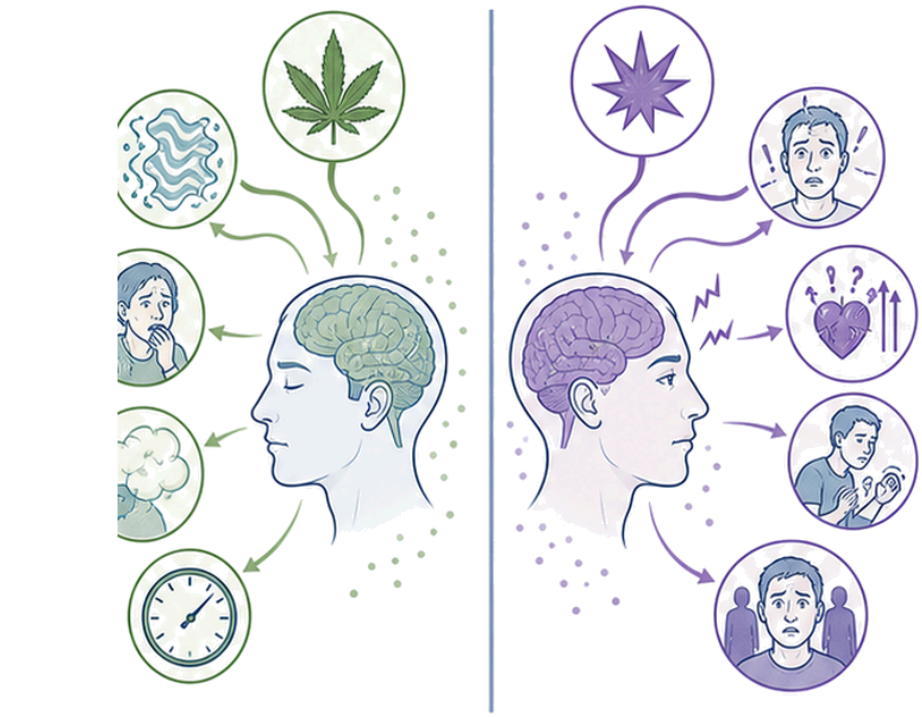


Fig 13.15 Acute cannabis effects may combine perceptual change, anxiety and cognitive slowing; stimulants more often produce intense arousal, sympathetic activation, stereotyped behaviour and paranoia or psychosis at higher exposure.

Why it matters clinically. A stimulant-intoxicated patient can look manic, look schizophrenic, or drop dead of an arrhythmia or a haemorrhagic stroke, so the discrimination is genuinely life-saving. The boundary between a stimulant-induced psychotic disorder and a primary psychosis is developed in the Other psychotic disorders, delusional syndromes and catatonia notes; the NDPS Act frame that governs access and prosecution sits in the Mental health legislation and forensic psychiatry notes. What this topic must nail down is the criterion set, the discriminators, and the one management truth: for stimulants, unlike alcohol or opioids, the drug cupboard is essentially empty.

22.1 The three drugs and how route sets the risk

The agents. Cocaine is a naturally occurring alkaloid of the coca plant, taken as snorted hydrochloride powder, injected in solution, or smoked as freebase or crack. Amphetamine and methamphetamine are synthetic phenylethylamines taken orally, nasally, intravenously or (methamphetamine) smoked; methylphenidate and modafinil are amphetamine-type substances

by mechanism (Kaplan and Sadock 2024; DSM-5-TR). **Route dictates danger.** Smoking and intravenous use give the fastest onset (seconds to blood-brain barrier), the most intense euphoria, and the steepest slide into compulsive use; cocaine euphoria correlates with the *rate of rise* of the serum level, not the absolute dose, which is exactly why crack and IV routes are the most addictive (Kaplan and Sadock 2024). **Kinetics.** Cocaine has a short half-life of roughly **50 to 90 minutes**, so intoxication is brief and bingeing is common; methamphetamine is far longer-acting, hence used fewer times a day but with a heavier dependence and worse prognosis (Kaplan and Sadock 2024).

PEARL

The single fact that unlocks stimulant addictiveness is the *rate* hypothesis: it is how fast the level rises, not how high it gets, that drives the reinforcing rush. That is why the same molecule (cocaine) is only moderately habit-forming snorted but ferociously so smoked as crack or injected. Combine cocaine with alcohol and the liver makes *cocaethylene*, a longer-acting, more cardiotoxic metabolite, which is why the drink-plus-cocaine combination kills more hearts than either alone.

22.2 Stimulant intoxication: the sympathomimetic euphoriant picture

The syndrome. Stimulant intoxication is the appearance of clinically significant behavioural or psychological change during or shortly after use, plus two or more physical signs (DSM-5-TR). The *psychological* change is euphoria with enhanced vigour, grandiosity, hypervigilance, talkativeness, interpersonal sensitivity, anxiety or anger, and stereotyped repetitive behaviour; chronic high-dose use flips this into affective blunting, fatigue and social withdrawal. The *physical* signs are frankly sympathomimetic: tachycardia (or bradycardia), pupillary dilation, raised (or lowered) blood pressure, sweating or chills, nausea, weight loss, psychomotor agitation or retardation, and at the severe end chest pain, arrhythmias, seizures, dyskinesias, dystonias or coma (DSM-5-TR). **The ICD-11 gloss** adds paranoid ideation (possibly delusional), transient auditory hallucinations, transient confusion and skin sores to the same core picture (ICD-11 6C46.3). A *with perceptual disturbances* specifier is added when hallucinations or illusions occur with intact reality testing.

GOOD TO REMEMBER

- **Stimulant intoxication (DSM-5-TR):** behavioural/psychological change (euphoria, hypervigilance, grandiosity, stereotypy) PLUS two or more physical signs (tachycardia, mydriasis, BP change, chills, nausea, weight loss, psychomotor change, chest pain, seizures) developing during or shortly after use.
- **The discriminator vs mania:** the physical sympathomimetic signs (mydriasis, tachycardia, sweating) and the short time-course, plus a positive urine screen, point to a substance rather than a primary manic episode.
- **Severe intoxication:** convulsions, cardiac arrhythmia, hyperpyrexia and death, the medical emergency that must be excluded first.

22.3 Stimulant psychosis and formication

The presentation. Heavy stimulant use produces paranoia in **50 to 70%** of people with cocaine use disorder and nearly 30% of methamphetamine users (Kaplan and Sadock 2024). Cocaine-

related psychosis characteristically involves *non-bizarre* persecutory delusions and misinterpretations (mistaking a car alarm for a police siren), and its signature perceptual sign is formication, the tactile hallucination of insects crawling in or under the skin, the classic *cocaine bugs*, which drives scratching and extensive skin excoriation (Kaplan and Sadock 2024; DSM-5-TR). **The label.** Brief paranoia within intoxication is *not* stimulant-induced psychotic disorder; the induced-disorder diagnosis is reserved for symptoms exceeding the quality or severity of intoxication (Kaplan and Sadock 2024). **Discriminators.** Prominent *visual* or *tactile* hallucinations point away from primary schizophrenia toward a toxic cause; methamphetamine psychosis is the hardest to separate from schizophrenia but usually remits within a week of abstinence. **Sensitisation.** Paranoia tends to appear *earlier* in successive binges (reverse tolerance), the opposite of ordinary tolerance.

WORKED EXAMPLE

A young man is brought in agitated, picking bleeding sores into his forearms, convinced the police have bugged his house. Pupils are dilated, pulse 118, BP 170/104. He describes bugs crawling under his skin. The dilated pupils, tachycardia and hypertension say sympathomimetic; the non-bizarre persecutory delusion plus formication say cocaine or methamphetamine, not primary schizophrenia. First move is a urine drug screen and an ECG, not an antipsychotic prescription for a presumed first-episode psychosis.

GOOD TO REMEMBER

- **Stimulant psychosis:** non-bizarre persecutory delusions plus tactile hallucinations; *formication* (cocaine bugs) is the pathognomonic clue and provokes skin excoriation.
- **The discriminator:** prominent visual/tactile hallucinations and remission within about a week of abstinence favour a stimulant-induced psychosis over primary schizophrenia (methamphetamine is the closest mimic).
- **First management step:** confirm with a urine drug screen, treat agitation, and observe for spontaneous remission before committing to a primary psychotic-disorder diagnosis.

22.4 The medical emergencies: cardiac, cerebrovascular, hyperthermic

Cardiovascular. Stimulants are potent sympathomimetics, so vasoconstriction plus raised myocardial demand can precipitate angina and myocardial infarction even in a young, otherwise healthy heart; methamphetamine additionally causes cardiomyopathy and cardiogenic shock (Kaplan and Sadock 2024). Chest pain is the single commonest reason a cocaine user reaches the emergency department. **Cerebrovascular.** Acute stimulant-driven hypertension predisposes to arterial haemorrhage, so *haemorrhagic stroke* and aortic dissection are on the table; ischaemic stroke and seizures also occur (Kaplan and Sadock 2024; DSM-5-TR). **Hyperthermic and neurologic.** Grand mal seizures are common in overdose, and severe intoxication produces *hyperpyrexia*, which together with rhabdomyolysis and cardiac arrhythmia is a recognised route to death (Kaplan and Sadock 2024). **Route-specific.** Snorting perforates the nasal septum; smoking causes bronchitis and pneumonitis; injecting brings HIV, hepatitis and endocarditis; methamphetamine's vasoconstriction-plus-bruxism produces *meth mouth*.

RULE **Treat the body before the mind.** In stimulant intoxication the first emergency is medical: get an ECG and check temperature and blood pressure, because MI, haemorrhagic stroke, seizure and hyperthermia kill faster than the psychosis.

GOOD TO REMEMBER

- **Cardiac:** vasoconstriction plus raised demand causes angina and MI even in young hearts; methamphetamine adds cardiomyopathy and cardiogenic shock.
- **Cerebrovascular:** acute hypertension precipitates haemorrhagic stroke and aortic dissection; ischaemic stroke and seizures also occur.
- **Hyperthermic:** severe intoxication gives hyperpyrexia, seizures and arrhythmia, the lethal triad; the first step is medical stabilisation, not sedation alone.

22.5 Stimulant withdrawal: the crash

The syndrome. Stimulant withdrawal is a mirror-image of intoxication: cessation or reduction of prolonged use, followed within a few hours to several days by *dysphoric mood* plus two or more of fatigue, vivid unpleasant dreams, insomnia or hypersomnia, increased appetite, and psychomotor retardation or agitation (DSM-5-TR). This is the *crash*, the profound low-energy, oversleeping, ravenous, anhedonic state that follows a binge; bradycardia is often present and is a reliable objective marker (DSM-5-TR). **The clinical hazard.** The crash is not, in itself, a medical emergency the way delirium tremens is, but its depressive symptoms can be severe and *suicidal ideation is a real risk* during withdrawal and in stimulant-induced mood disorders (Kaplan and Sadock 2024; DSM-5-TR). Craving is intense and cue-driven and may re-trigger use. **The mood trap.** Depressive symptoms cluster in withdrawal while manic-spectrum symptoms cluster in intoxication, so a binge-crash cycle can convincingly imitate bipolar disorder, and only a history and a drug screen separate them.

GOOD TO REMEMBER

- **Stimulant withdrawal (DSM-5-TR):** dysphoric mood PLUS two or more of fatigue, vivid unpleasant dreams, insomnia/hypersomnia, increased appetite, psychomotor change, within hours to days of stopping.
- **The signature:** the *crash*, with hypersomnia, hyperphagia and anhedonia; bradycardia is a reliable objective sign.
- **The first management priority:** screen for suicidality and manage supportively; withdrawal itself is not life-threatening but the depressive dip can be.

22.6 Making the diagnosis and the discriminators

The nosology. Both systems group cocaine and amphetamine-type substances under stimulants, with separate codes: DSM-5-TR uses stimulant use disorder plus stimulant intoxication, stimulant withdrawal and the stimulant-induced disorders; ICD-11 codes disorders due to cocaine (6C45) separately from disorders due to other stimulants including amfetamines and methamfetamine (6C46). **The key differentials.** Phencyclidine and cathinone (bath-salt) intoxication mimic stimulant intoxication and are separated only by the toxicology (Kaplan and Sadock 2024; DSM-5-TR). A primary manic, psychotic or anxiety disorder is separated by time-course: stimulant-induced symptoms attenuate over weeks of abstinence, so symptoms persisting

beyond a **1 month** abstinent period, or predating the drug, point to an independent disorder (DSM-5-TR).

Stimulant intoxication
euphoriant, sympathomimetic state during/after use; two or more physical signs required.

Stimulant-induced psychotic disorder
psychosis exceeding the quality/severity of intoxication; non-bizarre delusions and formication typical.

Stimulant withdrawal (crash)
dysphoria plus fatigue, hypersomnia, hyperphagia, vivid dreams after stopping prolonged use.

Reverse tolerance (sensitisation)
paranoia appearing earlier and at lower dose across successive binges.

FEATURE	INTOXICATION	WITHDRAWAL (CRASH)
Mood	**Euphoria, grandiosity (manic-like)**	**Dysphoria, anhedonia (depressive-like)**
Arousal	Hypervigilance, insomnia	Fatigue, hypersomnia
Appetite	Suppressed, weight loss	Increased (hyperphagia)
Pulse	Tachycardia (usually)	Bradycardia (reliable marker)
Pupils	Dilated (mydriasis)	Normal
Danger	MI, stroke, seizure, hyperthermia	Suicidal ideation, relapse craving

Intoxication and the crash are physiological opposites; the sympathomimetic signs and bradycardia are the quickest bedside discriminators.

TRAP **Do not diagnose bipolar disorder mid-binge.** A stimulant binge-crash cycle imitates mania then depression; commit to a mood-disorder label only after symptoms persist beyond a month of confirmed abstinence.

22.7 Management: no approved anti-craving agent, so treat supportively

The central truth. Unlike alcohol and opioids, there is *no* approved anti-craving or substitution pharmacotherapy for cocaine or amphetamine use disorder; prescription stimulants, dopamine agonists, anticonvulsants, antidepressants and antipsychotics have all failed to show conclusive benefit for cocaine use disorder, and prescription stimulants specifically should *not* be used for amphetamine dependence (BAP 2026, Level A). **So the evidence-based core is psychosocial:** for cocaine use disorder, community reinforcement approach, CBT, or contingency management combined with another behavioural intervention; for amphetamine or methamphetamine use disorder, contingency management combined with another behavioural intervention is the best-supported option (WHO mhGAP; BAP 2026). **Acute intoxication and agitation** are managed supportively with a calm environment and benzodiazepines for agitation and seizures, with cardiac and temperature monitoring. **Methamphetamine-associated psychosis** is treated with an antipsychotic, preferably olanzapine or quetiapine (BAP 2026, Level A/B). **Withdrawal (the**

crash) is managed supportively; no specific agent, including mirtazapine, modafinil or amantadine, has adequate evidence (BAP 2026). Only tentative, non-first-line signals exist (extended-release naltrexone plus bupropion, or atomoxetine, for methamphetamine), which is exactly what "no approved agent" means in practice.

50 to 90	50 to 70	1	0
COCAINE HALF-LIFE IN MINUTES (SHORT, HENCE BINGEING)	PER CENT OF COCAINE USERS WITH PARANOIA ON HEAVY USE	MONTHS ABSTINENT BEYOND WHICH PERSISTENT PSYCHOSIS SUGGESTS A PRIMARY DISORDER	APPROVED ANTI-CRAVING DRUGS FOR STIMULANT USE DISORDER

GOOD TO REMEMBER

- **Contingency management:** the best-evidenced intervention for stimulant use disorder; combine with another behavioural intervention (CBT, community reinforcement) (WHO mhGAP; BAP 2026). No approved anti-craving drug exists.
- **Olanzapine or quetiapine:** preferred antipsychotic for methamphetamine-associated psychosis (BAP 2026); most stimulant psychosis remits with abstinence and supportive care.
- **Benzodiazepine:** the workhorse for stimulant-induced agitation and seizures during acute intoxication, alongside cardiac and temperature monitoring (supportive care, not a specific antidote).

22.8 The India frame: a small but rising ATS problem inside a big treatment gap

The epidemiology and the gap. In Indian practice, cocaine and amphetamine-type stimulants are far less common than alcohol, opioids and cannabis, but amphetamine-type stimulants are a rising, mostly metropolitan and party-scene problem, and the psychiatrist is often the first clinician to recognise a stimulant psychosis brought in as a "first-episode schizophrenia". The dominant service reality is the treatment gap: the substance-use treatment gap in India runs at roughly **91 per cent** overall, and about 73 per cent for the non-alcohol, non-tobacco substance use disorders that include stimulants, so most people with a stimulant problem never reach a de-addiction service (AIIMS Clinical Methods in Psychiatry 2024). **The service and legal frame.** Care is concentrated in government de-addiction centres and Drug De-addiction Programme (DDAP) units and the day care centre model rather than general practice, framed by the Narcotic Drugs and Psychotropic Substances Act (NDPS Act, 1985); the medico-legal detail belongs to the Mental health legislation and forensic psychiatry notes. **Why this matters for stimulants specifically.** Because there is no substitution therapy for stimulants, the buprenorphine (Indian brand Tidigesic) model that anchors opioid de-addiction has no stimulant equivalent, so the Indian answer, like the global one, is squarely psychosocial and community-delivered, which fits the workforce constraint the treatment gap describes.

INDIA

Two facts to hold together for the Indian viva. First, stimulants sit low in the Indian substance hierarchy behind alcohol, opioids and cannabis, but amphetamine-type stimulants are climbing in cities and the clubbing scene, so a young metropolitan patient with paranoia, dilated pupils and formication deserves a stimulant screen before a schizophrenia label. Second, there is no substitution or anti-craving drug to offer, so unlike the opioid pathway there is no buprenorphine-style bridge, and the realistic intervention is contingency management and brief motivation-based psychosocial work delivered close to the community, inside a de-addiction system already stretched by a treatment gap of roughly 91 per cent (IPS_CPG; AIIMS Clinical Methods in Psychiatry 2024).

HOLD THIS

Stimulant intoxication is a euphoriant, sympathomimetic state whose signature psychosis carries non-bizarre delusions and formication (cocaine bugs), whose real killers are MI, haemorrhagic stroke, seizure and hyperthermia, whose withdrawal is a depressive crash with suicide risk, and for which there is no approved anti-craving drug, so management is supportive plus contingency management.

23 · Tobacco and nicotine dependence

Of every substance in this paper, **tobacco** kills the most people and is the least treated, which is exactly why it is examined. The dependence itself is unglamorous: no dramatic intoxication, no life-threatening withdrawal, no delirium. What makes it a management topic worth marks is that the pharmacology of **smoking cessation** is clean, evidence-heavy and testable, and India is the second-largest tobacco-consuming country in the world, so an Indian examiner will want the assessment tool, the first-line drugs and the doses, not a sermon on the harms of **nicotine**.

Why it matters clinically. Nicotine dependence is a drug-and-dose topic. The marks sit in three places: recognising the dependence, grading its severity with the **Fagerstrom** Test for Nicotine Dependence, and choosing pharmacotherapy from three verified first-line options, **nicotine replacement** therapy (**NRT**), **varenicline** and **bupropion**. The reward circuitry that nicotine hijacks (mesolimbic dopamine release driven by alpha4beta2 nicotinic receptors on ventral-tegmental neurons) is developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and is not re-derived here. Two figures carry this topic: Fig 13.16, the FTND item map and its severity bands; and Fig 13.17, the three-drug cessation algorithm keyed to the quit date. The FTND form itself is reproduced in the scales gallery.

NIDA Clinical Trials Network

Fagerstrom Test for Nicotine Dependence (FND)

Segment: _ _

Visit Number: _ _

Date of Assessment: (mm/dd/yyyy) _ _/_ _/_ _ _ _

Do you currently smoke cigarettes?

☐No ☐Yes

If "yes," read each question below. For each question, enter the answer choice which best describes your response.

1. **How soon after you wake up do you smoke your first cigarette?**
   ☐Within 5 minutes ☐31 to 60 minutes
   ☐6 to 30 minutes ☐After 60 minutes
2. **Do you find it difficult to refrain from smoking in places where it is forbidden** (e.g., in church, at the library, in the cinema)**?**
   ☐No ☐Yes
3. **Which cigarette would you hate most to give up?**
   ☐The first one in the morning ☐Any other
4. **How many cigarettes per day do you smoke?**
   ☐10 or less ☐21 to 30
   ☐11 to 20 ☐31 or more
5. **Do you smoke more frequently during the first hours after waking than during the rest of the day?**
   ☐No ☐Yes
6. **Do you smoke when you are so ill that you are in bed most of the day?**
   ☐No ☐Yes

Comments:

Heatherton TF, Kozlowski LT Frecker RC (1991). The Fagerström Test for Nicotine Dependence: A revision of the Fagerström Tolerance Questionnaire. British Journal of Addiction 86:1119-27.

FTND (Heatherton et al., 1991); reproduced from the NIDA CTN government-hosted form, freely reproducible with acknowledgement.

Fig 13.16 The Fagerstrom Test for Nicotine Dependence (FTND)

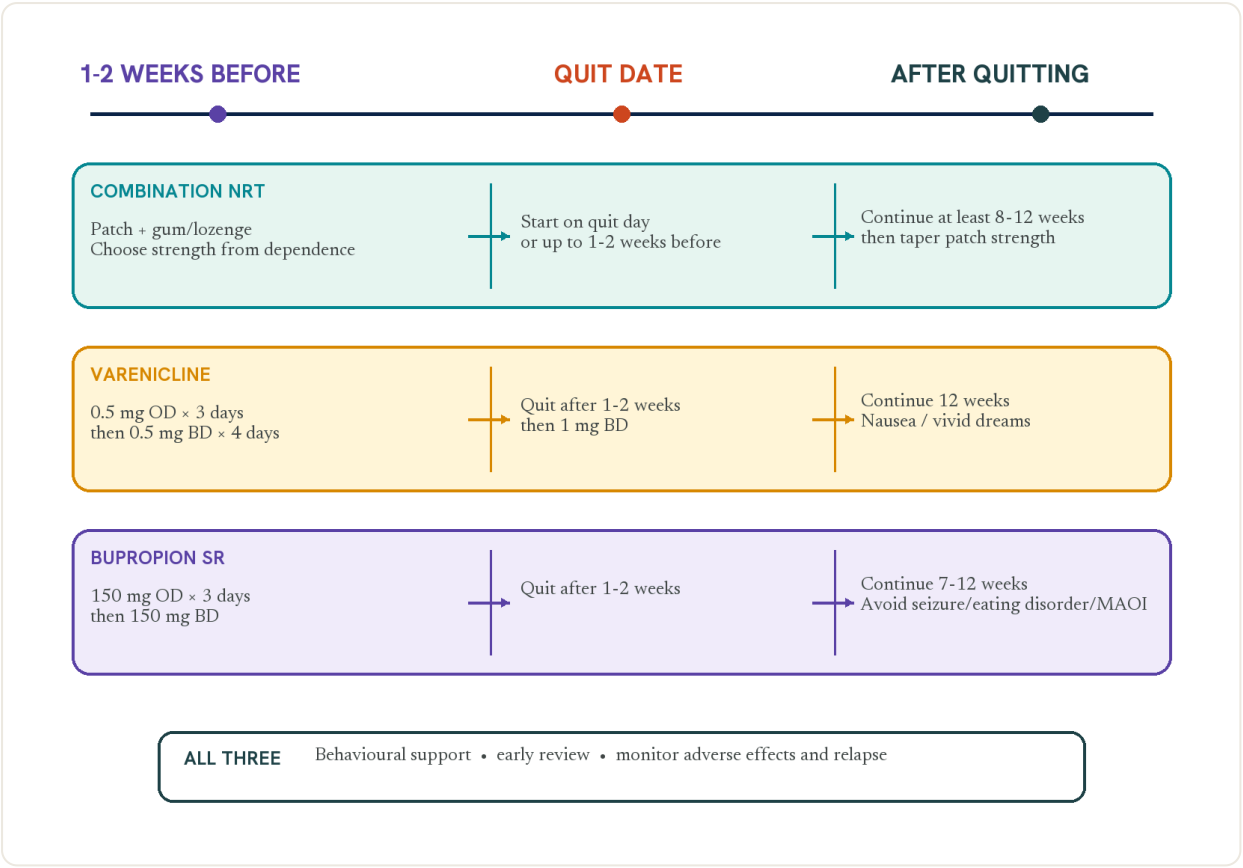


Fig 13.17 The three first-line smoking-cessation options keyed to the quit date. Combination NRT may start on or before the quit day; varenicline and bupropion are started 1 to 2 weeks beforehand, then continued with behavioural support and review after quitting.

23.1 What nicotine dependence is, and how it differs from other drugs

The dependence. Nicotine produces a genuine substance-use disorder that meets the same dependence criteria as any other drug: tolerance, a characteristic withdrawal syndrome, loss of control, and continued use despite harm (ICD-11 codes it under *disorders due to use of nicotine*; DSM-5-TR calls it *tobacco use disorder*). What separates it phenomenologically is the near-absence of a binge or intoxication phase, tobacco has little of the euphoric high/intoxication stage that dominates alcohol, opioid or stimulant use, so the disorder is driven almost entirely by withdrawal relief and by fast, heavily reinforced learning across dozens of daily doses (Tasman 2024, Kaplan and Sadock 2024).

The withdrawal syndrome. Nicotine withdrawal begins within hours of the last cigarette, peaks in the first few days and largely settles over 2 to 4 weeks: irritability, anxiety, restlessness, difficulty concentrating, increased appetite and weight gain, low mood and craving. It is unpleasant and drives relapse, but it is never a medical emergency, the contrast the examiner wants against alcohol and sedative withdrawal (Kaplan and Sadock 2024).

GOOD TO REMEMBER

- **Nicotine dependence (tobacco use disorder):** a true dependence syndrome (tolerance + a real withdrawal syndrome + loss of control) but with minimal intoxication phase (tobacco use disorder in DSM-5-TR); withdrawal is irritability, anxiety, poor concentration, appetite/weight gain and craving, begins within hours, peaks in days, resolves over 2 to 4 weeks, and is *never* life-threatening, the discriminator against alcohol/sedative withdrawal.

23.2 The receptor target: the alpha4beta2 nicotinic receptor

Where the drugs act. Nicotine binds neuronal nicotinic acetylcholine receptors, and the subtype that carries the reward is the alpha4beta2 receptor on dopaminergic neurons of the ventral tegmental area, whose activation drives dopamine release in the nucleus accumbens (Stahl; KDT). This single receptor is the reason the whole pharmacology hangs together: NRT occupies it with clean nicotine, varenicline is a *partial agonist* at it, and bupropion works around it entirely. Chronic exposure upregulates and desensitises these receptors, which is the molecular substrate of tolerance and of the withdrawal that appears when they are unoccupied.

23.3 Assessing severity: the Fagerstrom Test (FTND)

What it is. The Fagerstrom Test for Nicotine Dependence (FTND, Heatherton 1991) is the standard, most widely used measure of the *physical* severity of nicotine dependence. It is a brief 6-item self-report questionnaire; scores run from 0 to 10, and a higher score means heavier physiological dependence and predicts a worse withdrawal syndrome and greater difficulty quitting (Tasman 2024). It does not diagnose the disorder, it grades it, and the grade guides how intensive the pharmacotherapy needs to be (IPS guidelines direct clinicians to document the FTND for exactly this purpose).

The two heaviest items. The two items that carry most of the weight are the number of cigarettes smoked per day and the time from waking to the first cigarette; these two alone form the abbreviated 2-item Heaviness of Smoking Index (HSI). The single most useful clinical marker is time-to-first-cigarette: a smoker who lights up within **30 minutes** of waking is highly dependent and should be offered the higher-strength forms (the 4 mg gum or lozenge rather than the 2 mg) (Tasman 2024).

FTND SCORE (0 TO 10)	DEPENDENCE BAND	PRACTICAL IMPLICATION
0 to 2	very low / minimal	brief advice may suffice
3 to 4	low	behavioural support, consider NRT
5 to 6	**moderate**	offer pharmacotherapy; FTND >= 6 = high severity
7 to 10	high / very high	higher-strength NRT or varenicline; combination NRT

FTND severity bands; a score of 6 or higher marks high-severity dependence and a heavier withdrawal, so pharmacotherapy is intensified accordingly (Tasman 2024). The instrument form is reproduced in the scales gallery.

GOOD TO REMEMBER

- **FTND (Fagerstrom Test for Nicotine Dependence):** 6-item self-report, scored 0 to 10, grades *physical* dependence (not a diagnosis); score **>= 6** = high severity and heavier withdrawal; the two key items (cigarettes/day + time-to-first-cigarette) form the Heaviness of Smoking Index; first cigarette within 30 minutes of waking = high dependence, choose the higher-strength forms.

RULE **Grade before you treat.** Document the FTND (or at least cigarettes/day and time-to-first-cigarette) on every tobacco user, then match pharmacotherapy intensity to the score, high dependence gets combination NRT or varenicline, not a single low-dose patch.

23.4 The three verified first-line options and how to choose

The BAP position (lead). The British Association for Psychopharmacology (BAP) states the first-line treatments for nicotine dependence in adults are, alongside behavioural support, combination NRT, varenicline, cytisine, or a nicotine e-cigarette, offered with behavioural support but still offered if behavioural support is declined (BAP 2026). Crucially, BAP tells clinicians *not* to withhold varenicline over the outdated neuropsychiatric-safety concerns, including in people with mental illness. This is the verified first-line set and must anchor any answer.

What the other guidelines say. The Indian Psychiatric Society (IPS guidelines) frames every clinical contact around the 5As (Ask, Advise, Assess, Assist, Arrange), documents the FTND to set pharmacotherapy intensity, and names NRT as first-line with varenicline the most effective monotherapy and bupropion an alternative (IPS 2014). NICE recommends, combined with behavioural support, combination short-plus-long-acting NRT, varenicline, cytisinicline or a nicotine-containing e-cigarette as the options most likely to achieve stopping, and prescribing bupropion, NRT or varenicline before the quit date (NICE 2021). WHO mhGAP endorses brief intervention for all tobacco users in general settings and NRT/bupropion/varenicline where available (WHO mhGAP 2016).

AGENT	MECHANISM	LINE (PER BAP/IPS)
NRT (patch + gum/lozenge)	clean nicotine agonist, occupies alpha4beta2	first-line; combination > single-form
Varenicline	alpha4beta2 *partial* agonist	first-line; most effective monotherapy
Bupropion	noradrenaline-dopamine reup-take inhibitor	first-line alternative; less effective

The three cessation pharmacotherapies mapped to mechanism and guideline line; all three are verified first-line (varenicline the most effective single agent, combination NRT the strongest NRT approach) (BAP 2026, IPS 2014).

23.5 Nicotine replacement therapy: the patch, gum and lozenge

The principle. Nicotine replacement therapy gives back clean, slow-delivered nicotine to occupy the alpha4beta2 receptor and suppress withdrawal and craving, without the tar, carbon monoxide and carcinogens of combusted tobacco, then the dose is tapered off. It roughly doubles quit rates over placebo (Kaplan and Sadock 2024). NRT splits into a long-acting form (the transdermal patch, steady background level) and short-acting forms (gum, lozenge, spray, inhaler, for breakthrough craving).

The patch. The transdermal patch (Indian brand Nicotinell, generic nicotine) delivers continuous nicotine and comes in **21, 14 and 7 mg** per 24-hour strengths; a smoker of more than 10 cigarettes a day starts on the **21 mg/24 h** patch, then steps down through 14 and 7 mg over the

course of treatment (IPS 2014; KDT). It is started on the quit day or 1 to 2 weeks before, and continued for at least 8 to 12 weeks. Its weakness is that it cannot be self-titrated for sudden craving, which is why it is paired with a short-acting form.

Gum and lozenge. Nicotine gum (Indian brand Nicotex, generic nicotine polacrilex) and the lozenge each come in **2 mg and 4 mg** pieces; the 4 mg strength is for the highly dependent smoker (first cigarette within 30 minutes of waking), the 2 mg for the lighter smoker. Gum is chewed slowly and "parked" against the cheek, not chewed continuously, and acidic drinks (coffee, cola, juice) must be avoided for 15 minutes before use because they block buccal absorption (Tasman 2024). The evidence-based headline is that *combination* NRT, a long-acting patch plus a fast-acting gum or lozenge, is more effective than any single-form NRT, and this is what the guidelines now recommend as first-line (BAP 2026, NICE 2021).

WORKED EXAMPLE

A 44-year-old man smokes 25 cigarettes a day and lights his first within 5 minutes of waking; his FTND is 8 (high). You do not reach for a single 7 mg patch. You set a quit date, start a 21 mg/24 h patch (Nicotinell) for the background level, and add 4 mg nicotine gum (Nicotex) for breakthrough craving, this combination NRT, plus brief behavioural support, is first-line for a heavily dependent smoker (BAP 2026). You plan at least 8 to 12 weeks, then a stepped taper of the patch strength.

GOOD TO REMEMBER

- **NRT (nicotine patch Nicotinell; gum Nicotex; generic nicotine):** clean agonist replacement that occupies alpha4beta2 and roughly doubles quit rates; patch **21/14/7 mg**/24 h stepped down, gum/lozenge **2 mg or 4 mg** (4 mg for the highly dependent); combination (patch + fast-acting form) beats single-form NRT and is first-line; NRT is the only pharmacotherapy licensed in pregnancy (prefer intermittent forms, after behavioural support).

23.6 Varenicline: the alpha4beta2 partial agonist, most effective monotherapy

Mechanism. Varenicline (Indian brand Champix, generic varenicline) is a selective *partial agonist* at the alpha4beta2 nicotinic receptor. As a partial agonist it does two useful things at once: it mildly stimulates the receptor, giving enough dopamine to blunt withdrawal and craving, while simultaneously *blocking* nicotine from binding, so that a cigarette smoked on treatment delivers little reward (KDT; Stahl). It is the most effective single cessation agent (IPS 2014, BAP 2026).

The dose and titration. Varenicline is titrated up to avoid nausea, then held at the target dose for 12 weeks. The verified regimen: **0.5 mg once daily for 3 days**, then **0.5 mg twice daily for 4 days**, then **1 mg twice daily for 12 weeks** (target 1 to 2 mg/day) (IPS 2014, BAP 2026). The quit date is set for 1 to 2 weeks after starting the drug, so the receptor is already partly occupied when the patient stops. Nausea is the commonest side effect; abnormal dreams and insomnia are frequent.

The neuropsychiatric-safety question. Varenicline carried a historic black-box warning for mood change and suicidal ideation. The large EAGLES trial did not confirm an excess of serious neuropsychiatric events, and the warning has since been downgraded; BAP is explicit that

varenicline should *not* be withheld over these outdated concerns, including in people with mental illness, though monitoring of mood remains sensible in major mental illness (BAP 2026, IPS 2014).

GOOD TO REMEMBER

- **Varenicline (Champix; generic varenicline):** selective alpha4beta2 nicotinic *partial* agonist, the most effective cessation monotherapy; dose **0.5 mg OD x3 days, 0.5 mg BD x4 days, then 1 mg BD for 12 weeks**, quit date set 1 to 2 weeks after starting; nausea is the commonest adverse effect; the old neuropsychiatric black-box warning is downgraded (EAGLES), so do not withhold it in mental illness but monitor mood.

TRAP **Do not deny varenicline to the mentally ill.** The neuropsychiatric black-box warning has been downgraded and BAP says not to withhold it, refusing the most effective cessation drug to a smoker with depression or schizophrenia (the group who smoke most and die soonest) is now a guideline error, not a caution.

23.7 Bupropion: the NDRI alternative and its seizure caution

Mechanism and place. Bupropion (Indian brand Bupron SR, generic bupropion; the smoking-cessation brand internationally is Zyban) is an atypical antidepressant that inhibits noradrenaline and dopamine reuptake (an NDRI). In cessation it works around the nicotinic receptor entirely, providing dopaminergic tone without nicotine. It is a first-line *alternative*, less effective than varenicline, and it earns its keep when a smoker also has depression, because it treats both (a dual indication) (IPS 2014, BAP 2026).

The dose. Verified regimen: bupropion SR **150 mg once daily for 3 days**, then **150 mg twice daily** (target 150 to 300 mg/day), started **1 to 2 weeks before the quit day** and continued 7 to 12 weeks; it can be combined with NRT (IPS 2014, BAP 2026). The dose-limiting hazard is seizures: bupropion lowers the seizure threshold, so it is contraindicated in anyone with a seizure history, an eating disorder (anorexia or bulimia raise seizure risk), or on a MAOI, and is used with caution in bipolar disorder.

GOOD TO REMEMBER

- **Bupropion (Bupron SR / Zyban; generic bupropion):** noradrenaline-dopamine reuptake inhibitor, first-line *alternative* (less effective than varenicline), doubly useful when depression coexists; dose **150 mg OD x3 days then 150 mg BD** (150 to 300 mg/day), start 1 to 2 weeks before quit day, 7 to 12 weeks; the signature caution is *lowered seizure threshold*, so it is contraindicated in seizure history, eating disorders and concurrent MAOI.

23.8 The smoking-cessation CYP1A2 interaction: the trap after quitting

Smoke, not nicotine, induces CYP1A2. The polycyclic aromatic hydrocarbons in tobacco *smoke* (not the nicotine) induce the hepatic enzyme CYP1A2. Several psychotropics are CYP1A2 substrates, above all clozapine and olanzapine, but also haloperidol, fluvoxamine and duloxetine. A smoker on clozapine runs a lower plasma level because the enzyme is induced; when that patient *stops smoking*, the induction lifts over about a week and plasma levels rise, potentially to toxicity (Maudsley 2021, BAP 2026).

The management point. On stopping smoking, monitor and consider dose reduction of CYP1A2-metabolised drugs (clozapine and olanzapine first), guided by therapeutic drug monitoring; a rough guide is a possible need to reduce clozapine by up to a quarter over the first week of abstinence. Note that NRT does *not* prevent this, because it is the combustion products, not the nicotine, that drive the induction (Maudsley 2021). This is a classic examined interaction and a genuine ward hazard when an inpatient is made to stop smoking.

COMMON TRAP

Do not assume a patient on clozapine who quits smoking is now "safer". Stopping smoking removes the CYP1A2 induction, clozapine and olanzapine levels climb over the following week, and a stable patient can tip into toxicity (sedation, seizures, myocarditis risk). Anticipate it, monitor levels, and reduce the dose, and remember nicotine replacement will not shield the level, because smoke, not nicotine, was the inducer.

INDIA

India is one of the largest tobacco-consuming nations, and the pattern is distinctive: *smokeless* tobacco (khaini, gutkha, zarda, betel-quid, applied between gum and cheek) rivals or exceeds smoked forms (bidi, cigarette). Two consequences for the exam. First, varenicline is the guideline choice for *smokeless* tobacco users, where it raises quit rates by about 35% over placebo (BAP 2026), and the FTND, built around cigarettes, fits smokeless use poorly. Second, there is a large treatment gap: the National Tobacco Control Programme and tobacco-cessation clinics exist but reach a fraction of users, and while varenicline (Champix), bupropion (Bupron) and NRT (Nicotinell patch, Nicotex gum) are all marketed in India, cost keeps varenicline out of reach for many, so an NRT-plus-brief-intervention approach delivered through the general OPD, the 5As model IPS endorses, is the realistic default. Tobacco is not scheduled under the NDPS Act, which is why it is sold openly despite being the deadliest, the medico-legal frame for NDPS-scheduled drugs sits in the Mental health legislation and forensic psychiatry notes.

6	21	1	12
FTND HIGH-SEVERITY CUT-OFF (OUT OF 10)	PATCH STARTING STRENGTH, MG PER 24 H	VARENICLINE TARGET, MG TWICE DAILY	WEEKS OF PHARMACOTHERAPY

MNEMONIC

V beats B, and Combo beats Single

For choosing a cessation drug: *V*arenicline is the most effective single agent; *B*upropion is the weaker alternative (and the one with the seizure caution); and for NRT, *Combo* (patch + gum/lozenge) beats any *Single* form. That one line encodes the whole first-line hierarchy the examiner wants.

23.9 Special populations and the behavioural backbone

Pregnancy. In pregnancy, behavioural support is preferred; NRT (intermittent forms preferred over the patch) is offered only if behavioural support alone is insufficient, because NRT is the *only* pharmacotherapy licensed in pregnancy, varenicline and bupropion are not used (BAP 2026).

The pregnancy-and-substance frame more broadly sits in the Perinatal/women's mental health and emergency psychiatry notes.

Adolescents. Under-18s should not be offered varenicline, bupropion or cytisinicline (NICE 2021); behavioural treatment (motivational interviewing, brief intervention, CBT, contingency management) is the mainstay, and if any NRT is used the patch is the only form with demonstrated adolescent benefit (IPS 2014).

Behavioural support is not optional. Every guideline pairs the drug with behavioural support: brief telephone/quit-line counselling and structured 4-to-8-session counselling added to pharmacotherapy roughly double abstinence over drug alone (IPS 2014). The general MI and CBT technique behind this sits in the Psychotherapies, clinical assessment, MSE and nosology notes. The clinical rule is simple: offer pharmacotherapy *and* behavioural support, but still offer the drug if the patient declines the support (BAP 2026).

HOLD THIS

Grade with the FTND (>= 6 = high severity), then offer a first-line drug plus behavioural support: varenicline (Champix) 0.5 mg OD, up to 1 mg BD for 12 weeks is the most effective single agent; combination NRT (Nicotinell patch 21 mg + Nicotex gum) beats single-form NRT; bupropion (Bupron SR) 150 mg OD then BD is the alternative but is contraindicated with a seizure history, and after quitting, clozapine/olanzapine levels rise as smoke-induced CYP1A2 lifts.

24 · Sedative-hypnotic (benzodiazepine) dependence

The class that a psychiatrist most often makes dependent is one the psychiatrist prescribed. A **sedative** or **hypnotic** drug (the benzodiazepines, the older barbiturates, and the newer non-benzodiazepine "z-drug" hypnotics) is given for anxiety or insomnia, works well for a few weeks, and then, kept going for months, produces tolerance, dose-escalation and a physical dependence that is difficult to reverse. Examiners like this topic precisely because it is iatrogenic and preventable: they can ask you to name the withdrawal features (rebound anxiety and insomnia, the characteristic perceptual disturbances, and seizures on abrupt cessation), to explain why a short-acting agent withdraws worse than a long-acting one, and to lay out the one management principle that carries the whole answer, a gradual, individualised taper, usually after a switch to an equivalent dose of a long-acting agent.

Why it matters clinically. This is the mirror image of the alcohol story: the same GABA-A receptor, the same cross-tolerance, and the same hyperexcitable rebound when the drug is removed, which is why a benzodiazepine covers alcohol withdrawal and why **benzodiazepine withdrawal** itself looks like a slow-motion alcohol withdrawal. The receptor pharmacology behind the GABA-A adaptation is developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and is assumed here. The management is guideline-anchored and unusually clean, so this is a place to be exact: get the taper principle, the equivalence conversions and the withdrawal time-course cold.

24.1 What the dependence is: iatrogenic low-dose versus non-iatrogenic high-dose

The two clinical pictures. Benzodiazepine dependence splits into two forms that behave differently (Maudsley Prescribing Guidelines 2021). The *iatrogenic* (therapeutic-dose) form arises from low daily doses prescribed over many years for anxiety or insomnia; the patient is often not drug-seeking, takes the drug as prescribed, and is dependent in the sense that stopping produces a withdrawal syndrome. The *non-iatrogenic* form is high-dose, often illicitly obtained and intermittently consumed, frequently as part of polysubstance use, where daily intake may exceed **100 mg diazepam-equivalent**. The distinction sets the setting and pace: the low-dose patient can usually be tapered as an outpatient over months, the high-dose polysubstance user often needs a structured inpatient or specialist withdrawal.

Dependence is not the same as addiction. Physical dependence (neuroadaptation producing withdrawal on cessation) is the expected consequence of chronic exposure and can occur at therapeutic doses without any addiction, that is, without craving or compulsive use (Companion to Psychiatric Studies). The best estimate is that after **6 months** of continuous benzodiazepine exposure the risk of dependence is in the region of **45%**, and the single most important determinant is duration of treatment, the longer the exposure the higher the risk.

GOOD TO REMEMBER

- **Benzodiazepine dependence:** a physical dependence (neuroadaptation, not necessarily addiction) that splits into iatrogenic low-dose (therapeutic doses over years, not drug-seeking) and non-iatrogenic high-dose (illicit, often more than 100 mg diazepam-equivalent per day, usually polysubstance); the risk is roughly 45% after 6 months of continuous use, and duration of treatment is the strongest determinant; the discriminator from addiction is the absence of craving and compulsion in the typical therapeutic-dose patient.

24.2 The z-drugs: same receptor, same dependence, marketed as different

What they are. The z-drug hypnotics, zolpidem, zopiclone, zaleplon and eszopiclone, are non-benzodiazepine agents that act at the same benzodiazepine site of the GABA-A receptor and were introduced with a reputation for less tolerance, dependence and rebound. That reputation was based on short-term studies (Kaplan and Sadock 2024). More recent data show that tolerance, physical dependence and rebound insomnia all do occur with z-drugs, along with the class hazards of falls and complex sleep-related behaviours (sleep-driving, sleep-eating with amnesia). Because zolpidem has a short elimination half-life it causes little daytime carry-over but can produce next-morning memory impairment, and concern about adverse effects lowered the recommended zolpidem immediate-release dose to **5 mg**.

Why they matter for the exam. Treat a z-drug dependence exactly like a benzodiazepine dependence: convert to a diazepam equivalent and taper, or, where inter-dose withdrawal is a problem, switch to a longer-acting benzodiazepine first. A useful equivalence is that **zopiclone 7.5 mg** is about diazepam 5 mg, and eszopiclone 3 mg is about diazepam 10 mg (Maudsley Deprescribing Guidelines 2024).

PEARL

The "z" in z-drugs stands for the drug names (Zolpidem, Zopiclone, Zaleplon, esZopiclone), not for "zero dependence". They bind the benzodiazepine site of GABA-A, so they share cross-tolerance with benzodiazepines and alcohol, and are managed with the same taper. An Irish methadone-programme sample found 23% were misusing zopiclone, so do not assume a hypnotic is "safe" because it is not called a benzodiazepine.

24.3 The withdrawal syndrome: rebound anxiety and insomnia, perceptual disturbance, seizures

The core features. Benzodiazepine withdrawal is a hyperexcitable state that resembles alcohol withdrawal but is unusual in two ways: it is *delayed* compared with most withdrawal states, and it combines affective features with distinctive *perceptual disturbances* (Companion to Psychiatric Studies). The affective and physical core is rebound anxiety, insomnia (rebound anxiety and insomnia are the commonest early features), anxious dysphoria, daytime fatigue and a flu-like phase (sweating, anorexia, muscle aches, headache). The perceptual features are characteristic: heightened sensitivity to sound, light and touch (hyperacusis, photophobia), a "temporal-lobe" distortion of the environment (doors or walls appearing to slope), depersonalisation, and bizarre paraesthesiae including a sensation of "walking on cotton wool" (Kaplan and Sadock 2024; Companion). The dangerous end of the spectrum is seizures and, rarely, a withdrawal delirium.

Seizures and the abrupt-cessation risk. Fits are rare when a therapeutic-dose regimen is stopped but the risk rises sharply with abrupt cessation, high dose and short-acting high-potency agents; abrupt discontinuation of alprazolam can cause seizures and be life-threatening (Maudsley Deprescribing Guidelines 2024). This is the single reason a benzodiazepine or z-drug is never stopped abruptly from a dependent patient: the taper exists to prevent the seizure and the perceptual crisis, not merely to ease discomfort.

FEATURE CLUSTER	WHAT THE PATIENT REPORTS	EXAM DISCRIMINATOR
Rebound affective	Rebound anxiety, insomnia, anxious dysphoria, irritability, poor concentration	**rebound anxiety and insomnia are the earliest and commonest features**
Physical / flu-like	Sweating, tremor, nausea, anorexia, muscle aches, headache, hyperreflexia	overlaps alcohol withdrawal (shared GABA-A basis)
Perceptual (near-specific)	Hyperacusis, photophobia, distorted surroundings, depersonalisation, "cotton-wool" paraesthesiae	**perceptual distortion and depersonalisation are the near-signature of benzodiazepine withdrawal**
Severe / dangerous	Myoclonus, seizures, delirium	seizures mainly with abrupt cessation of high-dose or short-acting agents

Benzodiazepine withdrawal clusters; the affective rebound plus unique perceptual disturbance is what distinguishes it (Companion to Psychiatric Studies; Kaplan and Sadock 2024).

GOOD TO REMEMBER

- **Benzodiazepine withdrawal syndrome:** a delayed hyperexcitable state whose triad is rebound anxiety and insomnia, a distinctive perceptual disturbance (hyperacusis, photophobia, depersonalisation, "cotton-wool" paraesthesiae, temporal-lobe environmental distortion), and, at the severe end, seizures on abrupt cessation; the first management step is never to stop abruptly, so a dependent patient is always tapered; the discriminator from alcohol withdrawal is the delayed onset and the perceptual-distortion component.

24.4 The time-course: why the half-life sets the onset

Onset tracks elimination half-life. The onset of withdrawal is governed by the drug's elimination half-life, shorter half-life means quicker and often more severe onset, while its duration is set by how long the brain takes to re-adapt, not by how fast the drug clears (Maudsley Deprescribing Guidelines 2024). With a short-acting, high-potency agent (lorazepam, alprazolam) withdrawal begins within a day or so and is more intense, sometimes with inter-dose withdrawal even before the drug is stopped. With a long-acting agent (diazepam, with its long-acting active metabolite) symptoms are delayed, and after stopping a long-acting benzodiazepine the classic perceptual-affective phase described above starts some **5 to 7 days** later (Companion to Psychiatric Studies). This is the pharmacological reason for switching to a long-acting agent before tapering: it smooths and delays the withdrawal so the reduction is tolerable.

A trap hidden in the co-drinker. An alcohol-dependent patient also taking a long-acting benzodiazepine can have the onset of alcohol-withdrawal seizures or delirium postponed by up to several weeks, because the benzodiazepine holds the GABA-A receptor; when its level finally falls, delirium can emerge late and be misread as a postoperative or medical complication (Kaplan and Sadock 2024).

COMMON TRAP

Do not taper too fast, and do not read a slow-onset withdrawal as "the patient is fine". Because a long-acting benzodiazepine delays withdrawal by days to weeks, a reduction that looked well tolerated at review can precipitate the perceptual-affective syndrome, or a seizure, only later. The corresponding error in the co-drinker is calling a late-emerging delirium a surgical or medical complication when it is delayed alcohol or benzodiazepine withdrawal unmasked as the long-acting agent clears.

24.5 The management principle: switch to a long-acting agent, then taper gradually

The one rule that carries the answer. The guideline-verified management of sedative-hypnotic dependence is a *gradual, individualised dose reduction*, and abrupt discontinuation is avoided (VA/DoD, strong recommendation to gradually taper the benzodiazepine; NICE safe-prescribing guidance). The standard method is to convert the patient's benzodiazepine (or z-drug) to an equivalent dose of a long-acting agent, usually diazepam, because its long duration of action mitigates the inter-dose peaks and troughs and smooths withdrawal (Maudsley Deprescribing and Prescribing Guidelines). Then reduce in a slow, step-wise manner, proportionate to the current dose so the decrements get *smaller as the dose falls*, a common rule of thumb being a

reduction of about one-eighth of the daily dose per step, with the next step only when symptoms from the last have settled.

How long, and what does not help. Tapering is titrated to the individual: some patients can complete it in under 6 months, many take longer, and it is minimised but not always prevented by slow reduction over **3 to 6 months** or more (Kaplan and Sadock 2024). Two negatives are examinable: a 2018 Cochrane review found no add-on drug that reliably facilitates the withdrawal, and you should not treat withdrawal with another dependence-forming drug, or with sodium valproate or buspirone (Maudsley Deprescribing Guidelines 2024). What does help is psychosocial support, patient education and CBT alongside the dose reduction. Alprazolam withdrawal is notoriously the hardest, as the dose falls below about 1 to 1.5 mg the receptor down-regulates paradoxically and symptoms intensify even on a slow taper; substituting an equivalent dose of a longer-acting agent for the last steps can help.

AGENT	APPROX. DOSE EQUAL TO DIAZEPAM 5 TO 10 MG	NOTE FOR TAPERING
Diazepam	5 to 10 (the reference agent)	long-acting, active metabolite; the switch target
Chlordiazepoxide	25 (about diazepam 10)	long-acting; also the alcohol-withdrawal agent
Lorazepam	1 (about diazepam 10)	short-acting, high potency; harder withdrawal
Alprazolam	1 (about diazepam 10 to 20)	high potency; hardest taper, switch for final steps
Temazepam	10 (about diazepam 5)	short-acting hypnotic
Zopiclone (z-drug)	7.5 (about diazepam 5)	convert then taper as diazepam
Eszopiclone (z-drug)	3 (about diazepam 10)	convert then taper as diazepam

Approximate diazepam-equivalence for the common switch-and-taper; values are guide figures for planning, individualise to response (Maudsley Deprescribing Guidelines 2024).

GOOD TO REMEMBER

- **Diazepam (the taper agent):** the long-acting benzodiazepine to which the patient's shorter-acting agent is switched at an equivalent dose before a slow step-wise reduction (reductions become smaller as the dose falls, roughly one-eighth per step, over 3 to 6 months or longer); chlordiazepoxide 25 mg, lorazepam 1 mg and zopiclone 7.5 mg are each roughly diazepam 5 to 10 mg; the signature caution is never to stop abruptly (seizure risk) and not to add valproate, buspirone or another dependence-forming drug, none of which reliably helps.

24.6 What the guidelines say: BAP, the Indian Psychiatric Society, NICE and WHO

BAP. The British Association for Psychopharmacology (BAP) evidence-based framework for substance misuse endorses the standard approach of a gradual, medically supervised benzodiazepine withdrawal rather than abrupt cessation, with psychosocial support, and treats sedative-hypnotic dependence within the general principle of managing withdrawal, substitution

where needed, and prevention of complications (BAP 2012). BAP does not endorse an add-on pharmacotherapy that reliably eases the taper, consistent with the Cochrane finding above.

The Indian Psychiatric Society, NICE and WHO. NICE safe-prescribing and withdrawal guidance is the most explicit: convert to an equivalent diazepam dose where helpful, then reduce gradually and step-wise with shared decision-making and scheduled review, avoiding abrupt discontinuation (NICE). The VA/DoD guideline makes it a strong recommendation to gradually taper the benzodiazepine for patients needing withdrawal management, and NICE separately addresses the harder case of co-existing alcohol and benzodiazepine dependence, best managed with *one* benzodiazepine (chlordiazepoxide or diazepam), the dose covering both requirements, over an extended inpatient period of 2 to 3 weeks or longer (NICE; Maudsley 2021). The WHO mhGAP frame keeps sedative use short-term and cautions against long-term prescribing, reinforcing the prevention side. At the level of the Indian Psychiatric Society (IPS guidelines), the substance-use CPGs (Basu, Ghosh, Lal, Murthy) set out the general assessment-and-management architecture, the SBIRT screening frame, the ASI-based biopsychosocial assessment, the NDPS Act and Mental Healthcare Act interface, and MI as the foundational counselling style, all of which apply to sedative-hypnotic dependence; a benzodiazepine-specific IPS taper recommendation could not be confirmed from the available corpus and is flagged under gaps rather than stated.

INDIA

Benzodiazepine dependence is a genuinely Indian problem because these drugs are cheap, widely prescribed for anxiety and insomnia, and, despite scheduling under the Narcotic Drugs and Psychotropic Substances (NDPS) Act, 1985, often accessible over the counter in practice; alprazolam (Indian brand Alprax, also Restyl) is among the most prescribed. The Indian substance-use treatment gap and the concentration of formal care in de-addiction centres and Drug De-addiction Programme units mean many dependent patients are managed in general practice with little structured tapering, so the exam-safe message, switch to a long-acting agent and taper gradually with psychosocial support, is exactly the practice point to carry into an Indian clinic. The NDPS scheduling and prescriber compliance detail sits in the Mental health legislation and forensic psychiatry notes.

MNEMONIC

"SWITCH then SLIP"

SWITCH to a long-acting agent (diazepam) at an equivalent dose; then SLIP the dose down, Slow, step-wise, Longer as needed, Individualised, Psychosocial support alongside. Never a cliff; always a slope.

24.7 Assessment, monitoring and the special situations

What to assess and monitor. Establish the drug, dose, duration and any polysubstance use (especially opioids and alcohol), and estimate the total diazepam-equivalent daily dose. During the taper, monitor withdrawal symptoms and level of sedation at each review, and slow or pause

the reduction if symptoms are intolerable rather than pushing through. There is no scale specific to benzodiazepine withdrawal in routine use analogous to CIWA-Ar; the assessment is clinical, though the general SUD screening instruments (AUDIT for alcohol, DAST for drugs, ASSIST for general use) belong in the wider workup and their cut-offs are reproduced in the scales gallery.

The situations that change the plan. In pregnancy, benzodiazepines are not major teratogens but should ideally be discontinued gradually before conception; if a woman is found pregnant on a benzodiazepine, withdraw gradually over as short a time as is safe, mindful of withdrawal-seizure risk (Maudsley Deprescribing Guidelines 2024). In overdose, flumazenil reverses benzodiazepine-induced sedation and respiratory depression but is used selectively, it can precipitate seizures (particularly in mixed overdose, for example with tricyclics, or in the benzodiazepine-dependent patient) and has a much shorter half-life than most benzodiazepines, so the patient must be observed for re-sedation (Maudsley Prescribing Guidelines 2021). In the co-existing alcohol-and-benzodiazepine patient, use one benzodiazepine to cover both and extend the inpatient regimen.

RULE **Never a cliff, always a slope.** A sedative-hypnotic or z-drug is never stopped abruptly in a dependent patient; switch to an equivalent dose of a long-acting agent and reduce gradually and step-wise, titrated to the patient's withdrawal symptoms.

TRAP **Do not reach for an add-on to "cover" the taper.** No add-on drug reliably eases benzodiazepine withdrawal (Cochrane 2018), and you must not use another dependence-forming agent, sodium valproate or buspirone; the taper itself, plus psychosocial support and CBT, is the treatment.

5 to 7 days	45%	3 to 6 months	100 mg
ONSET AFTER STOPPING A LONG-ACTING BENZODIAZEPINE	DEPENDENCE RISK AFTER 6 MONTHS CONTINUOUS USE	TYPICAL GRADUAL TAPER DURATION, OR LONGER	DIAZEPAM-EQUIVALENT PER DAY MARKING NON-IATROGENIC DEPENDENCE

HOLD THIS

Sedative-hypnotic (benzodiazepine and z-drug) dependence is a physical dependence whose withdrawal is a delayed hyperexcitable syndrome of rebound anxiety and insomnia, a distinctive perceptual disturbance, and seizures on abrupt cessation; the one management principle, guideline-verified across BAP, NICE and VA/DoD, is a gradual individualised taper, usually after switching to an equivalent dose of a long-acting agent such as diazepam, never an abrupt stop.

25 · Inhalants, hallucinogens, NPS and caffeine

This is the tail of the substance paper, the group of drugs that never carry a whole question but reliably supply a one-line MCQ or a "compare and contrast" limb. The examiner wants three discriminations kept crisp: the **inhalant** that kills a healthy adolescent on the first sniff, the **hallucinogen** that produces no physical dependence and no dangerous withdrawal, and the fact that everyday **caffeine** has two formal DSM-5-TR diagnoses with numbered criteria. Get those three right and the low-yield block is safe.

Why it matters clinically. Two of these substances kill (inhalants by sudden cardiac death, high-dose caffeine by seizures and arrhythmia) and the rest are examined as pure discriminators: no withdrawal for hallucinogens, a bladder for ketamine, an unpredictable label for **novel psychoactive** substances. The reward-pathway anatomy behind why any of these are reinforcing sits in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the substance-induced-psychosis boundary (LSD, PCP, cannabinoids) sits in the Other psychotic disorders, delusional syndromes and catatonia notes. Figure opportunities are flagged in metadata for Ra to draw.

25.1 Inhalants and solvents: what they are and how they act

The class. Inhalants are volatile substances that are sniffed or "huffed" for a rapid intoxication: **solvent**s and glues containing toluene, aerosols, cleaning fluids, nail-polish remover, lighter fluid, paint thinner, petrol, and the gases (butane, propane, nitrous oxide). ICD-11 codes them as *disorders due to use of volatile inhalants* (6C4B). The defining features for the exam are that this is overwhelmingly a drug of *adolescents and street children*, that it is cheap and legal, and that intoxication is fast on and fast off (Kaplan and Sadock 2024, Tasman 2024).

The intoxication. **Inhalant use** produces a brief alcohol-like intoxication that begins within about **5 minutes** and clears in **1 to 2 hours**: euphoria then disinhibition, belligerent or assaultive behaviour, apathy and impaired judgement, with dizziness, nystagmus, slurred speech, unsteady gait, depressed reflexes, tremor, blurred vision and diplopia, progressing at higher doses to stupor and coma. Physical give-aways are a perioral rash ("glue-sniffer's rash"), solvent breath odour and residue on the face and hands (Kaplan and Sadock 2024).

GOOD TO REMEMBER

- **Inhalant/volatile-solvent intoxication:** volatile inhalants (toluene glue, aerosols, petrol, butane, nitrous oxide) sniffed mainly by adolescents/street children; intoxication onset within **5 minutes**, clears in **1 to 2 hours**; alcohol-like picture (euphoria then belligerence, ataxia, nystagmus, slurred speech), with the diagnostic clues of perioral "glue-sniffer's rash", solvent breath and facial residue; management is supportive in a low-stimulation setting.

25.2 Sudden sniffing death syndrome

The emergency. The single highest-yield inhalant fact is sudden sniffing death syndrome: a young, physically healthy solvent user drops dead, typically after a startle or sudden exertion during or just after huffing. The mechanism is catecholamine-sensitised myocardium, the volatile hydrocarbon sensitises the heart to adrenaline, so a surge of catecholamines (from being startled, chased or exercising) triggers a fatal ventricular arrhythmia (ventricular fibrillation) and cardiac arrest (Kaplan and Sadock 2024, Tasman 2024). It can happen on the first exposure, which is what makes it examinable and tragic. The practical corollary: do *not* startle or chase an intoxicated huffer, and adrenaline-driven resuscitation is relatively contraindicated because the heart is already catecholamine-sensitised.

The other lethal routes. Beyond the arrhythmia, inhalants kill by asphyxiation and suffocation (bag over the head), aspiration of vomitus, and direct CNS/respiratory depression; chronic use

causes toluene leukoencephalopathy, peripheral neuropathy, cerebellar signs, and hepatic, renal and bone-marrow toxicity (Kaplan and Sadock 2024).

WORKED EXAMPLE

A 15-year-old is caught by a shopkeeper sniffing correction fluid, bolts when chased, runs 50 metres and collapses. He has no cardiac history. This is sudden sniffing death syndrome: the toluene has sensitised his myocardium and the adrenaline surge of being chased has thrown him into ventricular fibrillation. The teaching point the examiner wants is the sequence, healthy adolescent, solvent, startle/exertion, arrhythmic sudden death, and that the person who chased him inadvertently triggered it.

GOOD TO REMEMBER

- **Sudden sniffing death syndrome:** sudden cardiac death in a young, healthy inhalant user, precipitated by a startle or exertion during/after huffing; mechanism is myocardial catecholamine sensitisation by the volatile hydrocarbon leading to fatal ventricular fibrillation; can occur on the first use; the management rule is do not startle or chase the user, and avoid adrenergic drugs in resuscitation.

RULE **Keep an intoxicated huffer calm.** The one management principle for inhalant intoxication is a low-stimulation, non-confrontational approach, startling, chasing or agitating the user can precipitate the fatal arrhythmia of sudden sniffing death.

TRAP **Do not give a benzodiazepine to sedate an agitated inhalant user.** Benzodiazepines potentiate the CNS and respiratory depressant effect of inhalants; marked agitation is controlled with a low-dose antipsychotic (for example haloperidol), not a benzodiazepine (Kaplan and Sadock 2024).

25.3 Hallucinogens: LSD, psilocybin and mescaline

The class. The classical hallucinogens are serotonergic agonists acting principally at the **5-HT2A** receptor: LSD (lysergic acid diethylamide), psilocybin (magic mushrooms), mescaline (peyote) and DMT. They produce a "trip", perceptual intensification and distortion, synaesthesia, depersonalisation and derealisation, altered time sense and mood lability, in a *clear sensorium* without delirium (Tasman 2024). The two facts that carry the marks are pharmacological, not phenomenological.

The two examined facts. First, hallucinogens produce *rapid tolerance* (tachyphylaxis, a trip loses potency over consecutive daily doses, with cross-tolerance between LSD, psilocybin and mescaline) but *no clinically significant physical dependence and no dangerous withdrawal syndrome*, the sharp discriminator against alcohol, opioids and sedatives (Tasman 2024). Second, the acute danger is behavioural, not physiological: the "bad trip" (acute panic/dysphoric reaction, managed by reassurance/"talking down" in a calm environment, with a benzodiazepine if needed and an antipsychotic reserved for frank psychosis), and rarely a prolonged hallucinogen-induced psychosis.

GOOD TO REMEMBER

- **Classical hallucinogens (LSD, psilocybin, mescaline):** 5-HT2A agonists producing perceptual distortion in a clear sensorium; key discriminators, *rapid tolerance* with cross-tolerance but *no physical dependence and no dangerous withdrawal*; the acute problem is the panic "bad trip" (managed by talking down plus a benzodiazepine, antipsychotic only for psychosis), not autonomic instability.

25.4 Hallucinogen persisting perception disorder (flashbacks)

The syndrome. Hallucinogen persisting perception disorder (HPPD) is the re-experiencing, *after the drug has cleared* and while sober, of perceptual symptoms first felt during intoxication: geometric hallucinations, flashes and trails of colour, haloes around objects, false peripheral movement, intensified colours, positive after-images, and macropsia/micropsia. To be a disorder these "flashbacks" must cause distress or impairment (DSM-5-TR; Tasman 2024). Reality testing is intact, the person knows the perception is not real, which separates HPPD from a psychosis. Flashbacks can be triggered by stress, cannabis, or emergence into a dark environment.

GOOD TO REMEMBER

- **HPPD (hallucinogen persisting perception disorder):** spontaneous re-experiencing of drug-era perceptual disturbance (trails, haloes, geometric/colour hallucinations, micropsia) occurring sober, days to years after use; reality testing is preserved (the discriminator from psychosis); commonest after LSD, often triggered by stress/cannabis/darkness.

25.5 Dissociatives: PCP and ketamine

The class. The **dissociative** anaesthetics are NMDA-receptor antagonists: phencyclidine (PCP, "angel dust") and ketamine. They block the NMDA-receptor channel, producing dissociation, analgesia and anaesthesia with a distinctive intoxication quite unlike the serotonergic hallucinogens (Kaplan and Sadock 2024). PCP intoxication is the dangerous one for the exam: violence and unpredictability, analgesia (loss of pain response, so self-injury), and the near-pathognomonic sign of *vertical and horizontal nystagmus* with hypertension, plus ataxia, at higher doses catatonia, rigidity, myoclonus, hyperthermia and rhabdomyolysis, and death from respiratory failure or arrhythmia. Management is a low-stimulation environment, a benzodiazepine for agitation, an antipsychotic for psychosis, and avoidance of restraint (which worsens rhabdomyolysis) (Kaplan and Sadock 2024).

Ketamine misuse. **Ketamine misuse** ("Special K") gives a shorter dissociative "K-hole"; the signature chronic harm the examiner wants is *ketamine-induced ulcerative cystitis*, a painful, contracted, ulcerated bladder from heavy recreational use (Maudsley 2021). Note the double life: the same molecule, at sub-anaesthetic dose, is an approved rapid-acting antidepressant (esketamine), so ketamine appears in both the mood and the substance papers.

GOOD TO REMEMBER

- **PCP / ketamine (dissociatives):** NMDA-receptor antagonists; PCP intoxication is violent and unpredictable with analgesia and the near-signature *vertical + horizontal nystagmus with hypertension*, risking rhabdomyolysis (avoid restraint) and death from respiratory failure; the examined chronic harm of ketamine misuse is *ulcerative cystitis* (contracted, ulcerated bladder); manage with low stimulation, benzodiazepine for agitation, antipsychotic for psychosis.

25.6 Novel psychoactive substances (NPS)

The category. Novel psychoactive substances (**nps**, "legal highs", "designer drugs") are synthetic compounds engineered to mimic a traditional drug's effect while staying one step ahead of scheduling law. The exam-relevant families are the synthetic cannabinoid receptor agonists ("Spice", "K2", far more potent and toxic than natural cannabis, causing agitation, psychosis, seizures and deaths), the synthetic cathinones ("bath salts", mephedrone/MCAT, MDPV, amphetamine-like stimulants driving the "chem-sex" scene), and novel dissociatives and psychedelics (New Oxford; Maudsley NEPTUNE guidance 2015).

Why they are hard. The teaching point is unpredictability: potency, contamination and content vary wildly, harm profiles are poorly characterised, and many NPS (like GHB) are *not detected on routine urine drug screens*, so a stimulant-toxidrome patient with a negative screen should raise NPS. There is no specific antidote; management is supportive, benzodiazepine-led symptomatic care as per the NEPTUNE framework (Maudsley 2021).

GOOD TO REMEMBER

- **NPS (novel psychoactive substances / "legal highs"):** synthetic drugs mimicking traditional agents, chiefly synthetic cannabinoids ("Spice"/"K2", more toxic than cannabis, cause psychosis/seizures) and synthetic cathinones ("bath salts", mephedrone); unpredictable potency and content, frequently *missed on routine urine drug screens*; no specific antidote, supportive benzodiazepine-led care (NEPTUNE).

25.7 Caffeine intoxication

The drug. Caffeine is the most widely used psychoactive substance in the world, an adenosine-receptor antagonist metabolised by CYP1A2 with a half-life of about **4 to 6 hours**. DSM-5-TR recognises four formal caffeine diagnoses, of which **caffeine intoxication** and caffeine withdrawal are the two to memorise (caffeine-induced anxiety disorder and caffeine-induced sleep disorder are the other two; caffeine use disorder remains a condition for further study) (Kaplan and Sadock 2024, DSM-5-TR).

The criteria. The DSM-5-TR criteria for caffeine intoxication are recent consumption usually well in excess of **250 mg** (about 2 to 3 cups of brewed coffee), plus *five or more* of twelve signs, restlessness, nervousness, excitement, insomnia, flushed face, diuresis, GI disturbance, muscle twitching, rambling thought/speech, tachycardia or arrhythmia, periods of inexhaustibility, psychomotor agitation, causing distress or impairment. The key differential is that this mimics a panic attack, generalised anxiety, mania, stimulant intoxication and akathisia, so ask about the coffee/energy-drink before diagnosing anxiety (DSM-5-TR). Very high doses (grams) cause

seizures and arrhythmia; serum levels above **100 mcg/mL** may be lethal and the lethal dose is roughly 10 g.

GOOD TO REMEMBER

- **Caffeine intoxication (DSM-5-TR):** recent intake usually > **250 mg** plus *5 or more* of 12 signs (restlessness, nervousness, insomnia, flushing, diuresis, GI upset, twitching, rambling speech, tachycardia/arrhythmia, inexhaustibility, psychomotor agitation) with distress; mimics panic/GAD/mania/akathisia (ask about the coffee first); very high doses cause seizures and arrhythmia; management is supportive as the short half-life (4 to 6 h) lets it self-resolve.

25.8 Caffeine withdrawal

The syndrome. **Caffeine withdrawal** is a genuine, DSM-recognised physical-dependence phenomenon that follows abrupt cessation of prolonged daily use: within **24 hours**, *three or more* of headache, marked fatigue/drowsiness, dysphoric or irritable mood, difficulty concentrating, and flu-like symptoms (nausea, vomiting, muscle pain/stiffness). *Headache is the hallmark*, diffuse, throbbing, movement-sensitive. It can follow doses as low as 100 mg/day, peaks over the first day or two and settles within about a week, and is a well-documented cause of post-operative and weekend headaches when the usual intake is missed (DSM-5-TR, Kaplan and Sadock 2024). It is unpleasant but never dangerous, and taper rather than abrupt stop prevents it.

GOOD TO REMEMBER

- **Caffeine withdrawal (DSM-5-TR):** abrupt cessation of prolonged daily use → within **24 hours**, *3 or more* of headache, fatigue/drowsiness, dysphoric/irritable mood, poor concentration, flu-like symptoms; *headache is the hallmark*; can occur from doses as low as 100 mg/day; benign and self-limiting; prevent by tapering; a classic cause of the post-operative and weekend headache.

COMMON TRAP

Do not misread a new-onset panic or anxiety presentation, or an inpatient's "unexplained" headache, without taking a caffeine history. High-dose caffeine intoxication is a textbook mimic of panic disorder, GAD and akathisia; caffeine-related headache from a missed morning coffee is a textbook mimic of a fresh headache disorder on the ward. The caffeine question is cheap and the diagnosis is missable.

INDIA

Two India-specific threads. Inhalants are the drug of India's street children and the urban poor: correction fluid, glue (the "dendrite"/tik-based adhesives), petrol and shoe-solution are cheap and unscheduled, and this is a paediatric-social problem the de-addiction services are poorly configured for, part of the wider substance-use *treatment gap*. Legally, most inhalants sit outside the Narcotic Drugs and Psychotropic Substances (NDPS) Act, which is precisely why they are freely available to minors, whereas LSD, ketamine and many NPS *are* scheduled, the NDPS/medico-legal frame is developed in the Mental health legislation and forensic psychiatry notes. Caffeine, delivered here mainly as strong tea (chai) and increasingly energy drinks among the young, is unscheduled everywhere and matters chiefly as a symptom-mimic in the OPD.

5	250	5	24
INHALANT INTOXICATION ONSET, MINUTES	CAFFEINE INTOXICATION THRESHOLD, MG	SIGNS NEEDED FOR CAFFEINE INTOXICATION (OF 12)	CAFFEINE WITHDRAWAL ONSET WINDOW, HOURS

HOLD THIS

Inhalants can kill a healthy adolescent on the first sniff (sudden sniffing death, a catecholamine-sensitised arrhythmia, so never chase or startle the user); hallucinogens do the opposite, no physical dependence and no dangerous withdrawal, only a panic "bad trip" and later flashbacks (HPPD); and caffeine is the everyday drug with two numbered diagnoses, intoxication (> 250 mg plus 5 of 12 signs) and withdrawal (3 of 5 within 24 hours, headache the hallmark).

26 · Behavioural addictions

A **behavioural addiction** is a disorder in which a rewarding *behaviour*, not a psychoactive substance, is pursued compulsively to the point of harm. The signal conceptual shift of ICD-11 was to carve out a small chapter called **Disorders due to addictive behaviours** and place **gambling disorder** and **gaming disorder** there, alongside the substance-use disorders, on the argument that the same reward-circuit machinery drives both (the dopamine and mesolimbic circuit mechanics belong to the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and are not re-derived here). This is a low-yield topic worth a compact, criterion-anchored pass: the exam task is to know that gambling moved from the impulse-control chapter into addiction, to state the three-part addiction template that both new syndromes share, and to know that gaming disorder is the genuinely new ICD-11 category while DSM-5-TR still parks internet gaming disorder in its research appendix.

Why it matters. The discrimination that earns marks is nosological. A **non-substance addiction** looks like a substance-use disorder shorn of the pharmacology: impaired control, escalating priority, and continuation despite harm, but with no ingested drug and (for gambling and gaming) no true physiological withdrawal. Getting the ICD-11-versus-DSM-5 placement right, and separating a genuine disorder from ordinary heavy gambling or gaming, is the whole of the topic. The medico-legal frame around online gambling and the NDPS Act sits in the Mental health legislation and forensic psychiatry notes.

26.1 The concept: what makes a behaviour an addiction

The template. ICD-11 defines a disorder due to addictive behaviours by three essential features that map exactly onto substance dependence minus the drug: impaired control over the behaviour (onset, frequency, intensity, duration, termination, context); *increasing priority* given to the behaviour so it takes precedence over other interests and daily activities; and *continuation or escalation despite negative consequences* (ICD-11 6C50/6C51; Clinical Methods in Psychiatry, AIIMS 2024). The pattern is present over an extended period, usually **12 months**, and causes significant distress or functional impairment. **What is deliberately absent.** Tolerance and withdrawal are *not* part of the ICD-11 essential features for gambling or gaming; there is no ingested substance and no pharmacological withdrawal syndrome, so the diagnosis rests on the behavioural triad, not on physiology (ICD-11 CDDR). **The move that examiners test.** In ICD-10,

pathological gambling (F63.0) sat among the habit and impulse-control disorders; ICD-11 reclassified it as a behavioural addiction because the accumulated evidence aligned it with the addictions rather than with pyromania and kleptomania (Clinical Methods in Psychiatry, AIIMS 2024).

RULE **Three features, not a drug.** A behavioural addiction is diagnosed on impaired control, escalating priority, and continuation despite harm, sustained over about 12 months, with no substance and no required physiological withdrawal.

PEARL

The reason gambling moved into the addictions and not, say, obsessive-compulsive disorder is *reward, not relief*: the gambler and the gamer chase a positively reinforcing high, whereas the person with OCD performs a ritual to *reduce* anxiety. Ego-syntonic pursuit of pleasure points to addiction; ego-dystonic neutralising of dread points to the compulsive spectrum.

26.2 Gambling disorder: the ICD-11 and DSM-5-TR criteria

ICD-11 (6C50). Gambling disorder is a persistent pattern of gambling behaviour, predominantly offline (6C50.0) or predominantly online (6C50.1), showing the three-feature addiction template applied to betting money or valuables, over an extended period of typically 12 months, with significant distress or impairment; it is not diagnosed if the behaviour is better explained by a manic episode (ICD-11 CDDR). **DSM-5-TR (F63.0).** DSM-5-TR keeps the name gambling disorder and places it as the sole non-substance disorder inside the Substance-Related and Addictive Disorders chapter. It requires **4 or more of 9** criteria in a 12-month period: needing to gamble with increasing amounts (tolerance), restlessness or irritability on cutting down (a withdrawal analogue), repeated unsuccessful efforts to stop, preoccupation, gambling when distressed, *chasing losses* (returning another day to get even), lying to conceal involvement, jeopardising a relationship or job, and relying on others for a financial bailout (DSM-5-TR). **Severity.** Mild is 4 to 5 criteria, moderate 6 to 7, severe 8 to 9. The most-endorsed criteria in mild disease are preoccupation and chasing losses (DSM-5-TR). **A DSM-5 change.** The old DSM-IV "illegal acts to finance gambling" criterion was dropped, taking the count from 10 to 9 and the threshold from 5 to 4.

FEATURE	ICD-11 GAMBLING DISORDER (6C50)	DSM-5-TR GAMBLING DISORDER (F63.0)
Chapter placement	**Disorders due to addictive behaviours**	**Substance-Related and Addictive Disorders (only non-substance member)**
Diagnostic logic	Three essential features (impaired control, priority, continuation despite harm)	Polythetic: 4 or more of 9 criteria
Time frame	Extended period, typically 12 months	Within a 12-month period
Online/offline	Specifiers 6C50.0 offline, 6C50.1 online	No online/offline specifier
Severity / course	Coded by remission; no criterion count	Mild 4-5, moderate 6-7, severe 8-9; episodic vs persistent
Exclusion	Not better explained by a manic episode	Not better explained by a manic episode

Gambling disorder across the two systems: the same construct reached by a feature list (ICD-11) or a criterion count (DSM-5-TR).

GOOD TO REMEMBER

- **Gambling disorder (DSM-5-TR):** 4 or more of 9 criteria over 12 months; the pathognomonic behaviour is *chasing losses* (returning to get even) and the desperation criterion is relying on others for a financial bailout.
- **The discriminator vs mania:** gambling driven only during a manic or hypomanic episode is *not* gambling disorder; the pattern must persist outside mood episodes (both systems exclude this).
- **The nosology point:** ICD-11 moved it from impulse-control (ICD-10 F63.0) into behavioural addiction; DSM-5-TR made it the only non-substance disorder in the addictions chapter.
- **First management step:** screen for the very high rates of comorbid mood, anxiety, substance and personality disorder and for suicidal ideation, which is common among treatment-seekers.

26.3 Gaming disorder: the genuinely new ICD-11 category

ICD-11 (6C51). Gaming disorder is the same three-feature template applied to digital or video gaming, predominantly online (6C51.0) or offline (6C51.1), over an extended period of typically 12 months, causing distress or impairment (ICD-11 CDDR). It is the flagship new addition to the chapter and, unlike gambling, does *not* involve wagering money; if the gaming is focused on wagers (for example internet poker), gambling disorder is the better label (ICD-11 CDDR). **DSM-5-TR status.** DSM-5-TR does not accept gaming as a formal disorder: it lists internet gaming disorder only in Section III, "Conditions for Further Study," with proposed criteria of **5 or more of 9** over 12 months (preoccupation, withdrawal, tolerance, unsuccessful control, loss of other interests, continued use despite problems, deception, mood-modification, and jeopardising a relationship or opportunity); it explicitly covers only non-gambling games (DSM-5-TR). **The demographic.** Gaming disorder is most prevalent in adolescent and young-adult males aged roughly 12 to 20 years, commonly co-occurs with ADHD, mood and anxiety disorders, and can be diagnosed after less than 12 months (for example 6 months) when the presentation is severe

(ICD-11 CDDR). Reported prevalence of internet gaming disorder averages about **4.7%** across countries (range 0.7 to 15.6%), with adolescent boys higher than girls (DSM-5-TR).

TRAP **Heavy gaming is not gaming disorder.** Daily long-duration play, common in adolescent males and during holidays, is not a disorder without the impaired control, escalating priority, and harm; cultural and peer-group norms must be weighed before diagnosing.

GOOD TO REMEMBER

- **Gaming disorder (ICD-11 6C51):** impaired control, increasing priority, continuation despite harm over about 12 months; *no wagering* (that would be gambling), and it can be diagnosed sooner than 12 months if severe.
- **DSM-5-TR internet gaming disorder:** still only a Section III condition for further study, 5 or more of 9 criteria, non-gambling games only.
- **The discriminator:** gaming disorder vs normal enthusiast play turns on functional harm and loss of control, not on hours alone; peer and cultural norms are considered.
- **Typical patient:** adolescent or young-adult male, often brought by parents, frequently with comorbid ADHD, mood or anxiety disorder.

4	5	12
OF 9 DSM-5-TR CRITERIA FOR GAMBLING DISORDER	OF 9 FOR DSM-5-TR INTERNET GAMING DISORDER (SECTION III)	MONTHS, THE TYPICAL ICD-11 PATTERN DURATION

26.4 Screening scales and the assessment

What the scales do. Behavioural addictions are rare in the general clinic, so routine screening is not required; assess comprehensively when a patient or family flags problematic gambling or gaming, and screen all substance-use patients for gambling given the overlap (Clinical Methods in Psychiatry, AIIMS 2024). **Gambling instruments.** The most widely used screen is the South Oaks Gambling Screen (SOGS); the Problem Gambling Severity Index (PGSI) and the Gambling Symptom Assessment Scale (G-SAS) are also used for severity and monitoring (Clinical Methods in Psychiatry, AIIMS 2024). The instrument forms are reproduced in the scales gallery; treat a positive screen as a prompt for full clinical assessment, never as the diagnosis. **The assessment core.** Map the behaviour onto the three features (control, priority, continuation despite harm), then document harm across the seven domains used for substance disorders (physical, psychological, social, occupational, financial, familial, legal), the significant abstinent attempts, and the comorbid psychiatric picture, distinguishing an independent mood disorder from behaviour occurring only within a manic episode (Clinical Methods in Psychiatry, AIIMS 2024).

INDIA

There is no national prevalence study of behavioural addictions in India, but interest is rising as smartphone and online-gaming penetration grows; the AIIMS clinical-methods teaching flags gaming disorder as an adolescent presentation and gambling as an adult one, and folds both into the standard addiction assessment rather than a separate service. The wider addiction treatment gap is stark: the national survey estimates a treatment gap around **91%** for substance use disorders, and behavioural addictions, being less recognised and rarely presenting, are even less likely to reach the de-addiction centre or the district day care service. When gambling or gaming does present, it is managed within the existing DDAP and de-addiction framework, not a bespoke pathway.

26.5 Management: psychosocial first, naltrexone the one drug

The mainstay is psychological. Cognitive-behavioural therapy and motivational interviewing are the evidence-based core for gambling disorder, supported by peer resources such as Gamblers Anonymous; the general MI and CBT technique is developed in the Psychotherapies, clinical assessment, MSE and nosology notes. **The one drug with likely effect.** No medicine is licensed for gambling disorder, but the opioid antagonist naltrexone (Indian brands Naltima or Nodict) is the only agent with likely effectiveness and is recommended by international and draft NICE guidance to reduce gambling severity, working by dampening mesolimbic dopamine release via GABAergic disinhibition in the ventral tegmental area (Maudsley 15th edition; Kaplan and Sadock 2024). It should be started in a specialist setting after baseline biochemistry, at **25 mg/day** increasing to **50 mg/day**, with efficacy reviewed at **4 to 6 weeks** and 6-monthly renal and liver monitoring (Maudsley 15th edition). Patients must be warned about the interaction with any concomitant opioid. **Alternatives.** Nalmefene, SSRIs, N-acetylcysteine, topiramate, lithium and modafinil have all been trialled with weaker evidence; naltrexone remains first among them (Maudsley 15th edition). Gaming disorder management is chiefly psychosocial and family-based; no drug is established.

TRAP **Dopamine agonists can cause gambling.** Pramipexole, ropinirole and aripiprazole (and other dopamine partial agonists) can induce or worsen an impulse-control disorder, including pathological gambling; always take a gambling history before and during dopaminergic prescribing, especially in Parkinson disease.

GOOD TO REMEMBER

- **Naltrexone (Naltima, Nodict) for gambling:** the only drug with likely effect; start 25 mg/day, titrate to 50 mg/day, review at 4 to 6 weeks; monitor LFTs and renal function; warn about the opioid interaction and do not start in a current opioid user.
- **Mechanism:** mu-opioid antagonism disinhibits GABA input to VTA dopamine neurons, cutting reward-related dopamine and gambling urges.
- **First-line overall:** CBT and motivational interviewing are the psychosocial mainstay; medication is adjunctive and unlicensed.

HOLD THIS

ICD-11 created a behavioural-addiction chapter holding gambling disorder (moved out of impulse control) and the new gaming disorder, both diagnosed on impaired control, escalating priority, and continuation despite harm over about 12 months; DSM-5-TR keeps gambling disorder (4 of 9 criteria) but leaves internet gaming disorder in the research appendix (5 of 9), and naltrexone titrated 25 to 50 mg/day is the one drug with likely benefit for gambling.

27 · Substance use in special populations

The generic assessment-and-management frame you have built for alcohol and opioids has to be re-tuned when the patient is a teenager, a pregnant woman, an older adult, or someone whose body is already carrying a serious medical illness. **Why it matters clinically.** The examiner uses **special populations** as a rapid probe of whether you can bend the rules safely: the screening tool changes, the drug you reach for changes, and the one contraindication that is inert in a fit 30-year-old becomes decisive. This is a low-tier recognition topic, so the aim is a short, confident list of the population-specific twists, with the deeper frames cross-referenced rather than re-derived.

Kept deliberately brief. The full **substance use in pregnancy** and fetal-alcohol detail, the antenatal-clinic workup and maternal withdrawal management sit in the Perinatal/women's mental health and emergency psychiatry notes; the underlying reward-circuit vulnerability of the adolescent brain sits in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the NDPS Act and the medico-legal frame around minors and capacity sit in the Mental health legislation and forensic psychiatry notes. Here we teach only what is population-specific: the tool, the dose, the caution.

27.1 The four populations and the single governing principle

The governing principle. In every special population the diagnosis of a substance use disorder is made by the *same* ICD-11 or DSM-5-TR criteria; what changes is the screening instrument, the pharmacotherapy that is safe, and the balance of risk. The four high-yield groups are the **adolescent**, the pregnant woman, the older adult, and the patient with serious **comorbid medical illness**. Get the population-specific tool and the population-specific drug caution for each and you have the whole topic.

Adolescent substance use

Substance use disorder with onset in the teens; screen with CRAFFT, treat with a family- and psychosocial-first approach, medication reserved and evidence-limited.

Substance use in pregnancy

Any maternal use in gestation; the priority is retention in agonist treatment (opioids) and safe managed withdrawal (alcohol, sedatives), never abrupt unsupervised detoxification.

Elderly substance use

Under-recognised late-onset or continuing use in older adults; alcohol and prescribed benzodiazepines dominate, pharmacokinetics shift, and interactions and falls are the danger.

Comorbid medical illness

Substance use alongside liver disease, HIV, hepatitis, cardiac or renal disease; the illness constrains both the withdrawal agent and the relapse-prevention drug.

27.2 Adolescents: CRAFFT, the developmental stakes, and a family-first approach

Screen with the right tool. Adult instruments such as AUDIT and CAGE are not validated for teenagers; the population-specific screen is the CRAFFT (Car, Relax, Alone, Forget, Family/Friends, Trouble), a six-item interview covering alcohol and other drugs together. A score of **2 or more** positive answers is the cut-off that flags a need for fuller assessment (Clinical Methods in Psychiatry, AIIMS 2024; Kaplan and Sadock 2024). The related BSTAD and S2BI screens serve the same purpose. The actual instrument form is in the scales gallery.

Why adolescence is the danger window. Roughly **80 per cent** of people with a substance use problem began using as teenagers, and the estimated risk of developing a disorder by age 18 is about **24 per cent** (Kaplan and Sadock 2024). Earlier onset means a higher chance the disorder persists into adulthood, and repeated use interferes with the rapid prefrontal and reward-circuit maturation still under way through the early twenties. Childhood ADHD, trauma and oppositionality are the strongest antecedent risks, so screening for a co-occurring psychiatric disorder is not optional.

Treatment is family- and psychosocial-first. The evidence base in **adolescent substance** use rests on family-based and psychosocial interventions (multidimensional family therapy, attachment-based family therapy, motivational and cognitive-behavioural work), not medication. Where pharmacotherapy is used it is narrow: buprenorphine-naloxone (Suboxone) is approved for opioid dependence in those **16 years and older** (Woody 2008), and bupropion (Bupron) at **300 mg/day** and nicotine replacement have adolescent tobacco-cessation evidence (Moolchan 2005; Muramoto 2007). Dual diagnosis is treated integrated and concurrently, never "get sober first".

WORKED EXAMPLE

A 16-year-old is brought after a road-traffic accident; he admits he had been drinking and had smoked cannabis, and that he uses alone and has forgotten things he did while high. That is three CRAFFT items (Car, Alone, Forget), well above the cut-off of 2, so he needs a full substance and psychiatric assessment, family engagement and a psychosocial plan, not a one-off warning.

GOOD TO REMEMBER

- **CRAFFT:** the six-item adolescent alcohol-and-drug screen (Car, Relax, Alone, Forget, Family/Friends, Trouble); the discriminator is that it is validated for teenagers where AUDIT and CAGE are not, the cut-off is a score of 2 or more positive answers, and a positive screen triggers full assessment plus screening for the near-universal comorbid psychiatric disorder (ADHD, trauma, conduct), with family-based psychosocial treatment as the first and main step.

27.3 Pregnancy: keep the agonist, manage withdrawal safely, never precipitate it

Opioids: maintain agonist treatment. The governing rule of **substance use in pregnancy** for opioid dependence is to *retain* the woman on opioid agonist maintenance, because unsupervised

withdrawal risks miscarriage, preterm labour and relapse. Methadone is the traditional first-line agonist in pregnancy and is preferred over buprenorphine in several guidelines, though buprenorphine (Tidigesic) may also be offered and is increasingly used; the woman already stable on one agent is kept on it (BAP; NICE). Two hard cautions: do *not* switch a stabilised woman from methadone to buprenorphine during pregnancy because of the precipitated-withdrawal risk, and split the methadone dose in the third trimester to blunt peak-and-trough fetal exposure. Naltrexone is not used for maintenance in pregnancy.

Alcohol and sedatives: hospitalise and taper gently. Pregnant women in alcohol or sedative withdrawal are admitted; benzodiazepines are used at the lowest effective dose for the shortest duration, and oxazepam is preferred for its intermediate half-life and absence of active metabolites (BAP). Parenteral thiamine is given before any glucose load, exactly as in the non-pregnant drinker. The teratogenic fetal-alcohol picture and neonatal abstinence syndrome are covered in the Perinatal/women's mental health and emergency psychiatry notes.

RULE **In pregnant opioid dependence, keep her on the agonist.** Retention on methadone or buprenorphine maintenance protects the pregnancy; supervised managed withdrawal, not abrupt detoxification, is the fallback if withdrawal is truly needed.

TRAP **Switching methadone to buprenorphine mid-pregnancy.** Buprenorphine is a partial agonist and will precipitate withdrawal in a woman stabilised on full-agonist methadone; do not switch agents in pregnancy, and never give naltrexone to a pregnant opioid-dependent woman.

GOOD TO REMEMBER

- **Opioid agonists in pregnancy:** methadone (traditional first-line, split the dose in the third trimester) or buprenorphine (Tidigesic) maintenance is continued through pregnancy at a retaining dose; the discriminators are that you never precipitate withdrawal by switching a methadone-stable woman to the partial agonist buprenorphine, you never use naltrexone, and for alcohol or sedative withdrawal you hospitalise and use the lowest-dose shortest-course benzodiazepine (oxazepam preferred) with parenteral thiamine before glucose.

27.4 Elderly and comorbid medical illness: the same drug, a different margin of safety

Elderly substance use is under-recognised. In older adults the picture is dominated by alcohol and long-prescribed benzodiazepines rather than illicit drugs, and it is routinely missed because the presentation is confounded with falls, confusion and "ageing". Age-related pharmacokinetic change (reduced volume of distribution, slower clearance, greater CNS sensitivity) means a "normal" dose behaves like a larger one, so withdrawal management shifts toward shorter-acting agents such as lorazepam and the whole approach is delivered in a supportive, non-confrontational, brief-intervention style (IPS_CPG). Anti-craving and detoxification doses are started lower and titrated more slowly.

Comorbid medical illness constrains the drug. With serious **comorbid medical illness** the diagnosis is unchanged but the agent is dictated by the organ that is failing. In established hepatic compromise the withdrawal benzodiazepine is switched from chlordiazepoxide to lorazepam or oxazepam, which lack oxidative hepatic metabolism; disulfiram is avoided in significant liver

disease and in cardiac disease; and every patient with current or past injecting use is screened at baseline and annually for HIV, hepatitis B and C, syphilis and tuberculosis. The comorbid psychiatric-illness (dual-diagnosis) frame is treated in the dual-diagnosis topic.

2	16	300
CRAFFT POSITIVE-ANSWER CUT-OFF FLAGGING NEED FOR FULL ASSESSMENT	MINIMUM AGE (YEARS) FOR APPROVED BUPRENORPHINE-NALOXONE IN OPIOID DEPENDENCE	BUPROPION DOSE (MG/DAY) WITH ADOLESCENT TOBACCO-CESSATION EVIDENCE

PEARL

The single organ that most often rewrites your prescription across all these populations is the liver: it pushes you off chlordiazepoxide onto lorazepam or oxazepam for withdrawal, off disulfiram for relapse prevention, and toward the lowest-dose shortest-course strategy you would already use in the pregnant woman and the older adult.

27.5 The India frame: reaching the special populations across the treatment gap

The gap is the theme. India's substance-use treatment gap is very large, and it falls hardest on exactly these special populations: adolescents outside any screening system, pregnant women whose drinking or opioid use is stigmatised and unasked, and older adults whose alcohol use is normalised. The response is organised around the de-addiction and drug-de-addiction programme (DDAP) network of centres, the Indian Psychiatric Society substance-use clinical practice guidelines, and delivery through the day care centre and trained non-specialist community workers (IPS_CPG). The NDPS Act frames access to controlled agonists and is covered in the Mental health legislation and forensic psychiatry notes.

Buprenorphine access shapes what is possible. In Indian outpatient practice buprenorphine-naloxone (4:1) is the first-line agonist, which matters for the pregnant and adolescent opioid-dependent patient because it is the accessible maintenance option; methadone is restricted to government OST clinics run under the National AIDS Control Organisation and select institutions (for example AIIMS NDDTC, NIMHANS), so a pregnant woman needing methadone is referred to a licensed OST centre rather than managed in private practice (IPS_CPG). Assessment in the Indian setting commonly uses the Addiction Severity Index or its Indian short-form.

INDIA

The special-population priority in India is upstream identification: ask every adolescent (CRAFFT), every antenatal patient, and every older adult about alcohol and drugs, because the treatment gap means most never reach a de-addiction service. Buprenorphine-naloxone is the accessible first-line agonist; methadone maintenance for a pregnant opioid-dependent woman must go through a NACO-licensed OST clinic, not a private prescription.

HOLD THIS

Same diagnostic criteria, different tool and different drug: CRAFFT (cut-off 2) for the adolescent, keep the agonist and never precipitate withdrawal in the pregnant opioid user, lorazepam or oxazepam and lower-and-slower for the elderly and the liver, screen for blood-borne virus in every injector.

Psychosocial treatment and relapse prevention

28 · Motivational interviewing

Almost every substance-use answer ends with a psychosocial limb, and the one the examiner most wants named is **motivational interviewing**. It matters because the core problem in addiction is not ignorance but **ambivalence**: the person genuinely wants to change and genuinely wants to keep using, at the same time. Confront that ambivalence head-on and it hardens; work *with* it and the person argues themselves toward change. Motivational interviewing (**MI**) is the collaborative, goal-directed conversational method, developed by William Miller and Stephen Rollnick, that does exactly this, and its manualised four-session research form is **motivational enhancement therapy**. For an Indian exam this is the highest-yield psychotherapy of the whole block, because it is deliverable by trained non-specialist workers, needs no drug, and is written into the IPS clinical practice guidelines as a first-line psychosocial intervention for the treatment gap.

Why it matters clinically. MI is where the guideline word "offer motivational enhancement therapy or brief intervention" turns into a technique you can actually do (IPS 2014). It is owned and fully taught here as a substance-use skill; the wider psychotherapy frame (general CBT, the broader MI evidence base) is developed in the Psychotherapies, clinical assessment, MSE and nosology notes and is not re-derived here. One figure carries this topic: Fig 13.18, the spirit-OARS-change-talk schematic. Get four things exact and you can answer anything asked: the spirit, the OARS micro-skills, what change talk is and how you evoke it, and how MET packages it all.

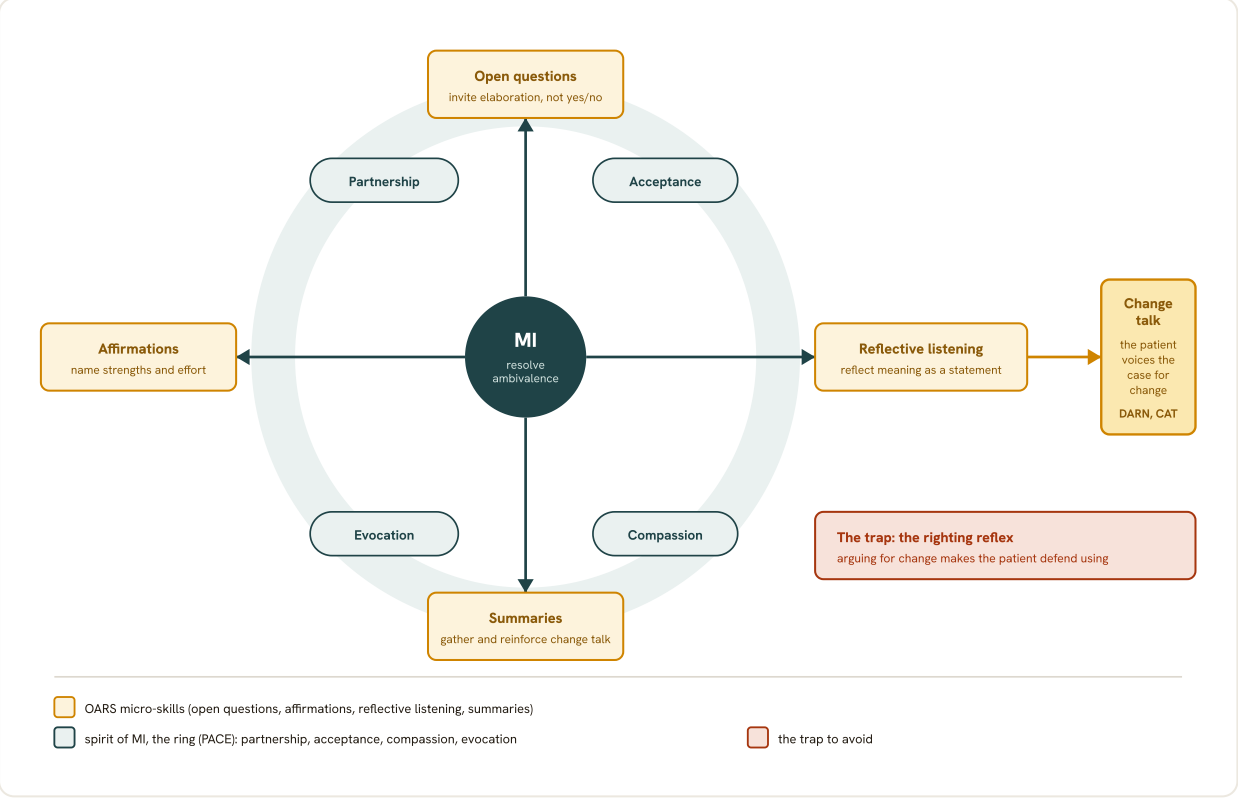


Fig 13.18 Motivational interviewing: the spirit and the OARS skills. The method sits at the centre, resolving ambivalence in favour of change. Around it are the four OARS micro-skills, open questions, affirmations, reflective listening and summaries, the moment-to-moment tools. Behind them is the ring that must hold them, the spirit of MI (PACE): partnership, acceptance, compassion and evocation. The whole point is to evoke the patient's own change talk (DARN, then CAT), while avoiding the righting reflex of arguing for change.

28.1 The definition: a collaborative method that resolves ambivalence in favour of change

What MI is. Motivational interviewing is "a collaborative, person-centred form of guiding to elicit and strengthen motivation for change" (Miller and Rollnick). It is *directional* without being directive: the clinician is steering toward a specific target (reduced or stopped use) but does so by drawing the arguments for change out of the patient rather than supplying them. It grew out of Miller's 1983 work with problem drinkers and became the standard motivational method across all addictive behaviours (Kaplan and Sadock 2024; Tasman 2015).

What MI is not. It is not persuasion, not education, not confrontation, and not a warm-up before the "real" therapy. The single most important error to avoid is the **righting reflex**, the clinician's instinct to fix the patient by arguing for change; because ambivalent people resolve tension by defending whichever side is attacked, arguing for change makes the patient argue for the status quo.

RULE **Let the patient voice the argument for change.** In MI the person, not the clinician, makes the case for changing; your job is to evoke and reinforce that self-motivational speech, never to supply it.

28.2 The spirit of MI: partnership, acceptance, compassion, evocation

The underlying stance. Before any technique comes the **spirit of mi**, the mindset without which the skills are hollow. Miller and Rollnick define it by four elements: *partnership* (a collaboration between two experts, the clinician on change and the patient on their own life, not an expert

acting on a passive recipient); *acceptance* (absolute worth, accurate empathy, autonomy support, and affirmation); *compassion* (actively promoting the patient's welfare, not the clinician's agenda); and *evocation* (drawing motivation out of the patient rather than installing it) (Tasman 2015; Kaplan and Sadock 2024).

Autonomy is the load-bearing idea. The clinician repeatedly affirms that the choice is the patient's, which paradoxically lowers defensiveness and frees the person to consider change. This is why MI works in mandated and reluctant patients where confrontation fails.

MNEMONIC

PACE

Partnership, **A**cceptance, **C**ompassion, **E**vocation, the four elements of the spirit of MI. If a technique is delivered without PACE it is not motivational interviewing, it is just a checklist.

28.3 The four processes: engaging, focusing, evoking, planning

The flow of a session. MI unfolds through four sequential-yet-recursive processes. *Engaging* builds the working relationship. *Focusing* agrees the change target (which behaviour, which direction). *Evoking* draws out the patient's own reasons for change, the heart of MI and what distinguishes it from generic counselling. *Planning* develops commitment and a concrete plan once the patient signals readiness (Tasman 2015). Move to planning too early and you re-open ambivalence; the plan must follow, not force, readiness.

WORKED EXAMPLE

A 34-year-old sent by his family for daily drinking says "I don't have a problem, my wife does." Rather than correcting him (the righting reflex), you *engage* ("tell me what a normal day looks like for you"), *focus* ("would it be alright to spend a few minutes on the drinking specifically?"), then *evoke* ("what do you notice is different on the mornings after you've drunk?"). His own answer, "I can't get to work on time," is change talk you elicited, not advice you imposed. Only when he says "maybe I should cut down" do you move to *planning*.

28.4 OARS: the four core micro-skills

The toolkit. The moment-to-moment skills of MI are captured by **oars**: **open questions**, **affirmations**, **reflective listening**, and **summaries**. These are the concrete verbal behaviours the examiner expects you to list and unpack (Miller and Rollnick; Tasman 2015).

Open questions

Questions that cannot be answered "yes/no", inviting the patient to elaborate ("what worries you about your smoking?") rather than closed interrogation.

Affirmations

Genuine statements recognising the patient's strengths, efforts and worth ("it took real effort to come today"), building self-efficacy, not empty praise.

Reflective listening

Reflecting back the patient's meaning as a statement, from simple repetition to complex reflection of underlying feeling; the signature MI skill and the main vehicle for empathy.

Summaries

Pulling together what the patient has said, especially their change talk, to reinforce it and steer the conversation ("so on one hand..., and on the other...").

MNEMONIC

OARS row you toward change

Open questions, **A**ffirmations, **R**eflective listening, **S**ummaries. Reflective listening is the paddle you use most; the others set direction.

28.5 Change talk and sustain talk: the currency of the method

Listen for the language of change. **Change talk** is any patient speech that favours change; *sustain talk* is speech that favours the status quo. MI is, at core, systematically evoking and reinforcing change talk while not amplifying sustain talk. Preparatory change talk is remembered as *DARN*, Desire ("I want to stop"), Ability ("I could stop"), Reasons ("my liver is suffering"), and Need ("I have to for my kids"); mobilising change talk is *CAT*, Commitment, Activation, and Taking steps, and predicts actual behaviour change (Miller and Rollnick).

How you evoke it. Ask evocative open questions, use the importance and confidence rulers ("on 0 to 10, why a 4 and not a 2?", which forces the patient to voice reasons for change), explore values, and look back or forward. Then reflect and summarise the change talk so the patient hears their own motivation echoed.

PEARL

The confidence and importance "rulers" are the single most exam-quotable MI technique. Asking "why are you at a 4 and not a 0?" makes the patient list reasons they *are* motivated (change talk); asking "why not a 10?" would elicit sustain talk, so you deliberately ask the lower-anchor version.

28.6 Rolling with resistance: working with discord, not against it

Do not wrestle. What older MI called "rolling with resistance" (now reframed as responding to *sustain talk* and *discord*) means: when the patient pushes back, you do not argue, you flow with it. Techniques are simple reflection, amplified reflection (reflecting the sustain talk slightly stronger so the patient themselves qualifies it), double-sided reflection (holding both sides of the ambivalence), shifting focus, and emphasising personal autonomy and choice (Miller and Rollnick; McCrady alcohol therapist guide). Resistance in MI is read as a signal that the clinician is pushing too hard, not as patient pathology.

TRAP **Do not argue with denial.** Meeting "I can quit any time" with "no you can't, look at your history" hardens the position; reflect it, roll with it, and let the discrepancy between the patient's goals and their behaviour do the work.

28.7 Developing discrepancy: the engine of motivation

The mechanism. Motivation rises when the patient perceives a gap between their present behaviour and their broader goals or values ("I want to be a present father" versus "I'm drunk most evenings"). The MI clinician gently develops and amplifies this *discrepancy*, letting the patient, not the clinician, articulate it. This is the classic Miller and Rollnick principle set, historically summarised as express empathy, develop discrepancy, roll with resistance, and support self-efficacy.

COMMON TRAP

Developing discrepancy is not shaming or guilt-tripping. If the patient feels judged, defensiveness returns and change talk dries up. The discrepancy must be surfaced within an accepting, affirming stance, the patient noticing the gap themselves, not the clinician rubbing their nose in it.

28.8 Motivational enhancement therapy: MI in its manualised form

What MET is. **Motivational enhancement therapy** (MET) is the standardised, manualised, brief form of MI developed for and validated in Project MATCH. It packages the MI spirit and OARS skills into a short structured course, classically **four sessions**, whose distinctive added ingredient is *personalised assessment feedback*: the patient's own results (for example liver enzymes, quantity-frequency, a scale score) are fed back in an MI style to evoke change talk (Kaplan and Sadock 2024; Tasman 2015). The IPS guidelines specify **met** as four structured sessions and place it, alongside CBT and relapse prevention, as a first-line psychological intervention for substance use in India (IPS 2014).

MET versus brief intervention versus FRAMES. MET is the full four-session package; a *brief intervention* is the shorter 5 to 15 minute opportunistic version for hazardous or harmful use not yet meeting dependence, distilled by the FRAMES acronym: Feedback, Responsibility (the choice is yours), Advice, Menu of options, Empathy, and Self-efficacy (IPS 2014).

MNEMONIC

FRAMES

Feedback, **R**esponsibility, **A**dvice, **M**enu of options, **E**mpathy, **S**elf-efficacy, the active ingredients of an effective brief intervention, the short-contact cousin of MET.

INDIA

MI and MET are the parts of the substance-use toolkit that scale to India's treatment gap. The IPS clinical practice guidelines direct services to deliver "brief, motivation-based psychosocial interventions" with a strategic shift to community and home-based delivery by trained non-specialist health workers, precisely because MI needs no drug, no laboratory and no specialist, and works in the primary-care and de-addiction-centre settings where most Indian care happens (IPS 2014). WHO mhGAP likewise lists motivational interventions among the structured psychosocial options for alcohol dependence. So in an Indian answer, MET (four sessions) and brief intervention (5 to 15 minutes) are not optional extras, they are the front line of the psychosocial limb that pairs with every anti-craving drug and every OST induction.

28.9 Where MI fits: not a stand-alone cure but the motivational front end

The place in the pathway. MI/MET is most powerful early, to convert ambivalence into engagement and readiness, and it improves outcomes when combined with pharmacotherapy and with more skills-based work such as CBT and relapse prevention (IPS 2014). It is transdiagnostic across substances, so the same spirit and OARS skills serve alcohol, opioids, tobacco (motivational interviewing with personalised feedback is an evidence-based way to move ambivalent smokers toward cessation) and behavioural addictions. It is a way of being with the patient that can be layered onto any other intervention, not a rival to them.

4	4	5 to 15 min
STRUCTURED SESSIONS IN A STANDARD MET COURSE (IPS)	ELEMENTS OF THE SPIRIT OF MI: PARTNERSHIP, ACCEPTANCE, COMPASSION, EVOCATION	A BRIEF MOTIVATIONAL INTERVENTION FOR HAZARDOUS OR HARMFUL USE

GOOD TO REMEMBER

- **Motivational interviewing (MI):** a collaborative, person-centred, goal-directed method (Miller and Rollnick) that resolves ambivalence in favour of change; spirit = partnership, acceptance, compassion, evocation (PACE); skills = OARS (open questions, affirmations, reflective listening, summaries); the discriminating feature is that the patient, not the clinician, voices the change talk, and the cardinal error is the righting reflex.
- **Motivational enhancement therapy (MET):** the manualised, four-session brief form of MI validated in Project MATCH; its added ingredient is personalised assessment feedback; IPS lists MET (four sessions), CBT and relapse prevention as first-line psychological interventions and it scales to India's treatment gap via non-specialist delivery.

HOLD THIS

Motivational interviewing works with ambivalence, not against it: spirit is PACE (partnership, acceptance, compassion, evocation), skills are OARS (open questions, affirmations, reflective listening, summaries), the aim is to evoke and reinforce the patient's own change talk while rolling with sustain talk, and its manualised first-line form is MET, four structured sessions built around personalised feedback.

29 · The stages of change

Behaviour change in addiction is not an on-off switch but a process a person moves through over time, and the **stages of change** model, the core of the **transtheoretical** model (TTM) of

Prochaska and DiClemente, is the framework that names the steps of that process (Kaplan & Sadock 2024; Clinical Methods in Psychiatry, AIIMS 2024). First developed to explain why some smokers quit and others never even begin, it now organises how we think about any health behaviour, and in the addictions it does two jobs at once: it lets you *place* a patient (what is their readiness?) and it tells you what to *do* next (the stage-matched intervention). The model calls the process transtheoretical because it sits above and cuts across every school of therapy rather than belonging to one.

Why it matters in the exam. Examiners test whether you can name the stages in order, define each one crisply (especially the discriminators between **precontemplation** and **contemplation**, and between **preparation** and **action**), state the two verified time-anchors (action lasts one day to 6 months; maintenance is behaviour change sustained beyond 6 months), and, above all, match the intervention to the stage. The classic viva trap is giving an action-stage task to a contemplation-stage patient. The India device is genuine: the AIIMS assessment method makes the stage of change a formal item of the addiction interview, alongside the locus of control, and the IPS treatment-gap strategy leans on brief, motivation-based interventions that are explicitly stage-driven.

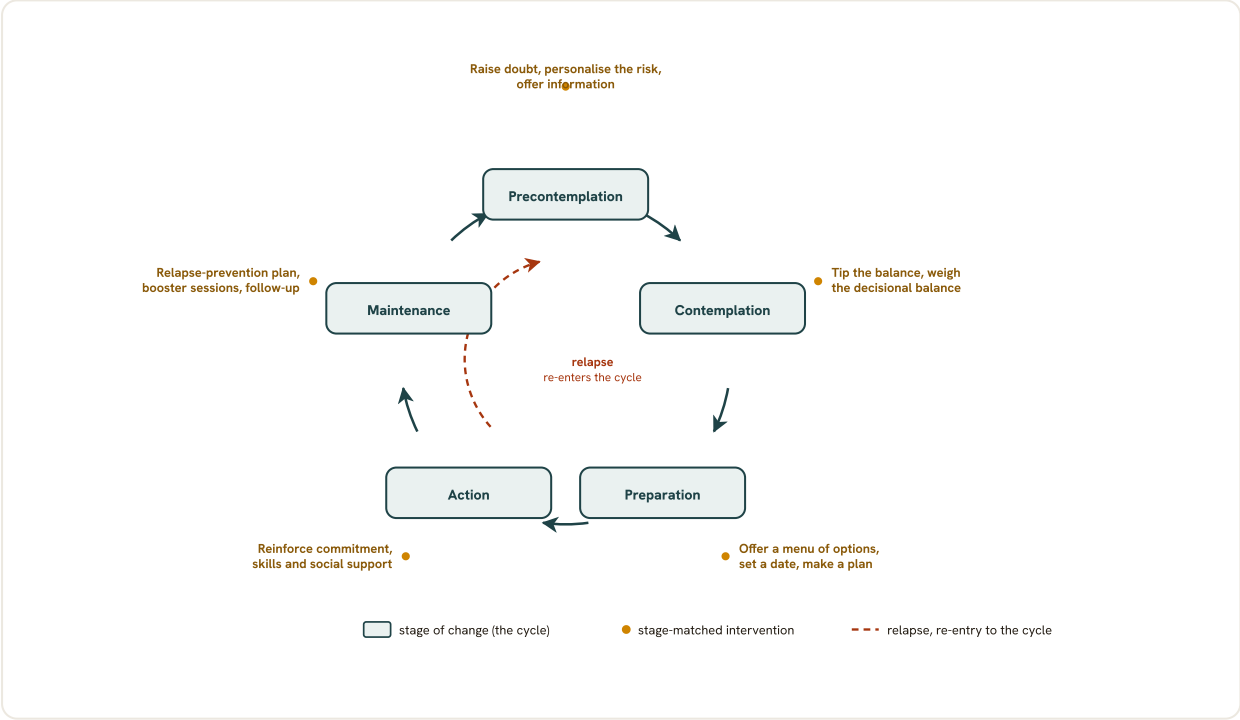


Fig 13.19 The stages of change and the stage-matched interventions. Change is a cycle, not a switch: a person moves from precontemplation through contemplation, preparation, action and maintenance, and relapse is a normal re-entry rather than a failure. Each stage calls for a different move, so the clinician matches the intervention to the stage rather than pushing action on someone who is still weighing it up: raise doubt in precontemplation, tip the decisional balance in contemplation, build a concrete plan in preparation, reinforce commitment and skills in action, and shore up the gains with relapse-prevention and follow-up in maintenance.

29.1 The transtheoretical model: change as a process, not an event

The idea. The transtheoretical model (TTM), proposed by Prochaska and DiClemente in 1983, postulates that adopting a new behaviour involves an evolution through a series of distinct **stages of readiness to change**, and that behaviour change develops over time rather than in a

single decisive moment (Kaplan & Sadock 2024). It grew out of work on why smoking-cessation interventions failed, and its enduring clinical value is that it reframes a "non-compliant" or "unmotivated" patient as simply someone at an earlier stage than the treatment assumes.

Two mediators drive movement. Progress between stages is pushed by two constructs. The **decisional balance** is the weighing of the pros against the cons of change: in the earlier stages (precontemplation, contemplation) patients see more cons than pros, and the balance tips toward pros as they move up (Kaplan & Sadock 2024). **Self-efficacy**, the person's confidence they can change, rises roughly linearly across the stages. Reading a patient's decisional balance and self-efficacy tells you which way they are about to move.

RULE **Assess the stage before you prescribe the task.** Motivation is a stage, not a trait; identify where the patient is on the cycle first, then choose the intervention that fits that stage.

29.2 Precontemplation: no intention to change, often here under pressure

Definition. In precontemplation the person has no intention to change in the foreseeable future. They may deny or be unaware that their substance use is a problem, and they often present only because of pressure from others, feeling coerced or threatened by treatment (Kaplan & Sadock 2024; Clinical Methods in Psychiatry, AIIMS 2024). The discriminator from contemplation is the absence of any recognised problem: the precontemplator does not yet see a reason to change.

What this looks like clinically. The family drags the man in; he insists his drinking is normal and the appointment a waste of time. Confrontation here provokes resistance and dropout. The AIIMS text notes that in exactly this precontemplation presentation, motivational-interviewing technique is what builds rapport and retains the patient in treatment.

29.3 Contemplation: aware of the problem, ambivalent, not yet committed

Definition. In contemplation the person is aware a problem exists and is seriously considering change, but has made no commitment to action. They are stuck between the wish to change and the perceived effort or loss it would cost, the hallmark **ambivalence** of this stage (Kaplan & Sadock 2024). Patients can dwell in contemplation for a long time; one study found people commonly remain contemplative for at least two years before moving on.

The discriminator. Contemplation differs from precontemplation by the presence of problem-recognition, and from preparation by the absence of a near-term plan or commitment. "I know I should cut down, but..." is the contemplation sentence. Pushing an action plan now, before ambivalence is resolved, is premature.

29.4 Preparation: committed and taking the first "baby steps"

Definition. In preparation the person intends to take measurable action in the near future (typically within the next month) and may already be taking small steps, the "baby steps", or reporting minor reductions in use; they may also have made an unsuccessful attempt in the past year (Kaplan & Sadock 2024; Clinical Methods in Psychiatry, AIIMS 2024). This is the stage of intention plus early behaviour, where the commitment that contemplation lacked has formed.

The discriminator. Preparation differs from contemplation by the presence of a plan and near-term commitment, and from action by the fact that the full, overt behaviour change has not yet begun; the changes so far are preparatory and partial.

29.5 Action and maintenance: overt change, then holding the gain past six months

Action. In action the person makes overt modifications to behaviour, experiences or environment to overcome the problem, the visible behaviour change everyone recognises as "doing something about it". The verified time-window for the action stage is **one day to 6 months** (Kaplan & Sadock 2024). Because the change is public, this is where patients get the most external reinforcement (compliments, praise), which itself helps sustain the effort.

Maintenance. After roughly six months of consistent change the person enters maintenance, where the work shifts to consolidating gains and preventing relapse; the operational threshold is remaining free of the problem behaviour, or consistently engaging in the incompatible behaviour, for **more than 6 months** (Kaplan & Sadock 2024; Clinical Methods in Psychiatry, AIIMS 2024). For many addictive behaviours maintenance is effectively lifelong. The purest end-point, **termination** (exiting the cycle with full confidence in every high-risk situation and no relapse-prevention work), is reached by few, which is why the working sixth stage in the addictions is relapse rather than termination.

WORKED EXAMPLE

A woman with alcohol dependence stops drinking and rebuilds her routine (action). Four months in she is clearly changed but not yet at the six-month mark, so she is still in the action stage, not maintenance. At a family wedding she drinks, and over the next weeks slides back into ambivalence, a lapse that becomes relapse and drops her to the contemplation stage. The clinician normalises this as the spiral nature of change, not as failure, and helps her re-enter preparation. The single skill on display is placing her correctly at each turn and matching the response to the stage.

29.6 Relapse as a stage: change spirals, and relapse is the rule not the exception

Definition. Relapse is the stage in which a person who had changed their behaviour falls back into the old pattern of problematic use (Clinical Methods in Psychiatry, AIIMS 2024). The AIIMS text explicitly lists six stages, precontemplation, contemplation, preparation, action, maintenance and relapse, treating relapse as a formal stage of the addiction model, which is the framing this topic teaches.

The spiral, not the line. People move through the stages in a spiral rather than a linear pattern; relapse is the rule rather than the exception, and it is common to regress to an earlier stage and cycle through again (Kaplan & Sadock 2024). The clinical instruction that follows is to educate the patient from the outset about the spiral nature of change and to normalise relapse, because a relapse read as total failure drives the patient out of treatment, whereas a relapse read as a re-entry point keeps them in the cycle.

TRAP **Treating relapse as failure.** Relapse is a predictable stage of the spiral; framing it as the end of treatment, rather than as a return to contemplation or preparation, loses the patient at the moment they most need to re-engage.

STAGE	CORE DEFINITION	TIME-ANCHOR / DISCRIMINATOR
Precontemplation	**No intention to change; problem not recognised; often here under pressure**	No problem-recognition (vs contemplation)
Contemplation	Aware of problem; ambivalent; no commitment	**Can persist about 2 years**
Preparation	Intends to act soon; making "baby steps"	Action intended within the next month
Action	**Overt behaviour change in progress**	One day to 6 months
Maintenance	Consolidating gains; preventing relapse	**Sustained beyond 6 months**
Relapse	Return to the old problematic pattern	Re-enters the spiral (to contemplation / preparation)

The six stages of change of the transtheoretical model, with the verified time-anchors and the key inter-stage discriminators (Kaplan & Sadock 2024; Clinical Methods in Psychiatry, AIIMS 2024). Relapse is treated as a stage per the AIIMS assessment framing.

6	1 day to 6	>6
STAGES: PRECONTEMPLATION, CONTEMPLATION, PREPARATION, ACTION, MAINTENANCE, RELAPSE	ACTION-STAGE DURATION, IN MONTHS	MONTHS OF SUSTAINED CHANGE DEFINING MAINTENANCE

29.7 Stage-matched interventions: the whole clinical payoff of the model

The principle. The reason to stage a patient is to deliver matched interventions: treatment is most effective when the clinician matches the goal and technique to the patient's current stage of change (Kaplan & Sadock 2024). Most treatments, including many addiction programmes, are action-oriented and wrongly assume everyone is in the action stage; giving action tasks to a contemplation-stage patient predictably produces failure or dropout. Aiming to move a patient just one stage can roughly double the chance they will engage in change on their own later.

The stage-to-technique map. The motivational-interviewing strategies are keyed to the stage, and the specific technique for each is what the wider Psychotherapies, clinical assessment, MSE and nosology notes develop as the general MI frame. Here the point is the pairing: *precontemplation* gets non-confrontational awareness-raising, rolling with resistance and developing discrepancy; *contemplation* gets the pros-and-cons of change (tipping the decisional balance), normalising ambivalence and building self-efficacy; *preparation* gets goal-setting, exploring options, reinforcing personal choice and drafting a concrete plan; *action* gets active support of self-efficacy and problem-solving; *maintenance* and *relapse* get relapse-prevention work (the Marlatt high-risk-situation and lapse-versus-relapse model, developed alongside this topic).

STAGE	MATCHED INTERVENTION (WHAT TO ACTUALLY DO)
Precontemplation	**Raise awareness, roll with resistance, develop discrepancy; do not confront**
Contemplation	Weigh pros and cons, normalise ambivalence, explore barriers, build self-efficacy
Preparation	**Clarify goals, explore options, reinforce choice, develop a plan**
Action	Support self-efficacy, problem-solve, reinforce the change
Maintenance / relapse	**Relapse prevention: identify high-risk situations, coping, re-entry after a lapse**

Stage-matched motivational-interviewing strategies (Kaplan & Sadock 2024, Table 27.4-8, adapted); the general MI technique is taught in the Psychotherapies, clinical assessment, MSE and nosology notes.

PEARL

The single most testable clinical rule of the model is the mismatch failure: an action task handed to a contemplation-stage patient. Whenever an addiction patient is labelled "unmotivated" or "non-compliant", re-read it as a staging error, they are almost always in precontemplation or contemplation, and the fix is a stage-matched motivational, not an action-oriented, intervention.

29.8 The Indian assessment context: staging is a formal item of the addiction interview

The frame. In the AIIMS Clinical Methods method, motivation is assessed as a dynamic phenomenon in three domains: whether motivation is fair, poor or doubtful; the *stage of change* per the transtheoretical model of Prochaska and DiClemente; and the **locus of control**, internal (change depends on my actions) versus external (it depends on fate, luck or powerful others) (Clinical Methods in Psychiatry, AIIMS 2024). Motivation must be assessed *per substance*: the same patient may have fair motivation to quit opioids but poor motivation to quit tobacco, and separately for quitting versus harm reduction (a man may be motivated to stop drink-driving but not to stop drinking).

Why it fits the treatment gap. India carries a very large substance-use treatment gap, and the IPS strategy to close it leans on brief, motivation-based psychosocial interventions delivered by trained non-specialist workers, with motivational enhancement therapy and relapse-prevention CBT as core, evidence-supported components (IPS 2014). Because those interventions are explicitly stage-driven, the transtheoretical model is the scaffold on which motivation-based Indian addiction care is built. The wider medico-legal and NDPS frame for coerced or diverted patients (who often present in precontemplation) sits in the Mental health legislation and forensic psychiatry notes.

INDIA

The AIIMS Clinical Methods in Psychiatry (2024) makes staging a formal, recorded item of the addiction history: stage of change (six stages, relapse included), the fair-poor-doubtful motivation grade, and internal-versus-external locus of control, assessed separately for each substance and for the quit-versus-harm-reduction goal. This dovetails with the IPS treatment-gap strategy of brief, motivation-based, non-specialist-deliverable care (motivational enhancement therapy, relapse-prevention CBT), so the transtheoretical model is the working backbone of Indian motivation-based addiction practice.

MNEMONIC

Please Come Prepared And Maintain Recovery

Precontemplation, Contemplation, Preparation, Action, Maintenance, Relapse, the six stages in order, with Relapse as the sixth stage feeding back into the spiral.

GOOD TO REMEMBER

- **Transtheoretical model (Prochaska and DiClemente, 1983):** six stages of change, precontemplation (no intention, no problem recognised), contemplation (aware, ambivalent, uncommitted, can last about 2 years), preparation (committed, near-term plan, baby steps), action (overt change, one day to 6 months), maintenance (sustained beyond 6 months), and relapse (return to the old pattern); movement is a spiral, driven by decisional balance and self-efficacy; the clinical payoff is stage-matched intervention, and the classic error is an action task given to a contemplation-stage patient.

HOLD THIS

Six stages in order, precontemplation, contemplation, preparation, action (one day to 6 months), maintenance (beyond 6 months), relapse, moving as a spiral in which relapse is the rule; match the intervention to the stage, and never hand an action task to a contemplation-stage patient.

30 · Relapse prevention (Marlatt)

Getting a person sober is the easy part; keeping them sober is the whole of the work, and **relapse prevention** is the cognitive-behavioural model that turns "staying stopped" from a matter of willpower into a set of teachable skills. Built by Alan Marlatt and Judith Gordon in the 1980s, the Marlatt model reframes relapse not as a moral collapse but as the predictable end-point of a chain: a **high-risk situation** meets a person who lacks a coping response, confidence drops, the substance is used, and a distorted appraisal of that first slip (the **abstinence violation effect**) tips a single lapse into a full relapse (Companion to Psychiatric Studies; Kaplan & Sadock 2024). Because every link in that chain is a target, the model is the theoretical spine under the relapse-prevention module of almost every structured addiction programme.

Why it matters in exams. Examiners want you to know that relapse prevention is a specific, named, evidence-based cognitive-behavioural intervention (not a vague "avoid triggers" homily), to reproduce the three empirical **determinants of relapse** that account for most slips, to define the **abstinence violation effect** and the **seemingly irrelevant decisions** that feed it, and to list

the two arms of treatment: the reactive **coping**-skills arm for the high-risk moment and the proactive lifestyle-balance arm for the background risk. The India device is genuine here: against a very large treatment gap, relapse prevention and motivation enhancement are named by the Indian Psychiatric Society as the core, non-specialist-deliverable psychosocial interventions for addiction (IPS 2014). This topic carries Fig 13.20, the Marlatt relapse-prevention model as a chain from high-risk situation through coping (or its failure) to lapse and the abstinence violation effect.

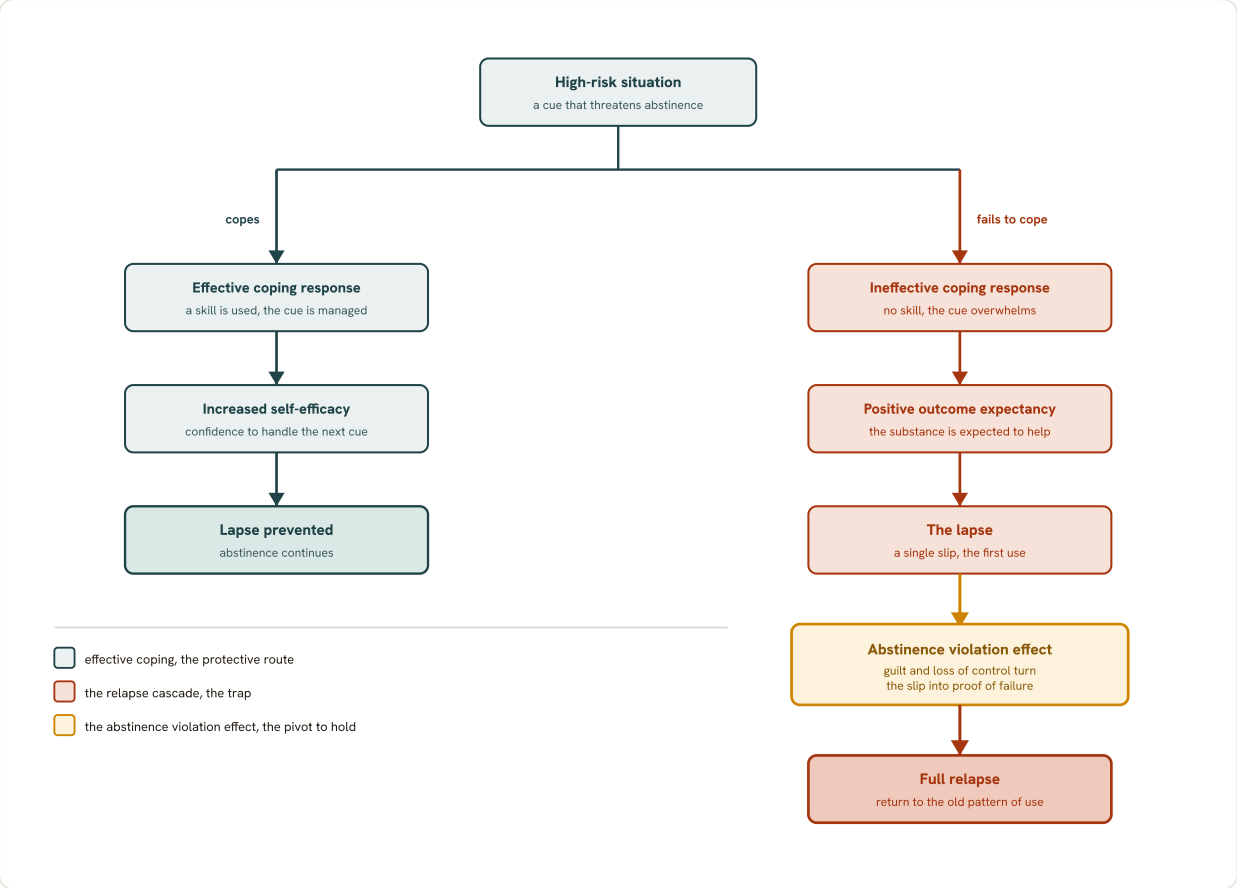


Fig 13.20 The Marlatt relapse-prevention model and the abstinence violation effect. A high-risk situation forces a choice. An effective coping response raises self-efficacy and the lapse is prevented, so abstinence holds. An ineffective response, driven by a positive outcome expectancy that the substance will help, leads to a lapse, a single slip. What decides whether that slip becomes a full relapse is the abstinence violation effect: guilt and a sense of lost control reframe the slip as proof of personal failure, and that self-attribution drives the return to the old pattern of use.

30.1 What relapse prevention is: a cognitive-behavioural self-management model

The definition. Relapse prevention is a cognitive-behavioural, self-management approach that teaches a person recovering from a substance use disorder to anticipate the situations that threaten abstinence, to build and rehearse the coping responses that carry them through, and to limit the damage if a slip occurs (Marlatt & Gordon; Companion to Psychiatric Studies). It sits in the **maintenance** phase of the stages-of-change cycle, the phase whose defining task is precisely to prevent a return to use and to keep the changes already made (the transtheoretical wheel is developed elsewhere in this chapter).

The premise. The model rests on a single reframe: relapse is a *process*, not an event. It does not descend out of nowhere; it is the visible end of a chain of antecedents that begins long before the

drink or the injection, which means each antecedent is a point at which the chain can be broken. That is what makes it teachable and testable (Kaplan & Sadock 2024).

RULE **Relapse is a process, not an event.** Treat every slip as the end of an identifiable chain of antecedents, and prevention becomes a matter of teaching skills at each link rather than exhorting willpower.

30.2 The high-risk situation: the pivot of the whole model

What it is. A high-risk situation is any circumstance that threatens a person's sense of control and raises the risk of a return to use (Marlatt & Gordon). It is the pivot of the model: what happens next depends entirely on whether the person has a coping response for it. If they do, and use it, self-efficacy rises and the risk of relapse falls; if they lack one or fail to deploy it, self-efficacy falls, an *expectancy* of the substance's positive effects moves to the front of the mind, and the probability of a lapse climbs sharply (Companion to Psychiatric Studies).

The clinical use. The first practical task of relapse prevention is therefore to help the patient identify *their own* personal high-risk situations, because these are idiosyncratic, and to catch the early warning signs that one is approaching, before the coping window has closed (Daley & Douaihy, Managing Your Substance Use Disorder; IPS 2014).

30.3 The determinants of relapse: the three that account for most slips

The taxonomy. When Marlatt and Gordon classified the situations in which relapses actually occurred, three **determinants of relapse** accounted for the large majority of them: **negative emotional states** (anger, anxiety, boredom, depression, frustration), **interpersonal conflict** (arguments and confrontations, most often with family or partner), and **social pressure** (both direct offers to use and the indirect pull of being around others who are using) (Companion to Psychiatric Studies; Kaplan & Sadock 2024). Negative emotional states are consistently the single commonest category. These three are the answer to "name the determinants of relapse".

Why it is high-yield. Naming these three lets you map any given patient's slips onto a known structure and pick the coping skill that fits: emotion-regulation and distress-tolerance for the affective determinant, communication and assertiveness training for the interpersonal one, and drink- and drug-refusal skills for the social-pressure one (Daley & Douaihy).

DETERMINANT OF RELAPSE	TYPICAL TRIGGER	COPING SKILL IT CALLS FOR
Negative emotional states	Anger, anxiety, boredom, depression, frustration (the commonest category)	Emotion regulation, distress tolerance, urge-surfing
Interpersonal conflict	Argument or confrontation, usually with family or partner	Communication and assertiveness training, conflict resolution
Social pressure	Direct offer to use, or indirect pull of a using peer group	Drink- and drug-refusal skills, avoiding using company

Marlatt and Gordon's three high-yield determinants of relapse, the trigger each represents and the coping skill it demands (Companion to Psychiatric Studies; Kaplan & Sadock 2024).

30.4 The abstinence violation effect: how one lapse becomes a relapse

The distinction first. The model draws a sharp line between a **lapse** (a single, discrete slip, one drink, one use) and a **relapse** (a full return to the prior pattern of dependent use). A lapse is not a relapse, and the whole point of the model is that the space between the two is where prevention still works (Daley & Douaihy).

The effect itself. The abstinence violation effect is the cognitive-affective reaction that turns a lapse into a relapse. After breaking a self-imposed rule of abstinence, the person experiences a burst of guilt and self-blame plus an *all-or-nothing* attribution, "I've blown it, my willpower has failed, I have no control, so I might as well keep going" (Companion to Psychiatric Studies; the McCrady CBT programme). The lapse is attributed internally, globally and to a stable personal failing rather than to the specific situation, which drives the mood lower and makes continued use feel inevitable. Left unchallenged, this appraisal, not the pharmacology of the first drink, is what converts the slip into a full relapse. The countermeasure is to pre-teach the patient that a lapse is a predictable, correctable event to learn from, not proof of failure, so the thought can be disputed the moment it appears.

TRAP **Treating a lapse as a relapse.** The clinician (or patient) who reads a single slip as total failure enacts the abstinence violation effect and helps cause the very relapse they fear; frame the lapse as a learning point and intervene in the gap.

30.5 Seemingly irrelevant decisions: the covert set-up for a lapse

The concept. Seemingly irrelevant decisions (also called apparently irrelevant decisions) are the small, individually innocent-looking choices that, in series, steer a person into a high-risk situation while preserving the illusion that the eventual lapse was unplanned and unavoidable. Marlatt's example is the recovering drinker who chooses the route home that happens to pass the old bar, or keeps alcohol in the house "for guests": each decision is defensible on its own, but together they set up the encounter with the high-risk situation (Marlatt & Gordon; Companion to Psychiatric Studies).

The clinical use. Teaching patients to spot their own seemingly irrelevant decisions moves prevention *upstream* of the high-risk situation itself: the safest place to break the chain is at the small choice, hours or days earlier, not at the moment of maximum craving. Each such decision is a fork with a low-risk and a high-risk branch, and the work is to make the low-risk choice consciously (Daley & Douaihy).

WORKED EXAMPLE

A man three months abstinent from alcohol agrees to host a cricket-match gathering, buys beer "for the friends", and keeps it chilled in his own fridge. Each step felt trivial and hospitable. By match-time he is alone in the kitchen beside cold beer after an argument with his wife: a seemingly-irrelevant-decision chain (host, buy, chill, keep) has delivered him into a high-risk situation stacked with two determinants at once, social pressure and interpersonal conflict. The lapse that follows will feel like it "just happened"; the model shows it was set up several innocent choices earlier.

30.6 Coping skills: the reactive arm for the high-risk moment

The core intervention. The reactive arm of relapse prevention is coping-skills training: equipping the person with a specific, rehearsed response for each high-risk situation so that when it arrives the response fires instead of the substance. The presence or absence of an effective coping response at the high-risk moment is, in the model, the single strongest predictor of whether that situation ends in a lapse (Marlatt & Gordon; Companion to Psychiatric Studies).

The toolkit. Coping skills are cognitive, behavioural and interpersonal: managing cravings by **urge-surfing** (riding the craving out on the knowledge that urges peak and fall within minutes rather than acting on it), challenging permission-giving thoughts, refusing offers assertively, resolving interpersonal conflict, regulating negative affect, and using a rehearsed emergency plan (leave the situation, wait it out, phone a support) (Daley & Douaihy; McCrady CBT programme). Crucially the skills are *practised*, often by role-play, before they are needed, and each successful use raises self-efficacy, which is itself protective.

PEARL

Cravings are self-limiting. The single most useful thing to tell a patient is that an urge is a wave, not a straight line: it rises, crests within a few minutes and falls whether or not they use. Urge-surfing exploits exactly this, and it reframes "I can't stand this craving" into "I only have to outlast it".

30.7 Lifestyle balance: the proactive arm that lowers background risk

The idea. The proactive arm targets the person's whole life, not just the high-risk moment. Marlatt framed it as **lifestyle balance**: the ratio of perceived "shoulds" (duties, obligations, stressors) to "wants" (pleasures, satisfactions). A life heavy with shoulds and starved of wants breeds a background sense of deprivation and a felt entitlement to indulge ("I deserve this"), which primes both the negative emotional states and the permission-giving thoughts that fuel relapse (Marlatt & Gordon; Daley & Douaihy).

The intervention. Restoring balance means deliberately building in non-chemical sources of pleasure and mastery, so-called *positive addictions* such as exercise, and using regular activities, relaxation, structured routine and a supportive recovery network to lower the baseline stress from which high-risk situations grow (Daley & Douaihy, Strategies for Balanced Living). Where the coping arm defuses the acute high-risk situation, the lifestyle arm reduces how often those situations arise in the first place.

GOOD TO REMEMBER

- **Abstinence violation effect (syndrome/concept):** the guilt-plus-loss-of-control cognitive reaction after a lapse ("I've blown it, might as well continue"), with an internal, global, stable attribution to personal failing; it is what converts a single lapse into a full relapse; the discriminator is that it is a cognitive-affective response to a slip, not the pharmacological effect of the substance; first management step is to pre-teach that a lapse is a correctable learning point and to dispute the all-or-nothing thought immediately.

30.8 Putting it together and the India frame: the two-arm model and the treatment gap

The whole model in one line. Relapse prevention runs on two arms: a reactive arm (identify high-risk situations and their determinants, spot the seemingly irrelevant decisions that lead into them, deploy a rehearsed coping response, and reframe any lapse to disarm the abstinence violation effect) and a proactive arm (lifestyle balance, positive addictions and a recovery network to lower background risk). Both are delivered on top of, not instead of, anti-craving pharmacotherapy where indicated (the disulfiram, naltrexone and acamprosate detail sits with the anti-craving topics of this chapter).

The India lens. India carries a very large substance-use **treatment gap**, with the national survey estimating that roughly **91%** of people with a substance use disorder receive no structured treatment, and care concentrated in government de-addiction centres and Drug De-addiction Programme units rather than general practice. Against that gap the Indian Psychiatric Society names cognitive-behavioural, motivation-enhancement and relapse-prevention approaches as the core, evidence-based psychosocial interventions for addiction, and pushes them toward community and home-based delivery by trained non-specialist workers precisely because relapse prevention is a structured, manualisable skill set that does not require a specialist to teach (IPS 2014). The NDPS Act frame and the wider medico-legal detail sit in the Mental health legislation and forensic psychiatry notes; the wider MI and general-CBT technique sits in the Psychotherapies, clinical assessment, MSE and nosology notes.

INDIA

Relapse prevention is the most exportable of the addiction psychotherapies for the Indian context: it is protocol-driven, teachable to a counsellor or trained non-specialist, and family-embeddable, which matters where a co-resident relative is often the recovery monitor. The IPS clinical practice guidelines pair a structured relapse-prevention and motivation-enhancement package with anti-craving pharmacotherapy and family-based supervision as the standard maintenance offer, and the community and home-based delivery model is the strategic response to the roughly 91% treatment gap. The de-addiction centre and the district day care service are where the model is most often taught.

3	2	91%
DETERMINANTS OF RELAPSE (NEGATIVE AFFECT, INTERPERSONAL CONFLICT, SOCIAL PRESSURE)	ARMS: COPING SKILLS PLUS LIFESTYLE BALANCE	INDIA SUBSTANCE-USE TREATMENT GAP (NATIONAL SURVEY)

MNEMONIC

A HALT before you slip

The classic recovery cue **HALT** (Hungry, Angry, Lonely, Tired) names the everyday states that most often become high-risk situations; "Angry" and "Lonely" map onto Marlatt's negative-emotional-state and interpersonal determinants. Teaching the patient to HALT and check is a simple, non-specialist-deliverable coping trigger.

HOLD THIS
Marlatt's chain is: high-risk situation to no coping response to lapse to abstinence violation effect to relapse, so the three intervention points are coping skills at the situation, seemingly-irrelevant-decision awareness upstream of it, and reframing the lapse to break the abstinence violation effect.

31 · Brief interventions and FRAMES

Most hazardous drinkers and drug users are found not in a de-addiction bed but in a general clinic, presenting for something else, and caught only if someone screens and then *says something useful in the ten minutes that follow*. That short, structured, opportunistic conversation is the **brief intervention**, and the examiner's favourite way to test whether you know its anatomy is the acronym **FRAMES**. It matters because brief intervention is the highest-reach tool in the whole substance block: it needs no drug, no laboratory and no specialist, it works precisely at the reversible hazardous-and-harmful stage, and it is written into the Indian guidelines as the front line against the treatment gap (IPS 2014). Get the six FRAMES elements, the delivery model that wraps around them, and how they relate to motivational enhancement therapy, and you can answer anything asked here.

Why it matters clinically. A screen only labels risk; the brief intervention is what you actually *do* about a positive AUDIT before the person is dependent. Its verified place is hazardous and harmful use not yet meeting dependence criteria, delivered in roughly **5 to 15 minutes** (IPS 2014). The underlying conversational skill is motivational interviewing, owned and taught fully in the Psychotherapies, clinical assessment, MSE and nosology notes and applied to substances alongside this topic; here the focus is the packaged short-contact structure, its scaffold FRAMES, and the delivery frame **SBIRT**.

31.1 What a brief intervention is: the short opportunistic conversation for the not-yet-dependent

The definition. A brief intervention is a time-limited, structured conversation, typically one to four short contacts of **5 to 15 minutes**, that aims to reduce risky substance use in people who are not seeking treatment and are not yet dependent (Tasman 2015; IPS 2014). It is opportunistic: it is delivered off the back of a positive screen, in the setting where the person already is, by whoever is there, rather than requiring a referral to a specialist first.

Who it is for. The evidence base is strongest for **hazardous** and **harmful** drinking, and by extension risky use of other substances, in people who have not yet crossed into dependence (Tasman 2015; IPS 2014). For dependence, a brief intervention is not enough on its own; it becomes the motivational front end that leads into fuller psychosocial treatment and pharmacotherapy.

RULE **Brief intervention targets hazardous and harmful use, not dependence.** Its job is early, at the reversible end flagged by a positive screen; established dependence needs assisted withdrawal, anti-craving pharmacotherapy and structured psychosocial treatment, with the brief intervention only as the motivational entry point.

31.2 FRAMES: the six active ingredients of an effective brief intervention

The scaffold. When researchers dismantled the brief interventions that actually worked, the common components distilled into the acronym FRAMES: **feedback responsibility advice menu empathy self-efficacy** (Bien, Miller and Tonigan 1993; Tasman 2015). It is the single most exam-quotable structure in this topic, because it converts a vague "give some advice" into a checkable six-part conversation.

Feedback

Personalised, non-judgmental feedback about the person's own use and its risks, ideally against population or clinical norms ("your intake is in the top few per cent for men your age").

Responsibility

Explicit emphasis that the choice to change is the patient's own ("it's up to you what you do with this"); this autonomy statement lowers defensiveness.

Advice

Clear, specific advice to cut down or stop, given plainly rather than implied.

Menu of options

A menu of alternative strategies and goals to choose from, so the person picks the route rather than being prescribed one.

Empathy

A warm, reflective, empathic counselling style throughout, not confrontation.

Self-efficacy

Active support for the person's optimism and belief that they *can* change, the ingredient that turns intention into action.

MNEMONIC

FRAMES

Feedback, **R**esponsibility, **A**dvice, **M**enu of options, **E**mpathy, **S**elf-efficacy, the six components that a brief intervention must contain to be effective. Responsibility (the choice is yours) and Empathy are what stop it collapsing into confrontation or a lecture.

31.3 Where FRAMES came from: the drinker's check-up and personalised feedback

The origin. With FRAMES as a guidepost, William Miller and colleagues built the "drinker's check-up", in which people received *feedback about their own drinking relative to population or clinical norms* and were then helped to explore what that feedback might mean for their motivation to cut down or stop (Miller et al. 1988; Tasman 2015). That personalised-feedback engine is the direct ancestor of the feedback step in motivational enhancement therapy.

Why feedback is the load-bearing element. The feedback is delivered in a motivational, non-confrontational way so the person, not the clinician, draws the conclusion. This is the hinge between a brief intervention and simple advice-giving: the discrepancy between the person's use and the norm does the persuading, evoking their own reasons to change rather than the clinician supplying them.

PEARL

Feedback and the empathic style are what separate a real brief intervention from a health lecture. Reeling off risks at a patient ("you'll wreck your liver") is advice without FRAMES; feeding back their own figures against a norm and letting them respond, while affirming that the choice is theirs, is the intervention that actually shifts drinking.

31.4 SBIRT: the delivery model that wraps around the brief intervention

The frame. The brief intervention lives inside a delivery model called SBIRT, for **screening brief intervention**, referral and treatment (Kaplan and Sadock 2024; APA practice guideline). It formalises a three-step pathway that a non-specialist can run in a general setting: *screen* everyone with a validated tool, deliver a *brief intervention* to those who screen positive at the risky level, and make a *referral to treatment* for those whose use is severe or dependent.

How the steps map to severity. The screen sorts people by risk, and the response is matched to it: reassurance and reinforcement for no or minimal use, a brief intervention for the moderate-risk hazardous or harmful user, and a warm referral to specialist treatment for the high-risk or dependent user (Kaplan and Sadock 2024). SBIRT was developed for and widely adopted in primary care and now runs in a broad range of clinical settings, including mental health services.

WORKED EXAMPLE

A 40-year-old man attends a general clinic for hypertension. You screen with the AUDIT and he scores **12**, in the hazardous-drinking band. You run FRAMES in ten minutes: *feedback* ("your score puts your drinking in the harmful range, well above most men"), *responsibility* ("what you do about that is entirely your call"), *advice* ("my clear advice is to cut down to within safe limits"), a *menu* ("some people set a daily cap, some have alcohol-free days, some use an app, which appeals?"), delivered with *empathy*, and closing on *self-efficacy* ("you managed to quit smoking two years ago, that same resolve will serve you here"). Had he scored above the dependence range you would instead have made a warm referral to treatment, the R and T of SBIRT.

31.5 Screening cut-offs that trigger a brief intervention

The numbers that launch the conversation. A brief intervention is not offered at random; a screening cut-off triggers it. On the AUDIT, a total of **8 to 15** suggests simple brief advice aimed at reducing hazardous drinking, **16 to 19** suggests brief counselling with continued monitoring, and **20 or more** warrants full diagnostic evaluation for dependence (Kaplan and Sadock 2024; Tasman 2015). On the WHO ASSIST, a per-substance involvement score in the **4 to 26** moderate-risk band (11 to 26 for alcohol) is the signal to deliver a brief intervention, with 27 or more directing to more intensive treatment. The scales themselves (the AUDIT, CAGE, DAST and ASSIST forms) are reproduced in the scales gallery.

SCREEN AND SCORE	RISK LEVEL	SBIRT RESPONSE
AUDIT 0 to 7	Low	Reassure, reinforce
AUDIT 8 to 15	**Hazardous / harmful**	**Brief intervention (brief advice)**
AUDIT 16 to 19	Harmful	Brief counselling, monitor
AUDIT 20 or more	Probable dependence	Refer for diagnostic evaluation / treatment
ASSIST 4 to 26 (11 to 26 alcohol)	**Moderate**	**Brief intervention**
ASSIST 27 or more	High	More intensive treatment / referral

Screening scores map onto the graded SBIRT response; the brief intervention lives in the moderate-risk middle band.

31.6 Brief intervention, MET and referral: three points on one continuum

How they relate. The three sit on a single continuum of intensity. A *brief intervention* is the shortest, 5 to 15 minutes of FRAMES for the not-yet-dependent. Motivational enhancement therapy (MET) is the fuller, manualised course, classically **four sessions**, that expands the same motivational spirit and adds structured personalised assessment feedback (Kaplan and Sadock 2024; IPS 2014). *Referral to treatment* is the onward step of SBIRT for those who need specialist care. FRAMES is the shared DNA: its feedback-and-autonomy engine runs through both the brief intervention and MET.

The Indian guideline placement. The IPS clinical practice guidelines list brief interventions (5 to 15 minutes) as evidence-based for hazardous and harmful use, and MET (four structured sessions) alongside CBT and relapse prevention as first-line psychological interventions for dependence, with combined psychosocial-plus-pharmacological care improving outcomes (IPS 2014).

TRAP **Do not deploy a brief intervention as the whole treatment for dependence.** Offering only FRAMES to a dependent drinker, instead of assisted withdrawal, an anti-craving agent and structured psychosocial treatment, is undertreatment; brief intervention is for the hazardous-harmful band, not for entrenched dependence.

31.7 Why brief interventions matter in India: the treatment gap and the non-specialist

The reach argument. Brief interventions are the part of the substance-use toolkit that scales to India's treatment gap, where the large majority meeting dependence criteria never reach the government de-addiction centres or the Drug De-addiction Programme (DDAP) units that hold most formal services. They need no drug, no laboratory and no specialist, which is exactly why the IPS guidelines direct services to deliver "brief, motivation-based psychosocial interventions" with a strategic shift toward community and home-based delivery by trained non-specialist health workers (IPS 2014). WHO mhGAP likewise places motivational and brief interventions among the structured psychosocial options for alcohol use.

INDIA

In an Indian answer, screening plus brief intervention is the front line against the substance-use treatment gap: a validated screen (AUDIT, ASSIST) in a primary-care or general-clinic hand, followed by 5 to 15 minutes of FRAMES, catches the hazardous drinker or user long before they would ever reach a de-addiction centre. The IPS substance-use guidelines build the pathway explicitly around brief, motivation-based intervention by non-specialist workers with community and home-based delivery (IPS 2014). Once a screen flags opioid use, the onward referral runs into opioid-agonist treatment, where buprenorphine is the Indian workhorse, prescribed within the Narcotic Drugs and Psychotropic Substances Act framework; that medico-legal and access detail is developed in the Mental health legislation and forensic psychiatry notes.

5 to 15	8	4
BRIEF-INTERVENTION CONTACT TIME IN MINUTES	AUDIT CUT-OFF TRIGGERING BRIEF ADVICE	MET STRUCTURED SESSIONS (FULLER FORM)

HOLD THIS

A brief intervention is 5 to 15 minutes of FRAMES (Feedback, Responsibility, Advice, Menu of options, Empathy, Self-efficacy) for hazardous and harmful use flagged by a positive screen (AUDIT 8 to 15), delivered inside the SBIRT model (screen, brief intervention, referral, treatment); MET is its four-session manualised sibling.

GOOD TO REMEMBER

- **Brief intervention:** 5 to 15 minute opportunistic FRAMES conversation for hazardous and harmful use not yet dependent; triggered by a positive screen (AUDIT 8 to 15), delivered inside SBIRT (IPS 2014).
- **FRAMES:** Feedback (personalised, against norms), Responsibility (choice is yours), Advice (clear), Menu of options, Empathy (non-confrontational), Self-efficacy (support optimism); the six components an effective brief intervention must contain.
- **SBIRT:** Screening, Brief Intervention, Referral to Treatment, the primary-care delivery model matching response to screened risk; brief intervention for moderate risk, referral for high risk / dependence (Kaplan and Sadock 2024).
- **MET:** motivational enhancement therapy, the manualised four-session expansion of FRAMES with structured personalised feedback; first-line psychosocial intervention in the IPS guidelines (IPS 2014).

32 · Twelve-step facilitation and self-help groups

Most of a person's recovery does not happen in a clinic; it happens in the weeks and months between appointments, and the oldest and most widely spread scaffold for that stretch is the mutual-help fellowship. **Alcoholics Anonymous** and its offspring turned the lived experience of recovering people into a free, ever-present, non-professional support network, and the **twelve-step** philosophy they run on has since been packaged by clinicians into a formal, manualised therapy, **twelve-step facilitation**, whose job is simply to get a patient engaged with the fellowship (Kaplan & Sadock 2024; Shorter Oxford Textbook of Psychiatry). For the exam this is a small but reliably tested cluster: know what a **self-help group** is, name the twelve steps'

organising idea, distinguish the fellowship (AA) from the clinician-delivered therapy that points people at it (TSF), and quote the evidence.

Why it matters in exams. Examiners want a clean separation of three things that candidates routinely blur: the peer fellowship (**aa**, **narcotics anonymous** and the wider family of anonymous groups), the twelve-step programme itself (the spiritual, abstinence-based recovery framework), and **twelve-step facilitation** therapy (a structured, professional intervention that is not the same as attending meetings). They also want the Project MATCH result, the one finding about who does best with TSF, and the India frame: a very large treatment gap in which free, self-sustaining, non-specialist mutual-help groups are exactly the kind of resource a resource-poor system needs.

32.1 What a self-help group is: peer-led, non-professional, free

The definition. A self-help group (mutual-help or mutual-aid group) is a voluntary association of people who share a common problem and meet, without professional leadership, to give each other support, information and encouragement toward recovery (Kaplan & Sadock 2024). The defining features are that it is *peer-led* (members help members; there is no therapist in charge), *non-professional* and unpaid, *free* and open-ended, and organised around a shared identity rather than a treatment contract. In addiction the archetype is Alcoholics Anonymous, and the model has since spread to Narcotics Anonymous, Cocaine Anonymous, Gamblers Anonymous, Nicotine Anonymous and family fellowships.

Why it matters. Because it costs nothing, needs no specialist and is available long after formal treatment ends, the self-help group is the maintenance-phase resource that fills the gap a time-limited clinical service cannot. Its strength, in the textbook's words, lies in the social support and the concrete plan for recovery it gives the member (Kaplan & Sadock 2024).

RULE **Refer, do not just recommend.** A self-help group is a maintenance-phase intervention in its own right; the clinician's job is active linkage (name the group, help find a local meeting, follow up on attendance), not a one-line "you could try AA".

32.2 Alcoholics Anonymous: the founding fellowship

What it is. Alcoholics Anonymous (AA) is a self-help organisation founded in the United States in 1935 (in Akron, Ohio) by two alcoholic men, a stockbroker (Bill Wilson) and a surgeon (Dr Bob Smith), and now present in most countries of the world (Shorter Oxford Textbook of Psychiatry; Tasman Psychiatry). Members attend group meetings, usually twice-weekly, on an open-ended long-term basis; in a crisis a member can obtain immediate help from other members by telephone. The organisation works on the firm belief that recovery requires *complete abstinence*, and it is explicitly non-professional and anonymous.

How it works. Newer members are paired with an experienced **sponsor** who guides them through the programme and is available between meetings; the group provides both confrontation and support for the newcomer (Kaplan & Sadock 2024). The alcoholic is asked to

accept powerlessness over alcohol, to draw on a "power greater than ourselves", and to work through the steps in fellowship with others in recovery.

PEARL

AA is a fellowship, not a treatment a doctor delivers, and it is not for everyone. The Shorter Oxford is candid that the emotional, confessional character of meetings and the evangelical, quasi-religious flavour of the twelve-step approach put some problem drinkers off. The correct exam line is that "anyone with a drink problem should be encouraged to try it", while recognising it will not suit all.

32.3 The twelve steps: the organising philosophy

The idea. Alcoholics Anonymous is built on a set of twelve steps, the fundamental principles to which members adhere (Shorter Oxford Textbook of Psychiatry). The programme is best remembered not as twelve items to recite but as a movement through three phases: an opening admission of powerlessness and unmanageability and a turning to a higher power (steps 1 to 3), a searching moral inventory, confession and readiness to change and to make amends (steps 4 to 9), and an ongoing maintenance of the new way of living plus carrying the message to others (steps 10 to 12). It is an abstinence-based, spiritually framed model of recovery.

What examiners test. That the first step is the admission "we were powerless over alcohol, that our lives had become unmanageable", that the model invokes a "power greater than ourselves", that step twelve is carrying the message to other alcoholics, and that the whole is a spiritual (though non-denominational) rather than a medical framework (Tasman Psychiatry, Table 72-10).

PHASE	STEPS	ORGANISING TASK
Surrender	1 to 3	Admit powerlessness and unmanageability; come to believe a greater power can restore; decide to turn will and life over to that power
Inventory and amends	4 to 9	Searching moral inventory, confession of wrongs, readiness to change defects, list those harmed and make direct amends
Maintenance and service	10 to 12	Continue personal inventory, prayer and meditation, and (having had a spiritual awakening) carry the message to other alcoholics

The twelve steps of Alcoholics Anonymous grouped into their three functional phases; the full step wording is reproduced centrally (Tasman Psychiatry, Table 72-10; AA World Services).

32.4 Narcotics Anonymous and the wider family of anonymous groups

What it is. Narcotics Anonymous (NA) is the drug-focused fellowship that grew directly out of AA, applying the same twelve-step structure and abstinence philosophy to recovery from opioids

and other drugs (Kaplan & Sadock 2024; Tasman Psychiatry). Alongside it sit Cocaine Anonymous, Nicotine Anonymous (NicA) and others, each a peer fellowship for a specific substance, all sharing the AA template: sponsorship, meetings, steps, complete abstinence.

The family groups. The model also extends to the people around the user. Al-Anon is a parallel fellowship (not formally affiliated with AA but sharing its structure and tenets) that supports the partners and family members of drinkers, and Alateen, sponsored by Al-Anon, does the same for their teenage children; Adult Children of Alcoholics (ACOA) is a related group (Tasman Psychiatry; Shorter Oxford). Al-Anon and AA meetings are often held jointly.

WORKED EXAMPLE

A man on buprenorphine maintenance for opioid dependence is stable on medication but isolated and bored, the classic background for a lapse. The clinician does not stop at the prescription: he links the man to a local Narcotics Anonymous meeting for peer support and a sponsor, and points the man's wife toward Al-Anon so the family stress that so often triggers relapse has its own outlet. Medication and mutual-help are complementary, not alternatives, and pairing them is standard maintenance practice (Kaplan & Sadock 2024).

32.5 Twelve-step facilitation therapy: the professional intervention, distinct from the fellowship

The definition. Twelve-step facilitation (TSF) is a structured, manualised, professionally delivered counselling programme whose explicit goal is to help a patient become actively engaged with a twelve-step fellowship such as Alcoholics Anonymous (Project MATCH; Epstein & McCrady, therapist guide). It is *not* the same as attending AA: it is a therapy the clinician runs, typically over about twelve sessions, that promotes the two behaviours known to matter, attending meetings and working the steps, and addresses the patient's ambivalence and obstacles to doing so.

Why the distinction is examinable. AA is a free peer fellowship; TSF is an evidence-based psychotherapy that points the patient at that fellowship. Twelve-step facilitation is described as a standard evidence-based treatment in most addiction services (Kaplan & Sadock 2024), whereas AA itself is a mutual-help organisation, not a clinical treatment. Confusing the two is the classic error here.

TRAP **Equating "going to AA" with "twelve-step facilitation".** TSF is a clinician-delivered, manualised therapy that *facilitates* engagement with the fellowship; AA attendance is the peer activity it promotes. They are tested as two separate things.

32.6 The evidence: Project MATCH and who does best with TSF

Project MATCH. The landmark trial was Project MATCH, a large randomised controlled comparison of three manualised psychological treatments for alcohol problems: twelve-step facilitation, motivational enhancement therapy (MET) and cognitive-behavioural coping-skills therapy (Project MATCH Research Group 1997; Shorter Oxford). The headline result was that the three treatments were broadly *equal* in efficacy, that the trial found few strong patient characteristics predicting which treatment suited whom (the "matching" hypothesis it was

designed to test largely failed), and that outcomes overall were good, with the brief four-session MET as effective as the two more intensive therapies.

The one matching finding to keep. One robust exception did emerge and it is high-yield: patients whose social network strongly supported drinking did particularly well with twelve-step facilitation, plausibly because AA gives them a new, abstinence-supporting social network to replace the drinking one (Epstein & McCrady; Longabaugh 1998). More broadly, TSF is associated with a greater likelihood of maintaining complete abstinence than other outpatient counselling (Project MATCH), and patients with fewer comorbid psychiatric problems tend to do better with the AA-type approach (Shorter Oxford).

GOOD TO REMEMBER

- **Project MATCH (trial):** RCT of TSF vs MET vs CBT for alcohol use disorder; the three were roughly equal and brief MET was as good as the intensive treatments; the discriminator to quote is that patients whose social network supported drinking did best with twelve-step facilitation; TSF is linked to higher rates of complete abstinence than other outpatient counselling.

32.7 Secular alternatives: SMART Recovery and the non-spiritual route

Why they exist. Because the spiritual, higher-power framing of the twelve steps does not suit everyone, a set of secular mutual-help alternatives has grown up. The most prominent is SMART Recovery (Self-Management And Recovery Training), a group programme built on cognitive-behavioural and motivational principles rather than surrender to a higher power; others include Rational Recovery, Women for Sobriety, Men for Sobriety and Moderation Management (Kaplan & Sadock 2024; Daley & Douaihy, Managing Your Substance Use Disorder). SMART Recovery is not incompatible with formal CBT and is a reasonable offer for the patient who declines AA on grounds of its religious tone.

The exam point. Know that a credible secular, CBT-based alternative to the twelve-step fellowships exists (SMART Recovery is the name to give), and that the choice between a twelve-step and a secular group can be matched to the individual patient's beliefs and preferences.

32.8 The India frame: the treatment gap and the place of mutual-help

The gap. India carries a very large substance-use **treatment gap**. The national survey found that roughly **14.6%** of Indians aged 10 to 75 use alcohol, with about 5.7 crore people having an alcohol use disorder, and the National Mental Health Survey put the treatment gap for substance use disorders at about **91.1%** overall (around **86.3%** for alcohol use disorder), meaning the large majority of affected people receive no structured care (Companion to Psychiatric Studies; Clinical Methods in Psychiatry, AIIMS 2024). Care that does exist is concentrated in government de-addiction centres and Drug De-addiction Programme (DDAP) units under the NDPS Act frame rather than in general practice.

Where mutual-help fits. Against that gap, free, self-sustaining, non-professional fellowships are structurally attractive: they need no specialist, cost nothing and continue indefinitely. The Indian Psychiatric Society guidelines name Alcoholics Anonymous referral, alongside twelve-step facilitation and the Community Reinforcement Approach, as evidence-supported components of

relapse prevention, embedded in a family-based model where a co-resident relative acts as recovery monitor (IPS 2014). AA and NA meetings do operate in Indian cities, though coverage is uneven and thinner outside metros, and the fellowships remain a useful adjunct rather than a substitute for pharmacotherapy and structured psychosocial care.

INDIA

Mutual-help groups map neatly onto India's constraints: they are free, run by peers, and outlast the brief window a stretched service can offer, which matters when roughly 9 in 10 people with a substance use disorder get no formal treatment. The IPS clinical practice guidelines fold AA referral and twelve-step facilitation into a family-embedded relapse-prevention package delivered through de-addiction centres and, increasingly, community and home-based non-specialist care. The NDPS Act and the de-addiction-programme structure sit in the Mental health legislation and forensic psychiatry notes; the wider MI and general-CBT technique sit in the Psychotherapies, clinical assessment, MSE and nosology notes.

1935	3	91.1%
AA FOUNDED (AKRON, OHIO) BY A STOCKBROKER AND A SURGEON	PROJECT MATCH TREATMENTS COMPARED: TSF, MET, CBT (ROUGHLY EQUAL)	INDIA SUBSTANCE-USE TREATMENT GAP (NATIONAL MENTAL HEALTH SURVEY)

MNEMONIC

HOW: Honesty, Open-mindedness, Willingness

The recovery-community cue **HOW** (Honesty, Open-mindedness, Willingness) names the three attitudes the twelve-step programme asks of a newcomer: honesty about powerlessness, open-mindedness to a power greater than oneself, and willingness to work the steps and make amends. It is a compact way to remember what "working the programme" actually demands.

HOLD THIS

Keep three things apart: the peer fellowship (AA and Narcotics Anonymous, free, non-professional, abstinence-based, twelve steps), the clinician-delivered therapy that engages patients with it (twelve-step facilitation, evidence-based, roughly equal to MET and CBT in Project MATCH), and the one matching finding worth quoting (patients whose social network supports drinking do best with twelve-step facilitation).

33 · Contingency management and community reinforcement

Two of the behavioural pillars of addiction psychotherapy sit on the same operant idea: if using a substance is a behaviour that has been powerfully reinforced, then not-using has to be reinforced back. **Contingency management** does this narrowly and directly, by paying out a tangible reward every time an objective marker of abstinence is met, while the **community reinforcement approach** does it broadly, by re-engineering the person's whole social world so that a sober life becomes more rewarding than a using one. Both are named, manualised, evidence-based interventions, and both are examinable as the concrete operant answer to "what psychosocial treatment, beyond CBT and motivation enhancement, has the strongest trial

evidence in substance use disorders" (Kaplan & Sadock 2024; New Oxford Textbook of Psychiatry).

Why it matters in exams. Examiners want the operant definition of **contingency management** (reinforcement of a target behaviour, not exhortation), the two reward formats (the **voucher** system and the prize-draw variant) with the idea of an escalating, reset-on-relapse schedule, the fact that it is the single most effective psychosocial approach for stimulant use disorder where no anti-craving drug exists, and the four things that make up the **community reinforcement approach** (**cra**). The India device is genuine: against a very large treatment gap these are low-cost, non-specialist-deliverable, family-embeddable methods, and CRA-style monitored disulfiram supervision by a co-resident relative is already standard practice in the Indian de-addiction model (IPS 2014). This is a brief, low-tier topic; keep the operant spine and the two named interventions.

33.1 Contingency management: the operant definition

The definition. Contingency management is the general application of operant principles to behaviour change: a target behaviour is reinforced by the consistent, immediate delivery of a reward, which strengthens that behaviour and displaces the undesired one (Kaplan & Sadock 2024). In substance use disorders the target is an objective marker of abstinence, most often a negative urine drug screen or a negative breath alcohol reading, and treatment attendance can be reinforced the same way. The reinforcement is delivered by *another person* who monitors the behaviour, which distinguishes it from self-reward and self-control techniques where the patient reinforces themselves (Shorter Oxford Textbook of Psychiatry).

The premise. Drug use is a reinforced behaviour, so abstinence has to compete on the same currency. Contingency management makes the reward for abstinence **immediate, tangible and certain**, precisely the properties that make the drug itself so reinforcing, so that in the moment of choice the reinforced alternative can win (New Oxford Textbook of Psychiatry).

RULE **Reinforce the objective marker, not the promise.** Contingency management rewards a verified negative test or attended session, delivered immediately by a monitor, never a self-reported or future intention to stay clean.

33.2 The four operational stages of contingency management

How it is actually run. A contingency-management programme is built in four stages: (1) *define and record* the target behaviour, with a trained monitor recording an objective marker; (2) choose the **reinforcer** and the schedule; (3) deliver the reinforcer consistently and immediately when the behaviour is met, and withhold it when it is not; and (4) fade the tangible reward toward natural social reinforcers (praise, feeling well, restored relationships) as gains consolidate (Shorter Oxford Textbook of Psychiatry; Kaplan & Sadock 2024). The fading step matters because a programme that never transfers to natural reinforcers cannot be sustained once the vouchers stop.

The token-economy cousin. The formalised, ward-based form of contingency management is the **token economy**, in which specified behaviours earn tokens redeemable for goods or

privileges; some add **response cost**, the withdrawal of a reward after a problem behaviour, and the combination of token reinforcement with response cost can be more effective than either alone (Kaplan & Sadock 2024).

33.3 The voucher system and the prize-draw variant

The voucher model. The classic form is the voucher-based system (Higgins): each negative drug screen earns a voucher of monetary value exchangeable for retail goods or services, never cash, and the value *escalates* with each consecutive negative screen so that a long clean run is worth progressively more, while a positive screen **resets** the voucher value to baseline. That escalate-and-reset schedule is the engine of the method, it makes each additional clean test more valuable than the last and makes a single lapse costly (Kaplan & Sadock 2024; New Oxford Textbook of Psychiatry).

The prize-draw variant. Because vouchers are expensive, a cheaper prize-based ("fishbowl") variant lets each negative screen earn a draw from a bowl of slips, most worth a small prize and a few worth a large one, so the same **incentive** effect is delivered at lower cost through intermittent, variable-magnitude reinforcement. Both formats reward the same objective abstinence marker; they differ only in how the reward is scheduled (Kaplan & Sadock 2024).

FEATURE	VOUCHER SYSTEM	PRIZE-DRAW (FISHBOWL) VARIANT
Reward earned for	Negative drug/alcohol screen or attendance	Negative drug/alcohol screen or attendance
Reward form	**Escalating-value voucher for goods (never cash)**	**Draw for a prize of variable magnitude**
Schedule	Escalates with consecutive negatives; resets on a positive	Intermittent, variable-magnitude reinforcement
Trade-off	Strong effect, higher cost	Lower cost, exploits variable reinforcement

The two reward formats of contingency management: the escalating voucher and the lower-cost prize draw, both reinforcing the same objective abstinence marker (Kaplan & Sadock 2024; New Oxford Textbook of Psychiatry).

33.4 Where contingency management earns its place: the stimulant gap

The high-yield indication. Contingency management is one of only three behavioural approaches (with CBT and twelve-step facilitation) that carry the strongest empirical grounding for **stimulant use disorder**, and it matters most there precisely because *no effective anti-craving medication exists* for cocaine or amphetamine dependence, so a robust psychosocial method carries the treatment (Kaplan & Sadock 2024; Tasman). Head-to-head, contingency management often outperforms other psychosocial approaches such as CBT for reducing drug use and improving treatment retention, and its benefit holds even in patients with comorbid serious mental illness (Shorter Oxford Textbook of Psychiatry; New Oxford Textbook of Psychiatry). It also works for smoking cessation and cannabis use disorder.

The limitation. Its main weakness is durability: the effect can fade once the reinforcement schedule ends, which is exactly why the fourth stage, fading to natural reinforcers, and pairing

with a skills-based intervention such as relapse prevention are built in (New Oxford Textbook of Psychiatry).

TRAP **Reading contingency management as "bribing addicts".** The reflex objection (paying people to do what they should do anyway) misreads an operant treatment with strong trial evidence, especially in stimulant use where it may be the single most effective psychosocial option; the real constraints are cost and durability, not principle.

33.5 The community reinforcement approach: re-engineering the social world

The definition. The community reinforcement approach (**cra**) is a broad behavioural, social-network treatment whose overall aim is to rearrange the drinker's or user's environment so that a sober life is more rewarding than a using one (Shorter Oxford Textbook of Psychiatry; Companion to Psychiatric Studies). Where contingency management reinforces one narrow marker, CRA reinforces a whole sober lifestyle by making the person's family, work, and social contacts the source of reward for positive change (Kaplan & Sadock 2024).

The four working parts. CRA is an amalgam of components: (1) *skills training*, including communication, problem-solving and assertive drink- or drug-refusal skills; (2) *relationship and family therapy*, engaging the partner and social network to reward sobriety; (3) *vocational and recreational* counselling to build non-using sources of satisfaction; and (4) frequently, disulfiram with *monitored compliance*, plus contingency management embedded within it (New Oxford Textbook of Psychiatry; Shorter Oxford Textbook of Psychiatry). Crucially, in CRA the family members are part of the therapist's working team, not themselves the subject of treatment (Companion to Psychiatric Studies).

WORKED EXAMPLE

A man with alcohol dependence starts supervised disulfiram, his wife agreeing to watch him take the morning dose and to praise each dosed, sober day rather than nag about past drinking. In clinic he rehearses refusing a drink at a family function, and the counsellor helps him re-enter a cricket club and pursue a job lead so his week fills with non-drinking rewards. Each element is a CRA component: monitored disulfiram, family as reward-monitor, refusal-skills training, and vocational and recreational re-engagement, together tilting his environment so sobriety pays.

33.6 CRA and family training, and the India frame

CRAFT. A named extension, **community reinforcement and family training** (CRAFT), works through the concerned family member of a person who will not yet engage in treatment, teaching the relative to reinforce non-using behaviour, withdraw reward around using, and guide the person toward help; it is one of the more effective ways of getting a treatment-refusing person into care (Daley & Douaihy). This family-as-agent logic maps closely onto Indian practice.

The India lens. India carries a very large substance-use **treatment gap**: the national survey estimated that around **91%** of people with a substance use disorder receive no structured treatment, with care concentrated in government de-addiction centres and Drug De-addiction Programme units under the NDPS-era policy framework rather than in general practice. CRA

and contingency management fit this setting well because they are low-cost, protocol-driven and deliverable by trained non-specialist workers, and the Indian Psychiatric Society already names the community reinforcement approach and twelve-step facilitation as evidence-supported options alongside family-based treatment in which a co-resident relative acts as recovery monitor and as the supervisor for any prescribed disulfiram (IPS 2014). The NDPS Act and the wider medico-legal frame sit in the Mental health legislation and forensic psychiatry notes; the general MI and CBT technique sits in the Psychotherapies, clinical assessment, MSE and nosology notes.

INDIA

Both methods are unusually exportable to the Indian de-addiction context. Contingency management needs only a monitor, an objective test and a modest reward, and CRA's core, family-supervised disulfiram plus refusal-skills and social re-engagement, is already how a district de-addiction centre or the day care service runs relapse prevention through a co-resident relative. Against the roughly 91% treatment gap the IPS clinical practice guidelines push exactly this non-specialist, community and home-based, family-embedded delivery (IPS 2014). Buprenorphine access under the opioid-substitution programme has widened the pharmacological base onto which these psychosocial methods are layered.

4
CRA COMPONENTS: SKILLS TRAINING, FAMILY/RELATIONSHIP THERAPY, VOCATIONAL/RECREATIONAL COUNSELLING, MONITORED DISULFIRAM PLUS CM

3
STRONGEST-EVIDENCE BEHAVIOURAL METHODS FOR STIMULANT USE DISORDER (CONTINGENCY MANAGEMENT, CBT, TWELVE-STEP FACILITATION)

91%
INDIA SUBSTANCE-USE TREATMENT GAP (NATIONAL SURVEY)

MNEMONIC

CRA has SORT

Skills training, **O**ccupational (vocational and recreational) counselling, **R**elationship and family therapy, and **T**ablet with monitored compliance (disulfiram). SORT recalls the four working parts of the community reinforcement approach.

GOOD TO REMEMBER

- **Contingency management (intervention):** operant reinforcement of an *objective* abstinence marker (negative drug screen or attendance) with an immediate, tangible reward delivered by a monitor; two formats, the escalating *voucher* that resets on a positive test and the lower-cost prize-draw variant; the discriminator is that another person delivers the reward for a verified behaviour (unlike self-reward); strongest-evidence psychosocial method for stimulant use disorder where no anti-craving drug exists; main limitation is fade after the schedule ends, so fade to natural reinforcers and pair with relapse prevention.
- **Community reinforcement approach (CRA, intervention):** broad social-network behavioural treatment that rearranges the environment so sobriety out-rewards using; four parts, skills/refusal training, family and relationship therapy, vocational and recreational counselling, and monitored-compliance disulfiram with embedded contingency management; the discriminator is that family are part of the treatment team, not the patients; CRAFT is the family-engagement extension for the treatment-refusing person; first practical step in the Indian model is enlisting a co-resident relative as recovery monitor and disulfiram supervisor.

HOLD THIS

Contingency management reinforces one objective abstinence marker with an immediate reward (escalating voucher or prize draw) and is the top psychosocial method for stimulant use where no drug helps; the community reinforcement approach reinforces the whole sober lifestyle through skills training, family/relationship therapy, vocational counselling and monitored disulfiram, with the family as the reward-delivering team.

Anti-craving and aversive pharmacotherapy

34 · Disulfiram

Disulfiram is the oldest medication for alcohol dependence, and it is examined less for pharmacological cleverness than for the one thing that makes it dangerous: it does nothing to the brain's craving, it only makes drinking *punishing*. It is an **aversive** (deterrent) agent, not an anti-craving agent. A patient who stays away from alcohol feels nothing; a patient who drinks on it suffers a violent, sometimes lethal, physical reaction. That single fact drives every exam point on this drug, the mechanism, the reaction, the dose and above all the **cautions**, so this fragment teaches the drug as a management decision, not a description.

Why it matters clinically. This is a management/drug topic, so the marks sit in the mechanism, the dose, the line and the monitoring. The two most tested, and most dangerous, errors are starting disulfiram in a patient who is still drinking (or intoxicated) and starting it in a patient with cardiac disease: both can precipitate a fatal reaction. Disulfiram is never a withdrawal treatment and never an emergency drug; it is a supervised, consented, maintenance-phase choice for a specific kind of patient. The mesolimbic reward anatomy that anti-craving agents act on, and that disulfiram deliberately does *not*, is developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the NDPS Act frame behind Indian de-addiction prescribing sits in the Mental health legislation and forensic psychiatry notes.

34.1 The mechanism: irreversible aldehyde-dehydrogenase inhibition

Where it acts. Alcohol is metabolised in the liver in two steps: alcohol dehydrogenase (ADH) converts ethanol to **acetaldehyde**, and then aldehyde dehydrogenase (ALDH) converts that toxic acetaldehyde to harmless acetate. Disulfiram *irreversibly* inhibits ALDH, blocking the second step (Stahl 2021; Maudsley 2021; New Oxford 2020). Because the inhibition is irreversible, the effect does not switch off when the drug is stopped: enzyme activity returns only as new ALDH is synthesised, which is why disulfiram's deterrent effect begins within about **12 hours** of the first dose and persists for roughly **7 to 14 days** after the last dose (Stahl 2021).

What accumulates. With ALDH blocked, any ingested ethanol is metabolised to acetaldehyde that cannot be cleared, so blood acetaldehyde rises to 5 to 10 times the level seen when the same amount of alcohol is metabolised normally (New Oxford 2020). Acetaldehyde is the noxious pivot: its accumulation, not disulfiram itself, produces the reaction. This is a deliberate,

pharmacological reproduction of the flush that people with an inherited inactive ALDH variant experience naturally.

MNEMONIC

"ALDH BLOCKED, ACETALDEHYDE STACKED"

Disulfiram irreversibly BLOCKS aldehyde dehydrogenase (ALDH), so acetaldehyde STACKS up when the patient drinks. Everything unpleasant in the disulfiram-ethanol reaction is acetaldehyde toxicity. Because the block is irreversible, stopping the tablet does not stop the danger for up to two weeks.

34.2 The disulfiram-ethanol reaction (DER): what the patient feels

The reaction defined. If a patient drinks alcohol while taking disulfiram, the accumulated acetaldehyde produces the **disulfiram-ethanol reaction** (the **der**, also called the disulfiram-alcohol reaction). Its cardinal features are cutaneous flushing, a throbbing headache, nausea and vomiting, and cardiovascular effects, tachycardia with hypotension, together with sweating, palpitations, tachypnoea (shortness of breath), giddiness and a distinctive sense of impending doom with severe anxiety (Maudsley 2021). The reaction is dose-dependent on both the disulfiram dose and the amount of alcohol taken.

Time-course. The onset is rapid, within about **30 minutes** of drinking; it becomes full-blown within roughly **1 hour** and usually subsides within about **2 hours** in a mild reaction, though it can last several hours. A crucial safety point for counselling and prescribing: because reactions can be triggered by alcohol-containing preparations the patient does not think of as "a drink", cough syrups, tonics, mouthwashes, aftershave, the patient must be warned about these, and warned that a reaction can occur if they drink for up to two weeks after stopping the drug (Stahl 2021).

WORKED EXAMPLE

A motivated man on disulfiram 250 mg daily for four months attends a family wedding and, under pressure, takes "just a small peg". Within twenty minutes his face is flushed and pounding, he is nauseated and vomiting, sweating, breathless, his heart is racing and his blood pressure has dropped. This is the disulfiram-ethanol reaction, the intended aversive consequence. In a mild case it is managed supportively (lie flat, fluids, observe) and settles within a couple of hours. The teaching point is that this is the drug *working*, and it is also exactly why a patient with cardiac disease must never be on it, because the same reaction there can mean a myocardial infarction or arrhythmia.

GOOD TO REMEMBER

- **Disulfiram-ethanol reaction (DER):** the acetaldehyde-mediated reaction on drinking, flushing, throbbing headache, nausea and vomiting, tachycardia with hypotension, sweating, dyspnoea and a sense of impending doom; onset about 30 minutes, full-blown within 1 hour, usually settling within 2 hours; the first management step is supportive (lie flat, fluids, monitor), and a severe reaction (shock, myocardial infarction, arrhythmia, seizures, coma) is a medical emergency.

34.3 How disulfiram works clinically: aversion, not craving

An aversive agent. The therapeutic effect is the *anticipation* of the reaction: knowing that a drink will make them violently ill, the patient does not drink. Disulfiram is therefore an aversive deterrent, an assisted form of behavioural control, rather than a neurochemical anti-craving drug like acamprosate or naltrexone (New Oxford 2020). It does not reduce craving at all, which is both its limitation and the reason compliance is poor: a patient who wants to drink simply stops the tablet a few days beforehand.

Why supervision is the whole game. Because the drug only works if it is actually taken, the evidence is stark: *supervised* disulfiram outperforms placebo and, in some analyses, out-performs acamprosate and naltrexone for maintaining abstinence, whereas *unsupervised* disulfiram is little better than placebo (New Oxford 2020; Maudsley 2021). This is why every guideline ties disulfiram to observed dosing by a reliable family member or carer, a model that fits Indian de-addiction practice especially well.

34.4 The dose and the Indian brands

Standard dosing. The usual oral dose is **250 to 500 mg daily**, typically 250 to 500 mg daily in the first week and **250 mg daily** for maintenance, with a maximum of 500 mg daily (Stahl 2021; IPS 2014). It is often taken at night because it can cause mild sedation, and no taper is needed to stop it (though the enzyme block, and therefore the risk of a reaction, persists for up to two weeks after the last tablet). Guidelines differ slightly on the maintenance figure, NICE anchors to 200 mg daily, IPS to 250 mg daily, which is a legitimate range rather than a contradiction; the safe, examinable core is 250 mg daily with a 200 to 500 mg daily range.

The Indian brands. In Indian practice disulfiram is prescribed as the brands Esperal or Dizone (each a 250 mg scored tablet); the generic is disulfiram (KDT 2019). Lead with the brand at the bedside, but the generic stays primary. Note the older Indian textbook practice of an alcohol *challenge test* under supervision to demonstrate the reaction before discharge, now largely abandoned as unsafe and unnecessary.

PARAMETER	VALUE
Mechanism	irreversible aldehyde-dehydrogenase (ALDH) inhibition
Starting / first-week dose (mg daily)	250 to 500
Maintenance dose (mg daily)	250 (range 200 to 500; NICE anchors 200)
Maximum dose (mg daily)	500
Onset of deterrent effect	within about 12 hours of first dose
Effect persists after stopping	about 7 to 14 days (irreversible block)
Indian brands	Esperal, Dizone (250 mg tablet)
Baseline monitoring	liver function tests, urea and electrolytes

The examinable disulfiram data: an ALDH-inhibiting aversive agent, 250 to 500 mg daily, effect lasting up to two weeks after stopping (Stahl 2021; NICE 2011; IPS 2014).

TRAP **Disulfiram is not a craving drug and not a withdrawal drug.** It has no anti-craving action and no role in detoxification or the acute withdrawal syndrome; giving it to "help withdrawal" or expecting it to reduce urges is wrong, it is a maintenance-phase aversive deterrent that only works when taken under supervision.

34.5 The critical cautions: never in a drinking or cardiac patient

Never while still drinking. The first absolute rule is that disulfiram is *never* started in a patient who is still drinking or intoxicated: with alcohol already on board, the first dose triggers the reaction directly, and it must be begun only after a documented period of abstinence, at least **24 hours** after the last drink (BAP 2026; IPS 2014; NICE 2011; Stahl gives at least 12 hours as the minimum). This is why a still-drinking patient is a hard exclusion and a wrong answer if you start it there.

The cardiac contraindication and other exclusions. The **cardiac contraindication** is the second absolute: disulfiram is contraindicated in ischaemic heart disease (coronary artery disease), heart failure and significant arrhythmia, because the tachycardia and hypotension of a reaction can precipitate myocardial infarction, dangerous arrhythmia or cardiovascular collapse (Stahl 2021). The other important exclusions are significant hepatic impairment or cirrhosis (disulfiram is itself hepatotoxic), current psychosis (past or present), severe renal impairment, peripheral neuropathy, and pregnancy, particularly the first trimester (Stahl 2021). Because the drug is hepatotoxic, baseline and follow-up liver function tests are mandatory, along with baseline urea and electrolytes (NICE 2011; Stahl 2021).

Consent and supervision. Two procedural safeguards are examinable in their own right. First, informed consent: the patient must be fully and explicitly informed about the disulfiram-ethanol reaction, the hidden sources of alcohol, and the two-week carry-over, and must never be given the drug covertly. Second, supervised administration: ideally a co-resident family member or carer observes each dose, because the drug's whole efficacy depends on it actually being taken (BAP 2026; IPS 2014; NICE 2011).

COMMON TRAP

The single most dangerous prescribing error with disulfiram is starting it in a patient who has not stopped drinking (or who has coronary artery disease). Do not be reassured by a patient who says "I'll stop from tonight", confirm at least 24 hours of documented abstinence first, and screen the heart and liver before the first tablet. Starting disulfiram in a still-drinking or cardiac patient can be fatal, and that is exactly the scenario the examiner builds.

GOOD TO REMEMBER

- **Disulfiram (Indian brands Esperal, Dizone):** an irreversible aldehyde-dehydrogenase inhibitor that makes acetaldehyde accumulate on drinking, producing the aversive disulfiram-ethanol reaction; oral 250 to 500 mg daily (maintenance 250 mg daily) as a supervised, consented maintenance option in a motivated, abstinence-goal patient started at least 24 hours after the last drink; the signature cautions are that it is never given to a still-drinking or intoxicated patient, is contraindicated in cardiac disease and significant hepatic impairment, and requires baseline and follow-up liver function tests.

34.6 The guideline position: BAP, Indian Psychiatric Society, NICE and WHO

BAP leads. The British Association for Psychopharmacology (BAP) recommends reserving disulfiram for highly motivated, abstinence-goal patients with family or social support, ideally under supervised administration, and starting it at least 24 hours after the last drink (BAP 2026). BAP rates the evidence for supervised disulfiram highly (strength A in the supplement) but frames it as an option for a specific patient rather than a routine first choice, with acamprosate and naltrexone the first-line anti-craving agents for most people.

The other three. The Indian Psychiatric Society (IPS guidelines) offers disulfiram 250 to 500 mg daily under supervision as an aversive-therapy option, but *only* in motivated patients with a reliable family supervisor, after at least 24 hours of abstinence and with informed consent regarding the disulfiram-ethanol reaction, an explicitly family-supervised model (IPS 2014). NICE positions disulfiram as a second-line relapse-prevention option (200 mg daily, started at least 24 hours after the last drink, overseen by a family member or carer) for patients who want abstinence but for whom acamprosate or naltrexone is unsuitable or not preferred, with monitoring every two weeks for the first two months (NICE 2011; Maudsley 2021). WHO recommends disulfiram only in close-supervision settings for patients motivated for abstinence (WHO mhGAP). All four agree on the same spine: motivated abstinence-goal patient, supervised dosing, informed consent, started only after abstinence.

GUIDELINE	DISULFIRAM POSITION (ALCOHOL RELAPSE PREVENTION)
BAP (2026)	Reserve for highly motivated abstinence-goal patients with support; ideally supervised; start at least 24 hours after last drink (strength A)
Indian Psychiatric Society (2014)	250 to 500 mg daily supervised aversive therapy, only with a reliable family supervisor, after 24 hours abstinence and informed consent re the DER
NICE (2011)	Second-line option (200 mg daily) when acamprosate or naltrexone unsuitable or not preferred; carer-overseen; start at least 24 hours after last drink
WHO (mhGAP)	Only in close-supervision settings for patients motivated for abstinence

The disulfiram position across the four guidelines; BAP leads, and all four converge on a supervised, consented, motivated-abstinence use after documented sobriety.

INDIA

Disulfiram (Esperal, Dizone) fits Indian de-addiction practice unusually well precisely because its one requirement, an observer, is culturally available: a co-resident relative acts as the recovery monitor who supervises each dose, exactly the family-based model the Indian Psychiatric Society recommends (IPS 2014). In the wider treatment-gap picture, where the vast majority of Indians with alcohol dependence never reach specialist care and community and home-based delivery by trained non-specialists is being scaled up, a cheap, non-scheduled tablet supervised by a family member is a pragmatic anti-relapse tool. But the caution cuts the same way: in a de-addiction camp or busy outpatient setting the temptation to start it fast, before the patient has truly stopped drinking or before the heart and liver are checked, is exactly the error that turns a helpful drug into a lethal one.

RULE **Dry first, consented, supervised.** Start disulfiram only in a motivated abstinence-goal patient who has been off alcohol for at least 24 hours, only after screening out cardiac and significant hepatic disease, only with explicit informed consent about the reaction, and only where a reliable person can supervise the dose.

250 to 500 mg	24 hours	7 to 14 days	30 minutes
USUAL DISULFIRAM DAILY DOSE, MAINTENANCE 250 MG DAILY	MINIMUM ABSTINENCE AFTER LAST DRINK BEFORE STARTING	REACTION RISK PERSISTS AFTER STOPPING (IRREVERSIBLE ALDH BLOCK)	ONSET OF THE DISULFIRAM-ETHANOL REACTION AFTER DRINKING

HOLD THIS

Disulfiram (Esperal, Dizone) is an irreversible aldehyde-dehydrogenase inhibitor and an aversive deterrent, not an anti-craving or withdrawal drug: on drinking, acetaldehyde accumulates and produces the disulfiram-ethanol reaction (flushing, throbbing headache, nausea and vomiting, tachycardia and hypotension); give it 250 to 500 mg daily, supervised and consented, only to a motivated abstinence-goal patient started at least 24 hours after the last drink, and never to a patient who is still drinking, intoxicated, or has cardiac or significant hepatic disease, because there the reaction can kill.

35 · Naltrexone for alcohol use disorder

Alcohol is rewarding partly because it releases **endogenous opioids** that, in turn, drive dopamine release into the nucleus accumbens; block the opioid receptor and you blunt that reward, and the drinking loses its pull. That single idea is the whole of **naltrexone for alcohol**. It is the prototype **anti-craving** drug of alcohol use disorder, examined not as a description of dependence but as a management/drug topic: the marks are in the mechanism, the dose, the line and the monitoring. Naltrexone is not a detox drug and not a sedative; it is a relapse-prevention agent that reduces heavy-drinking days and craving in a patient who has already come through withdrawal (or who is cutting down), which is exactly why it earns its place beside acamprosate and disulfiram.

Why it matters clinically. This is the most tested anti-craving agent because it has the cleanest mechanism, a landmark trial (the **COMBINE study**), two dosage forms (oral daily and a monthly long-acting injectable), and one hard contraindication that a wrong answer fails, that it must

never be given to a current opioid user. The opioid and mesolimbic-dopamine reward anatomy it interrupts is developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and is not re-derived here; the NDPS Act frame behind Indian de-addiction prescribing sits in the Mental health legislation and forensic psychiatry notes.

50	380	7 to 10	12
ORAL DAILY DOSE (MG), START AT 25	XR INJECTABLE DOSE (MG) MONTHLY IM	OPIOID-FREE DAYS NEEDED BEFORE STARTING	NUMBER-NEEDED-TO-TREAT, HEAVY-DRINKING RELAPSE

35.1 The mechanism: a mu-opioid antagonist that blunts alcohol's reward

How it works. Naltrexone is a competitive, essentially pure mu-opioid antagonist (with weaker kappa and delta antagonism); it binds the mu receptor and initiates no signal (Kaplan and Sadock 2024). Drinking alcohol triggers the release of endogenous opioids (beta-endorphin), which disinhibit ventral-tegmental dopamine neurons and increase dopamine release into the nucleus accumbens, the felt "reward" of a drink. Because a mu-opioid antagonist sits on that receptor and blocks the opioid step, it blunts the enjoyment of heavy drinking and can increase abstinence (Stahl's Substance Use). The upshot is that a lapse produces less reward, so the drive to keep drinking through to intoxication is weakened.

What it is not. Naltrexone has no agonist action, so it produces no "high", no reinforcement, no meaningful withdrawal on stopping and no diversion value; it is a non-scheduled drug prescribable in any clinical setting (Kaplan and Sadock 2024). Crucially, it can be used not only in an abstinent patient but also in one who is still drinking and trying to cut down, because its job is to strip the reward from the alcohol rather than to enforce a prior abstinence (Stahl's Substance Use).

> **PEARL**
>
> Separate naltrexone's mechanism from acamprosate's: naltrexone is a mu-*opioid* antagonist that reduces the *reward* of drinking and best suits the "reward drinker" who drinks for the buzz; acamprosate is a glutamate/NMDA modulator that dampens the protracted *hyperglutamatergic* negative-affect state and best suits the abstinent patient staying dry. They act on different arms of addiction, which is why combining them adds no benefit (COMBINE study).

35.2 The clinical effect: reduces heavy-drinking days and craving

What it actually delivers. Naltrexone's signature effect is that it **reduces heavy drinking**: across a large meta-analysis (53 trials, n = 9,140) its most consistent benefit is preventing the return to heavy drinking and reducing the percentage of drinking days and heavy-drinking days (Kaplan and Sadock 2024). The two original 1990s double-blind trials, in which 50 mg/day was started after at least 7 days abstinent, found naltrexone-treated patients more likely to stay abstinent (**54% vs 31%**) and much less likely to relapse to heavy drinking (**25% vs 52%**); a patient who did lapse was less likely to progress to heavy drinking on naltrexone than on placebo (Kaplan and Sadock 2024).

Craving and the modest overall effect. By reducing the opioid-mediated reward, naltrexone also lowers cue-induced craving, and it works best in high-craving patients and "reward drinkers" (positive-reinforcement drinkers, PREDICT study). Honestly framed, the effect size is modest, with a number-needed-to-treat of about **12** to prevent one return to heavy drinking (VA/DoD), but its good safety profile means it should be offered to essentially any patient with alcohol use disorder who has no contraindication (Kaplan and Sadock 2024).

RULE **Offer an anti-craving agent to every alcohol-dependent patient after withdrawal.** Naltrexone (or acamprosate) plus a structured psychosocial intervention is the standard of care for relapse prevention; the pharmacotherapy is an adjunct to psychosocial treatment, never a substitute for it.

35.3 The evidence base and the COMBINE study

The landmark trial. The COMBINE study (Anton et al, JAMA 2006) was a large multisite US trial (11 academic sites) that tested naltrexone and acamprosate, alone and combined, against placebo, each with either medical management or a more intensive combined behavioural intervention. Its headline result: a **100 mg** dose of naltrexone with medical management was more effective than placebo at increasing percent days abstinent and reducing heavy-drinking days (Kaplan and Sadock 2024). This is the single most quotable trial for naltrexone in alcohol use disorder.

The two negatives worth memorising. COMBINE found *no* benefit from adding acamprosate, either alone or on top of naltrexone, and *no* added benefit from combining naltrexone with acamprosate over naltrexone alone (Tasman 2024; Kaplan and Sadock 2024). It also showed that specialist behavioural therapy added little once naltrexone plus medical management was in place. The exam-safe summary is: naltrexone plus medical management works; adding acamprosate to it does not.

FINDING IN COMBINE (2006)	RESULT
Naltrexone 100 mg + medical management vs placebo	better: more abstinent days, fewer heavy-drinking days
Acamprosate vs placebo	no significant benefit
Naltrexone + acamprosate vs naltrexone alone	no added benefit of the combination
Intensive behavioural therapy added to naltrexone + MM	little additional benefit

The COMBINE study in one table: naltrexone with medical management is the effective arm; adding acamprosate adds nothing (Anton et al 2006; Kaplan and Sadock 2024).

MNEMONIC

COMBINE = Naltrexone wins, combo adds nothing

Read the trial name against its own result: it "combined" drugs and behavioural therapy, and the lesson is that the *combinations* did not help, only naltrexone-with-medical-management beat placebo. Acamprosate neither worked alone nor added to naltrexone.

35.4 The oral form: 50 mg a day (start 25 mg)

The dose. Oral naltrexone for alcohol use disorder is given at **50 mg/day** (25 mg and 50 mg tablets), usually started at 25 mg for a few days to check tolerability, then raised to 50 mg (IPS 2014; NICE 2011). It is begun after medically assisted withdrawal, combined with a structured psychosocial intervention, and typically continued for around 6 months (NICE 2011). Oral bioavailability is about 60%; the active metabolite 6-beta-naltrexol prolongs its action, and the mu blockade after an oral dose lasts up to about 72 hours (Kaplan and Sadock 2024).

Tolerability and monitoring. The common complaints are nausea, headache, dizziness and low mood; these usually settle. Naltrexone is *dose-relatedly* hepatotoxic, but at the therapeutic 50 mg/day it is not hepatotoxic in practice; the documented liver injury was at a sixfold higher 300 mg dose (Kaplan and Sadock 2024). Nonetheless baseline and periodic liver function tests are advised, and it is avoided in acute hepatitis or hepatic failure (NICE 2011; BAP 2026).

GOOD TO REMEMBER

- **Naltrexone (oral; commonly-used Indian brands Nodict or Naltima):** competitive pure mu-opioid antagonist that blunts the opioid-mediated reward of alcohol and reduces heavy-drinking days and craving; oral dose **50 mg/day** (start 25 mg), continued about 6 months with a psychosocial intervention; first-line anti-craving agent after detox; signature caution is precipitated withdrawal if given to a current opioid user (needs a 7-to-10-day opioid-free window), and monitor LFTs for dose-related hepatotoxicity.

35.5 The long-acting injectable: 380 mg IM monthly

Extended-release naltrexone. The long-acting injectable form (XR-NTX, brand Vivitrol) delivers **380 mg** deep intramuscularly once every 4 weeks, using a Medisorb microsphere depot that gives total naltrexone exposure three- to fourfold higher than daily oral dosing, with an elimination half-life of 5 to 10 days (Kaplan and Sadock 2024). A pivotal multisite trial of IM long-acting naltrexone in alcohol dependence showed the 380 mg preparation produced about a **25%** reduction in heavy-drinking days over 6 months, and the effect was larger in patients who had a few days of lead-in abstinence before the first injection (Kaplan and Sadock 2024).

Why the injectable matters. The daily tablet's weakness is adherence, a patient who wants to lapse simply skips it; a single monthly injection removes that daily decision and roughly doubles treatment retention versus oral (Kaplan and Sadock 2024). That is the whole clinical case for the depot: not greater intrinsic efficacy, but guaranteed exposure across the month.

FORM	ROUTE AND SCHEDULE	DOSE (MG)	NOTE
Oral naltrexone	tablet, once daily	50 (start 25)	first-line; adherence-limited; blockade ~72 h
XR-NTX injectable (Vivitrol)	deep IM, every 4 weeks	380	for poor adherence; retention ~2x oral

The two naltrexone forms for alcohol use disorder; the monthly injectable exists to solve the adherence failure of the daily tablet (Kaplan and Sadock 2024).

35.6 The guideline position: BAP first, then IPS, NICE and WHO

BAP (lead position). The British Association for Psychopharmacology (BAP) rates naltrexone strength A and recommends *preferring* naltrexone (oral daily or the monthly extended-release injection) for people with high craving or who are still drinking; it must not be started within a week of any opioid use, and it is avoided for 12 months after long-acting buprenorphine (BAP 2026). BAP also notes that in comorbid bipolar disorder naltrexone is preferred first-line, and that combining acamprosate and naltrexone gives no added benefit. This is the verified first-line anti-craving position and must anchor any answer.

IPS, NICE and WHO. The Indian Psychiatric Society is explicit that naltrexone 50 mg/day PO (titrated from 25 mg) is first-line anti-craving pharmacotherapy after detoxification, combined with a structured psychosocial intervention (IPS guidelines 2014). NICE recommends oral naltrexone after assisted withdrawal in moderate-to-severe dependence, starting 25 mg/day to a 50 mg/day maintenance dose, with an individual psychological intervention and at least monthly supervision for 6 months (NICE 2011). WHO mhGAP offers naltrexone to reduce the return to heavy drinking, and recommends the long-acting injectable where adherence is poor (WHO mhGAP 2016). WFSBP likewise rates oral naltrexone 50 mg/day at its highest recommendation grade for relapse prevention (WFSBP).

GOOD TO REMEMBER

- **Guideline line for naltrexone in alcohol:** BAP prefers it (strength A) for high craving or still-drinking patients, oral daily or monthly injectable; the Indian Psychiatric Society makes oral naltrexone 50 mg/day (start 25 mg) first-line anti-craving after detox; NICE and WHO mhGAP concur, WHO adding the injectable where adherence is poor. All pair it with a psychosocial intervention.

35.7 The critical contraindication: never in a current opioid user

Why it precipitates withdrawal. Because naltrexone is a competitive antagonist, giving it while opioids still occupy the mu receptor displaces the agonist and abruptly strips away all opioid tone, throwing a physiologically opioid-dependent patient into acute, severe **precipitated withdrawal** within minutes (Kaplan and Sadock 2024). This applies even when naltrexone is being prescribed for *alcohol*, so a drinker who is also using opioids (or on an opioid analgesic) cannot simply be started on it. The required opioid-free window is about **7 to 10 days** for short-acting opioids, longer after methadone, and BAP specifically warns to avoid naltrexone for 12 months after long-acting buprenorphine (Kaplan and Sadock 2024; BAP 2026).

The other cautions. Naltrexone is avoided in acute hepatitis and hepatic failure and monitored with LFTs (dose-related hepatotoxicity), and a patient on it cannot be given opioid analgesia through the blockade, so an alternative analgesic plan is needed for surgery or trauma (BAP 2026; VA/DoD).

TRAP **Naltrexone into a current opioid user precipitates withdrawal, even when prescribed for alcohol.** An antagonist onto occupied mu receptors strips the agonist off and causes acute severe withdrawal; confirm an opioid-free interval of about 7 to 10 days (longer after methadone) with a negative urine opioid screen before the first dose, and never start it "to be safe" while opioids may still be on board.

INDIA

In Indian de-addiction practice naltrexone is one of the workhorse anti-craving drugs, because the daily oral tablet is cheap, non-scheduled and prescribable in any setting without the OST licensing that agonist maintenance requires under the Narcotic Drugs and Psychotropic Substances (NDPS) Act, 1985. Against the country's enormous alcohol treatment gap, an affordable oral tablet backed by a co-resident family supervisor who observes the dose (the same family-supervised model used for disulfiram in Indian de-addiction centres and the DDAP model) is a genuinely scalable option. The long-acting depot injection is *not yet routinely available* in Indian practice, so the adherence problem is real and is managed socially rather than pharmacologically. The IPS substance-use guideline places oral naltrexone 50 mg/day first-line for anti-craving after detox (IPS guidelines 2014).

HOLD THIS

Naltrexone is a mu-opioid antagonist that blunts alcohol's reward: oral 50 mg/day (start 25 mg) or 380 mg IM monthly, first-line anti-craving after detox, reduces heavy-drinking days and craving (COMBINE), and must never be started until the patient has been opioid-free for at least 7 to 10 days.

36 · Acamprosate

Where disulfiram works by punishment and naltrexone by blunting reward, **acamprosate** works by repair: it is a neuromodulator that damps down the over-active **glutamate** system left behind by chronic drinking, and so belongs squarely to **abstinence maintenance** in the patient who has *already* been detoxified. It is one of the three classic anti-craving agents, and examiners test it on a small set of exact facts: what it does to the excitatory-inhibitory balance (its **nmda modulation** of the glutamatergic system), that it is a maintenance drug and never a withdrawal treatment, the three-times-daily schedule, the weight-banded dose, and the one contraindication that a wrong answer fails, its **renal dosing** and the renal contraindication (Kaplan and Sadock 2024; Maudsley 2021).

Why it matters clinically. This is a management/drug topic, so the marks are in the drug, the dose, the line and the monitoring, not in a description of alcohol dependence. The two things that make acamprosate clean to answer are its mechanism (it normalises a hyperglutamatergic state rather than aversion or reward) and its safety signature (it is renally, not hepatically, cleared, which flips the usual liver-caution on its head and moves the caution to the kidney). The reward and mesolimbic-dopamine anatomy on which alcohol's pull is built is developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and

is not re-derived here; the NDPS Act frame behind Indian de-addiction prescribing sits in the Mental health legislation and forensic psychiatry notes.

36.1 What it is: a glutamatergic neuromodulator for maintaining abstinence

The one-line identity. Acamprosate (calcium acetyl-homotaurinate; Indian brand Acamprol, also marketed as Campral in the West) is a synthetic structural analogue of the amino-acid neurotransmitters, licensed to *maintain abstinence* in the detoxified alcohol-dependent patient (Kaplan and Sadock 2024; Maudsley 2021). It does not sober a person up, does not treat withdrawal, and produces no aversive reaction if the patient drinks; its whole role is to hold a patient who has stopped drinking in abstinence and to help them regain it after a slip.

Where it sits among the three agents. Of the classic trio, disulfiram (Indian brands Esperal, Dizone) is aversive, naltrexone (Indian brands Nodict, Naltima) is reward-blunting, and acamprosate is the neuromodulator that restores disturbed brain chemistry. It is best in the *relief* drinker, the person who drinks to quell the negative affect and hyperexcitability of protracted withdrawal, rather than the *reward* drinker who is better matched to naltrexone (Kaplan and Sadock 2024).

36.2 The mechanism: glutamate, NMDA modulation and the excitatory-inhibitory balance

The neuroadaptation it corrects. Alcohol is a central nervous system depressant that inhibits the NMDA glutamate receptor and enhances GABA. The brain compensates for chronic exposure by up-regulating NMDA receptors and increasing synaptic glutamate release, so that when alcohol is withdrawn there is unopposed excitation, a hyperglutamatergic state that underlies craving, negative affect, disturbed sleep and, at the extreme, withdrawal seizures and delirium tremens (Kaplan and Sadock 2024). Acamprosate acts on exactly this imbalance: it damps the excitatory **glutamate** signalling that persists after drinking stops and so helps restore the excitatory-inhibitory balance the chronic drinker has lost.

The NMDA modulation specifically. Its **nmda modulation** is subtle rather than a simple block: acamprosate behaves as an NMDA partial co-agonist, activating the receptor when glutamatergic tone is low but becoming inhibitory when NMDA activity is pathologically high, which is how it *restores equilibrium* in a disrupted system rather than shutting it down (Kaplan and Sadock 2024). It also acts on metabotropic glutamate receptors (mGluR5), releases the inhibitory neuromodulator taurine, and there is compelling recent evidence that the calcium moiety of the salt is itself important. Structurally it resembles GABA, glycine, aspartate and glutamate, so more than one system is engaged, but the examinable headline is glutamatergic, NMDA-modulating restoration of the excitatory-inhibitory balance, with no aversion and no reward-blockade.

> **PEARL**
>
> The three anti-craving drugs map cleanly onto three mechanisms: disulfiram is aversion (blocks aldehyde dehydrogenase, acetaldehyde piles up), naltrexone is anti-reward (blocks the opioid-mediated pleasure of alcohol), and acamprosate is neuromodulation (damps the hyperglutamatergic, NMDA-driven excitation of protracted withdrawal). Only acamprosate is a pure repair drug: no punishment, no receptor block, just normalisation of disturbed chemistry.

36.3 The indication: abstinence maintenance in the already-detoxified patient

Timing is the whole indication. Acamprosate is for **abstinence maintenance** and is started only after medically assisted withdrawal, once abstinence has been achieved, in moderate-to-severe dependence, and always alongside a psychosocial intervention (NICE 2011; IPS 2014). It should be begun as soon as possible after detoxification, because its effect is time-sensitive: the glutamate dysregulation it targets is highest in early abstinence and normalises over the following weeks, so a drug started late has less to correct (Kaplan and Sadock 2024). One nuance to hold: the British Association for Psychopharmacology notes a potential neuroprotective effect and suggests it can even be started *during* detoxification, whereas trial data show no benefit, and possibly harm, if it is used to treat acute withdrawal itself; the safe examinable line is start early, after abstinence, never as a withdrawal agent (BAP 2026; Maudsley 2021).

What it is not. Acamprosate does not diminish withdrawal symptoms, is not indicated for delirium tremens, and produces no disulfiram-type reaction on relapse. If the patient continues to drink for 4 to 6 weeks after starting it, treatment should be stopped (NICE 2011). It is usually continued for up to 6 months, longer where the patient perceives benefit (Maudsley 2021).

TRAP **Acamprosate is not a withdrawal drug.** It does not touch the acute withdrawal syndrome and is not for delirium tremens; started during active withdrawal it gives no benefit and may worsen outcomes. Detoxify first with a benzodiazepine, achieve abstinence, then start acamprosate to maintain it.

36.4 The dose and the three-times-daily schedule

The weight-banded dose to memorise. Acamprosate comes as a **333 mg** enteric-coated tablet and is given three times daily. For a patient over 60 kg the dose is two tablets three times a day, that is 666 mg three times daily, a total of **1998 mg/day**; for a patient under 60 kg the dose is reduced to **1332 mg/day** (typically two tablets in the morning and one at midday and one at night, or 666 mg twice daily) (Maudsley 2021; NICE 2011; Stahl). The three-times-daily schedule is a genuine limitation: absorption is poor and slow so frequent dosing is needed, and adherence suffers, with about half of patients discontinuing before 6 months, partly because of the TID burden (Kaplan and Sadock 2024).

Why the schedule is what it is. Bioavailability is only about 11%, food reduces absorption slightly (not enough to change dosing), and the drug is so slowly absorbed it behaves like a modified-release preparation, so steady state takes 5 to 7 days; pairing each dose with a meal is a practical adherence tip (Kaplan and Sadock 2024). A useful reframe for the patient is to make the act of taking the tablet, rather than the act of drinking, the frequent daily ritual (Stahl).

BODY WEIGHT	SCHEDULE	TOTAL DOSE (MG/DAY)
Over 60 kg	666 mg (two 333 mg tablets) three times daily	1998
Under 60 kg	reduced schedule (e.g. two tablets AM, one midday, one night)	1332

Weight-banded acamprosate dosing; tablet strength 333 mg, always three-times-daily, for abstinence maintenance after detoxification (Maudsley 2021; NICE 2011).

36.5 Renal dosing and the renal contraindication

The safety fact that flips the usual caution. Acamprosate bypasses the liver almost entirely: it is not hepatically metabolised, does not induce or inhibit cytochrome enzymes, and the absorbed fraction is excreted unchanged in the urine (Kaplan and Sadock 2024). Two consequences follow, and both are examinable. First, because it spares the liver, it is *safe in alcohol-related liver disease* and needs no dose change in Child-Pugh A or B cirrhosis, which is why it is preferred over naltrexone where hepatic function is deranged (BAP 2026; Stahl). Second, because it is renally cleared, the kidney becomes the organ of caution.

The renal rule. Acamprosate is *contraindicated in severe renal impairment*, and in mild-to-moderate impairment the dose is reduced, with 333 mg three times daily recommended for moderate impairment (Stahl; BAP 2026; WFSBP). In practice this means a baseline renal check before starting: NICE requires baseline urea and electrolytes (alongside liver function tests including GGT) and periodic monitoring, and severe renal impairment (broadly a creatinine clearance below the low-30s mL/min) rules the drug out (NICE 2011; Maudsley 2021). The single most serious adverse effect on record is acute renal failure, so renal function, not the liver, is what you monitor (Kaplan and Sadock 2024).

RENAL STATUS	ACAMPROSATE ACTION
Normal renal function	Standard weight-banded dose (1998 or 1332 mg/day)
Moderate impairment	Reduce to 333 mg three times daily
Severe impairment	Contraindicated, do not use
Hepatic impairment (Child-Pugh A/B)	No dose change needed, preferred where liver disease limits other agents

Acamprosate is renally cleared: reduce in moderate renal impairment, contraindicated in severe, but safe in liver disease (Stahl; BAP 2026; Maudsley 2021).

RULE **Check the kidney, not the liver.** Acamprosate is renally excreted and hepatically safe, so it is the anti-craving agent of choice in alcohol-related liver disease, but it must be dose-reduced in moderate renal impairment and stopped altogether in severe renal impairment.

36.6 Where the guidelines place it: BAP, IPS, NICE and WHO

Lead with BAP. The British Association for Psychopharmacology (BAP) positions acamprosate as a core relapse-prevention agent offered after medically assisted withdrawal to increase abstinence, usable safely in alcohol-associated liver disease but requiring dose adjustment in renal impairment and avoidance in severe renal impairment; it also flags that combining acamprosate with naltrexone gives no added benefit over either alone (BAP 2026). Within a WHO-mhGAP-style primary-care frame, BAP goes further and calls acamprosate the maintenance intervention with the strongest evidence of benefit for holding alcohol abstinence after detoxification (BAP 2026). This is the verified first-line-by-goal position and anchors any answer.

Then the other bodies. The Indian Psychiatric Society substance-use clinical practice guidelines (the Basu, Ghosh, Lal and Murthy tradition) grade acamprosate at strength A and offer it to maintain abstinence and prevent relapse, noting it also reduces heavy drinking in those who relapse; the IPS guidelines make it a parallel first-line anti-craving option alongside naltrexone 50 mg/day, particularly favoured where opioid co-use is anticipated or where hepatic enzymes are deranged, always combined with a structured psychosocial intervention (IPS 2014). NICE offers acamprosate (or oral naltrexone) after successful withdrawal in moderate-to-severe dependence, at 1998 mg/day reducing to 1332 mg/day if under 60 kg, with a comprehensive medical assessment and baseline urea/electrolytes and liver function first (NICE 2011). WHO recommends considering acamprosate, naltrexone or disulfiram to prevent relapse in alcohol dependence (WHO mhGAP 2016), and WFSBP grades it RG1, first-line with naltrexone, contraindicated in severe renal impairment (WFSBP).

GUIDELINE	ACAMPROSATE POSITION (ALCOHOL RELAPSE PREVENTION)
BAP	Core agent after assisted withdrawal; strongest maintenance evidence in primary care; liver-safe, renal dose-adjust
Indian Psychiatric Society (IPS guidelines)	Strength A; parallel first-line with naltrexone; favoured where opioid co-use or deranged LFTs; with psychosocial care
NICE 2011	Offer after withdrawal in moderate-severe dependence; 1998 mg/day (1332 if under 60 kg); baseline U&E and LFTs
WHO mhGAP 2016	Consider acamprosate, naltrexone or disulfiram to prevent relapse
WFSBP	RG1, first-line with naltrexone; contraindicated in severe renal impairment

Guideline-level placement of acamprosate; BAP-led, then Indian Psychiatric Society, NICE, WHO and WFSBP (verified from the drug-guideline supplement).

36.7 The India lens: the treatment gap, brand access and the de-addiction setting

Where it fits Indian practice. In the Indian de-addiction context, acamprosate (Acamprol) is a practical maintenance agent: it is non-scheduled and so falls outside the Narcotic Drugs and Psychotropic Substances (NDPS) Act, 1985 prescriber constraints that bind agonist opioid-substitution therapy, and its hepatic safety matters in a population where alcohol-related liver disease is common (IPS 2014). Against the large substance-use treatment gap, where most dependent drinkers never reach formal care and services cluster in government de-addiction centres and Drug De-addiction Programme (DDAP) units, acamprosate combines usefully with the community and home-based, non-specialist-delivered model the Indian guidelines push, and with the family-supervised approach already used for disulfiram.

The honest caveat. The three-times-daily schedule is a real adherence obstacle in this setting, and acamprosate's modest effect size (number needed to treat around 12 to prevent a return to

drinking) means it is offered as one option, chosen by patient preference and comorbidity, not as a magic bullet; the drug works only when it rides on a structured psychosocial intervention (IPS 2014; Kaplan and Sadock 2024).

INDIA

Acamprosate (Acamprol) is the anti-craving agent to reach for in the Indian drinker with liver disease: it bypasses the liver, so it is safe in cirrhosis where naltrexone (hepatotoxic, and blocked by any opioid co-use) is problematic. It is non-scheduled, prescribable in any de-addiction setting without NDPS-linked OST licensing, but the twice-or-thrice-daily dosing is a genuine adherence problem, so pair it with a co-resident family supervisor and a structured psychosocial programme, exactly the model Indian de-addiction care already runs on. Watch renal function, not the liver.

MNEMONIC

"CALM the glutamate, spare the LIVER, mind the KIDNEY, dose by THIRDS"

Acamprosate CALMs the hyperglutamatergic, NMDA-driven excitation of early abstinence; it SPAREs the liver (renally cleared, safe in cirrhosis); you must mind the KIDNEY (reduce in moderate, avoid in severe renal impairment); and it is dosed by THIRDS, 666 mg three times a day (1998 mg/day over 60 kg; 1332 mg/day under 60 kg).

1998 mg DAILY ACAMPROSATE DOSE IF OVER 60 KG (666 THREE TIMES DAILY)	**1332 mg** REDUCED DAILY DOSE IF UNDER 60 KG	**333 mg** TABLET STRENGTH; THE MODERATE-RENAL-IMPAIRMENT DOSE IS ONE THREE TIMES DAILY	**6 months** USUAL DURATION OF MAINTENANCE TREATMENT

GOOD TO REMEMBER

- **Acamprosate (Indian brand Acamprol; oral):** a glutamatergic neuromodulator (NMDA partial co-agonist that restores the excitatory-inhibitory balance disturbed by chronic alcohol) for abstinence maintenance in the already-detoxified patient, never for withdrawal or delirium tremens; dose 666 mg three times daily (1998 mg/day if over 60 kg; 1332 mg/day if under 60 kg), tablet 333 mg; the signature caution is that it is renally cleared, so it is safe in liver disease but must be dose-reduced in moderate and is contraindicated in severe renal impairment; combine with a psychosocial intervention and stop if drinking continues 4 to 6 weeks after starting.

HOLD THIS

Acamprosate is a glutamatergic, NMDA-modulating neuromodulator that restores the excitatory-inhibitory balance of protracted withdrawal, used for abstinence maintenance in the detoxified patient (not for withdrawal); it is dosed 666 mg three times daily, 1998 mg/day if over 60 kg and 1332 mg/day if under 60 kg, and because it is renally excreted and hepatically safe it is the anti-craving agent of choice in liver disease but is dose-reduced in moderate and contraindicated in severe renal impairment.

37 · Comparing the anti-craving agents

Three drugs dominate the maintenance-phase pharmacotherapy of alcohol use disorder, and the examinable skill is not knowing each one in isolation but placing them side by side: the

comparison of disulfiram, naltrexone and acamprosate as three fundamentally different strategies against the same illness. Disulfiram makes drinking *punishing* (aversive deterrence), naltrexone makes drinking *less rewarding* (reward-craving reduction), and acamprosate makes staying dry *easier* (abstinence maintenance). The individual drugs are taught in their own fragments; here the marks are in the head-to-head, so this is written as a comparison and a selection decision.

Why it matters clinically. The single highest-yield fact is that the anti-craving agents (naltrexone and acamprosate) are the two first-line choices after detoxification, and disulfiram is a deliberately second-choice, supervised agent for a specific motivated patient, not a default. A wrong first-line here is a critical error. The examiner tests the **anti-craving comparison** by contrasting mechanism, target, evidence and the one caution that excludes each drug, then by asking which agent for which patient. The mesolimbic-dopamine reward anatomy these drugs act on (and that disulfiram deliberately does not) is developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the NDPS Act frame behind Indian de-addiction prescribing sits in the Mental health legislation and forensic psychiatry notes. One figure carries this topic: Fig 13.21, a three-column concept map of the aversive versus reward-blunting versus abstinence-stabilising strategies with each drug's target, dose and key caution.

2	50	1998	24
FIRST-LINE ANTI-CRAVING AGENTS AFTER DETOX (NALTREXONE, ACAMPROSATE)	NALTREXONE ORAL DOSE (MG), START AT 25	ACAMPROSATE DOSE (MG OVER 60 KG), 666 THREE TIMES DAILY	HOURS ABSTINENT REQUIRED BEFORE STARTING DISULFIRAM

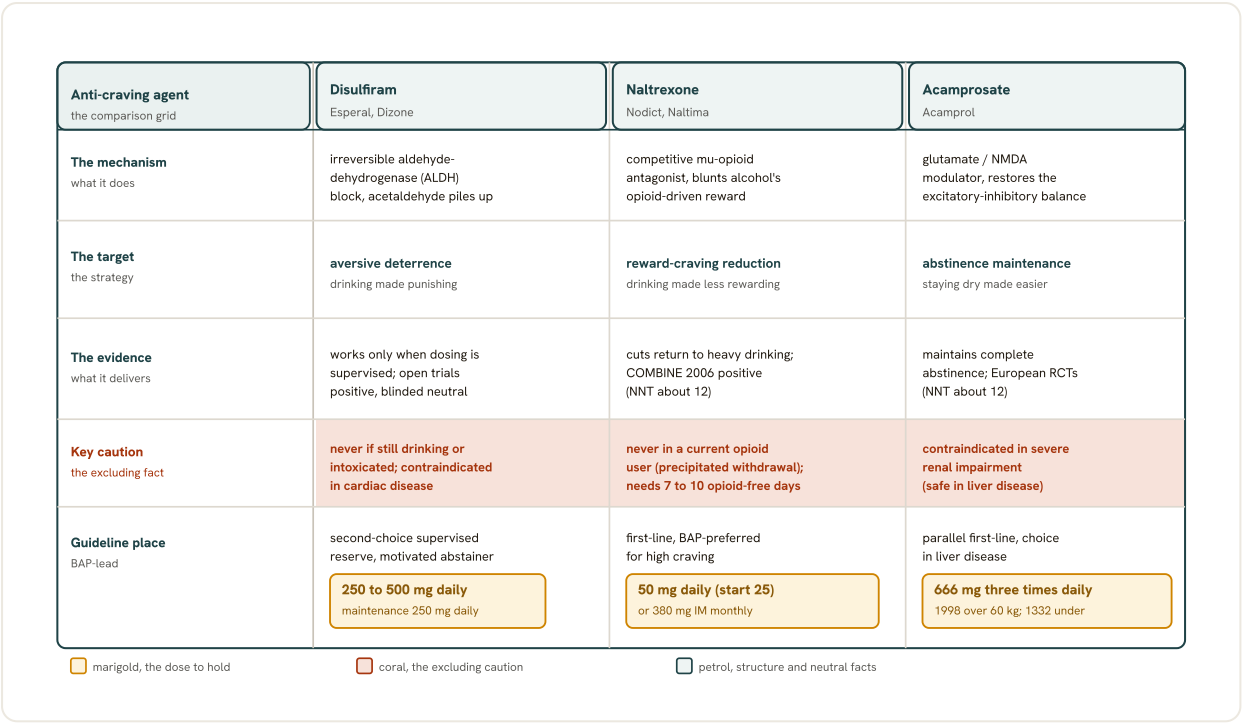


Fig 13.21 Anti-craving pharmacotherapy: disulfiram, naltrexone and acamprosate compared. Read down each column: disulfiram deters (ALDH block, aversive, supervised-only, never in a drinking or cardiac patient), naltrexone de-rewards (mu-opioid antagonist, first-line, never in an opioid user), and acamprosate anchors abstinence (glutamate/NMDA modulator, first-line, contraindicated only in severe renal impairment). Naltrexone and acamprosate are the two first-line anti-craving agents after detox; disulfiram is the supervised reserve. The marigold chips carry the examinable doses.

37.1 The three strategies at a glance: aversion, reward-blunting, abstinence-stabilising

Three different jobs. The clean framing is that the three agents attack three different arms of dependence. Disulfiram is an **aversive** deterrent: it does nothing to craving and instead makes drinking physically punishing, so it works by threat. Naltrexone is a reward-blunting anti-craving agent: it removes the pleasure from a drink, so a lapse yields less reward and the drive to keep drinking weakens. Acamprosate is an abstinence-maintaining neuromodulator: it settles the hyperglutamatergic negative-affect state of protracted withdrawal, so staying dry is easier (Kaplan and Sadock 2024; New Oxford). Only the last two are true anti-craving agents; disulfiram is grouped with them by indication (relapse prevention) but not by mechanism.

Why the distinction is examined. Candidates lose marks by calling disulfiram an "anti-craving" drug or by treating the three as interchangeable. They are not: they suit different patients, carry different contraindications, and sit on different guideline lines. The selection question flows directly from the mechanism, which is why the comparison is worth memorising as a single grid rather than three separate drug cards.

AGENT	STRATEGY / TARGET	MECHANISM (VERIFIED)	BEST-MATCHED PATIENT
Disulfiram (Esperal, Dizone)	aversive deterrence	irreversible aldehyde-dehydrogenase (ALDH) inhibitor → acetaldehyde accumulates on drinking	highly motivated, abstinence-goal, with a supervisor
Naltrexone (Nodict, Naltima)	reward-craving reduction	competitive mu-opioid antagonist → blunts alcohol's opioid-mediated dopamine reward	high-craving "reward drinker"; still drinking / cutting down
Acamprosate (Acamprol)	abstinence maintenance	glutamate / NMDA modulator (partial co-agonist) → restores excitatory-inhibitory balance	detoxified "relief drinker" holding abstinence; liver disease

The three-strategy grid: two anti-craving agents (naltrexone, acamprosate) plus the aversive deterrent disulfiram, matched to mechanism and patient (Kaplan and Sadock 2024; New Oxford).

MNEMONIC

"DISULFIRAM DETERS, NALTREXONE de-REWARDS, ACAMPROSATE ANCHORS"

Disulfiram DETERS by punishment (ALDH block, acetaldehyde reaction); naltrexone de-REWARDS by blocking the opioid-mediated buzz (mu antagonist, the reward drinker); acamprosate ANCHORS abstinence by calming the hyperglutamatergic state (NMDA modulator, the relief drinker). Three verbs, three mechanisms, three patients.

37.2 Mechanism head-to-head: ALDH block versus mu-opioid antagonism versus glutamate modulation

Disulfiram. Disulfiram irreversibly inhibits aldehyde dehydrogenase, the enzyme that clears acetaldehyde (the first metabolite of ethanol). On drinking, acetaldehyde accumulates and produces the aversive disulfiram-ethanol reaction (flushing, throbbing headache, nausea and vomiting, tachycardia with hypotension). It touches neither craving nor the reward pathway; the block is irreversible, so the danger persists for up to two weeks after the last tablet (Stahl 2021).

Naltrexone. Naltrexone is a competitive, essentially pure mu-opioid antagonist. Alcohol releases endogenous opioids that drive dopamine into the nucleus accumbens, the felt reward of a drink; blocking the mu receptor blunts that reward, so heavy-drinking days and cue-induced craving fall (Stahl's Substance Use; Kaplan and Sadock 2024). It works in the still-drinking patient because it strips the reward rather than enforcing prior abstinence.

Acamprosate. Acamprosate is a glutamatergic neuromodulator, an NMDA partial co-agonist that also acts on metabotropic glutamate (mGluR5) receptors. Chronic alcohol up-regulates NMDA receptors; on withdrawal this leaves an unopposed hyperglutamatergic state driving craving and negative affect. Acamprosate damps that excitation and restores the excitatory-inhibitory balance, with no aversion and no reward blockade (Kaplan and Sadock 2024; New Oxford).

PEARL

Match the anti-craving agent to the type of drinker. Naltrexone suits the *reward drinker* who drinks for the buzz (it removes the reward); acamprosate suits the *relief drinker* who drinks to quell negative affect and stay functional (it calms the glutamate storm). Disulfiram suits neither craving type, it suits the motivated abstainer who wants an external barrier against impulse. This is why combining naltrexone and acamprosate adds no benefit, they act on different arms and there is no synergy (COMBINE study).

37.3 The dose and monitoring lines, side by side

The three doses. The examinable doses are worth carrying as a set: disulfiram **250 to 500 mg daily** (maintenance 250 mg daily, oral); naltrexone **50 mg daily** orally (started at 25 mg, plus a 380 mg monthly IM injectable form); and acamprosate **666 mg** three times daily, giving 1998 mg daily over 60 kg and 1332 mg daily under 60 kg (IPS 2014; NICE 2011; Maudsley 2021). Each is a maintenance-phase agent, begun after (or, for naltrexone, sometimes during) a cut-down, and each is paired with a structured psychosocial intervention.

The monitoring split. The monitoring maps onto the metabolism. Disulfiram and naltrexone are both hepatically handled, so both need baseline and periodic liver function tests; acamprosate is renally cleared, so it is the safe choice in liver disease but must be dose-reduced in renal impairment (Kaplan and Sadock 2024; NICE 2011). This is a favourite discriminator: acamprosate watches the kidney, disulfiram and naltrexone watch the liver.

PARAMETER	DISULFIRAM	NALTREXONE	ACAMPROSATE
Oral dose (mg daily)	250 to 500 (maint. 250)	50 (start 25)	1998 (over 60 kg); 1332 (under 60 kg)
Schedule	once daily (often nocte)	once daily; 380 IM monthly	666 three times daily
Metabolism / clearance	hepatic (hepatotoxic)	hepatic (dose-related)	renal (not metabolised)
Key monitoring	LFTs; U&E	LFTs; opioid-free status	renal function (U&E)
Safe in liver disease?	no (contraindicated)	caution; avoid acute hepatitis / failure	yes (Child-Pugh A/B)
Onset condition	at least 24 h after last drink	at least 7 to 10 opioid-free days	as soon as possible after withdrawal

Dose, metabolism and monitoring for the three agents; note acamprosate's renal clearance makes it the liver-disease choice, and each drug's onset condition (BAP 2026; IPS 2014; NICE 2011; Maudsley 2021).

37.4 The evidence head-to-head: what each agent actually delivers

Naltrexone and acamprosate have the meta-analytic base. Both are supported by large meta-analyses, each with a number-needed-to-treat of roughly **12** to prevent one return to drinking; naltrexone's most consistent signal is reducing the return to *heavy* drinking, while acamprosate's is maintaining complete abstinence (Kaplan and Sadock 2024; VA/DoD). The landmark head-to-head is the COMBINE study (Anton et al, JAMA 2006): naltrexone with medical management

beat placebo, acamprosate showed no significant benefit in that US trial, and combining the two added nothing over naltrexone alone. European trials have been more favourable to acamprosate, so the two are treated as parallel first-line options rather than one being clearly superior.

Disulfiram's evidence is adherence-dependent. Disulfiram works only when its intake is *supervised*: in open trials with observed dosing it outperforms placebo, but in blinded trials where patients self-administer it does not, because an unsupervised patient who wants to drink simply stops the tablet first (Kaplan and Sadock 2024; New Oxford). This is the whole reason it is reserved for the motivated patient with a reliable supervisor, and why guidelines rank it below the two anti-craving agents.

AGENT	SIGNATURE OUTCOME	EVIDENCE ANCHOR
Naltrexone	reduces return to heavy drinking; lowers craving (NNT ~12)	COMBINE (2006); large meta-analyses
Acamprosate	maintains complete abstinence (NNT ~12)	European RCTs; meta-analyses
Disulfiram	effective only under supervised administration	open (supervised) trials positive; blinded trials neutral

What the evidence says each agent does; disulfiram's benefit is real but contingent on observed dosing (Kaplan and Sadock 2024; Anton et al 2006).

37.5 The cautions head-to-head: the one contraindication that excludes each drug

One killer caution per drug. Each agent has a signature exclusion that a well-set question hinges on. Disulfiram must never be started in a patient who is still drinking or intoxicated (the first dose triggers the reaction) and is contraindicated in cardiac disease, where the tachycardia and hypotension of the disulfiram-ethanol reaction can precipitate a myocardial infarction or arrhythmia; it needs at least 24 hours of documented abstinence, consent and supervision (BAP 2026). Naltrexone must never be given to a current opioid user, even when prescribed for alcohol, because as a competitive antagonist it displaces the agonist and throws a dependent patient into precipitated withdrawal; it needs a 7-to-10-day opioid-free window (longer after methadone, and BAP avoids it for 12 months after long-acting buprenorphine). Acamprosate's limiting caution is renal, it is dose-reduced in moderate and contraindicated in severe renal impairment, though it is safe in liver disease (Kaplan and Sadock 2024; NICE 2011; BAP 2026).

AGENT	THE ONE CAUTION THAT EXCLUDES IT	PRACTICAL GUARD
Disulfiram	still-drinking / intoxicated; cardiac disease; hepatic impairment	24 h abstinent + consent + supervision + LFTs
Naltrexone	current opioid use (precipitated withdrawal); acute hepatitis / failure	7 to 10 opioid-free days + negative urine opioid screen
Acamprosate	severe renal impairment	check renal function; dose-reduce if under 60 kg / moderate impairment

The signature contraindication of each anti-craving comparison partner, the level the examiner tests (BAP 2026; NICE 2011; Kaplan and Sadock 2024).

TRAP **Do not reach for disulfiram first, and never give naltrexone to a drinker who also uses opioids.** Disulfiram is a second-choice, supervised, consented aversive agent, not a first-line anti-craving drug; and naltrexone into a current opioid user precipitates severe withdrawal within minutes even when it is being prescribed for alcohol, so confirm an opioid-free window first.

37.6 The guideline-anchored selection: BAP first, then IPS, NICE and WHO

BAP (lead position). The British Association for Psychopharmacology (BAP) is the anchor for **guideline-anchored selection**. BAP rates naltrexone strength A and recommends *preferring* naltrexone (oral daily or the monthly extended-release injection) for patients with high craving or who are still drinking; acamprosate is likewise strength A for maintaining abstinence after withdrawal; and disulfiram, though strength A for efficacy, is explicitly *reserved* for highly motivated, abstinence-goal patients with family or social support and supervised administration, started at least 24 hours after the last drink (BAP 2026). BAP also notes that combining acamprosate and naltrexone gives no added benefit, and that in comorbid bipolar disorder naltrexone is preferred first-line. So the verified first-line anti-craving agents are naltrexone and acamprosate, with disulfiram positioned below them.

The Indian Psychiatric Society. The Indian Psychiatric Society is explicit that naltrexone 50 mg daily orally (titrated from 25 mg) is first-line anti-craving pharmacotherapy after detoxification, with acamprosate 666 mg three times daily a parallel first-line option, particularly where opioid co-use is anticipated or hepatic enzymes are deranged; both are combined with a structured psychosocial intervention (IPS guidelines 2014). The IPS guidelines place disulfiram 250 mg daily as supervised aversive therapy only in motivated patients with a reliable family supervisor, after at least 24 hours of abstinence and informed consent, exactly the second-choice, family-supervised framing that fits Indian de-addiction practice.

NICE and WHO. NICE recommends acamprosate or oral naltrexone (each with an individual psychological intervention) as the relapse-prevention options after assisted withdrawal in moderate-to-severe dependence, and positions disulfiram for patients with an abstinence goal *when acamprosate and naltrexone are unsuitable or not preferred*, which again ranks disulfiram below the two anti-craving agents (NICE 2011). WHO mhGAP takes the pragmatic line that acamprosate, disulfiram or naltrexone may all be offered to reduce relapse to heavy drinking, choosing the agent by patient preference and availability (WHO mhGAP 2016). The convergent, verified message across all four: the two anti-craving agents are first-line, disulfiram is the supervised reserve.

RULE **After detox, offer a first-line anti-craving agent (naltrexone or acamprosate) plus a psychosocial intervention; keep disulfiram as the supervised reserve.** BAP, the Indian Psychiatric Society and NICE all make naltrexone and acamprosate first-line and position disulfiram for the motivated abstinence-goal patient with supervision, or when the anti-craving agents are unsuitable.

37.7 Selecting an agent for the patient in front of you

The selection logic. The **selection of anti-craving** agent follows from goal, drinking type, comorbidity and organ function. Goal: a patient who wants controlled reduction or is still drinking suits naltrexone (it works while drinking continues); a patient committed to total abstinence suits acamprosate or supervised disulfiram. Drinking type: reward drinkers to naltrexone, relief drinkers to acamprosate. Comorbidity: comorbid opioid use forbids naltrexone (use acamprosate or disulfiram); comorbid nicotine dependence favours varenicline alongside; comorbid bipolar favours naltrexone (BAP 2026). Organ function: liver disease pushes toward acamprosate (renally cleared, hepatically safe) and away from naltrexone and disulfiram; renal impairment pushes away from acamprosate.

The disulfiram-specific gate. Disulfiram is selected only when three things line up: a genuinely motivated patient with a firm abstinence goal, a reliable co-resident supervisor, and no cardiac or significant hepatic disease, with documented abstinence and informed consent (IPS 2014; BAP 2026). If any of those is missing, choose an anti-craving agent instead.

WORKED EXAMPLE

A 42-year-old man with moderate-to-severe alcohol dependence and early cirrhosis has completed inpatient withdrawal and wants to stay dry. Naltrexone is relatively contraindicated by his liver disease; disulfiram is contraindicated (hepatotoxic, and he has no supervisor). The guideline-anchored choice is acamprosate (Acamprol) 666 mg three times daily, renally cleared and safe in Child-Pugh A/B cirrhosis, paired with a psychosocial intervention and family support, with renal function checked at baseline. If instead he were a high-craving "reward drinker" with a healthy liver and no opioid use, naltrexone 50 mg daily (start 25) would be first choice; disulfiram would enter only if he were strongly abstinence-motivated with a reliable home supervisor and a normal heart and liver.

INDIA

In Indian de-addiction practice the selection is shaped by a very large treatment gap, the family-supervised model, and access. Disulfiram (Esperal, Dizone) remains widely used because a co-resident relative can supervise each dose, the classic family-based recovery-monitor model the Indian Psychiatric Society endorses. Naltrexone (Nodict, Naltima) and acamprosate (Acamprol) are non-scheduled and so sit outside the NDPS Act, 1985 constraints that bind agonist opioid-substitution prescribing, making them prescribable in any de-addiction or Drug De-addiction Programme (DDAP) setting without special licensing. Acamprosate's hepatic safety matters where alcohol-related liver disease is common, though its thrice-daily dosing is a real adherence obstacle, so it too is paired with a family supervisor and a structured psychosocial programme.

GOOD TO REMEMBER

- **Disulfiram (Indian brands Esperal, Dizone):** irreversible ALDH inhibitor and aversive deterrent (not anti-craving); oral **250 to 500 mg daily** (maintenance 250) supervised and consented, only in a motivated abstinence-goal patient started at least 24 hours after the last drink; second-choice line; never in a still-drinking, intoxicated, cardiac or hepatic patient; monitor LFTs.
- **Naltrexone (Indian brands Nodict, Naltima):** competitive mu-opioid antagonist reducing the reward of drinking; oral **50 mg daily** (start 25; 380 mg IM monthly); first-line anti-craving after detox, BAP-preferred for high craving / still drinking; never in a current opioid user (precipitated withdrawal, needs a 7-to-10-day opioid-free window); monitor LFTs.
- **Acamprosate (Indian brand Acamprol):** glutamate / NMDA modulator for abstinence maintenance in the detoxified patient; **666 mg** three times daily (1998 mg daily over 60 kg; 1332 under 60 kg); parallel first-line anti-craving; renally cleared, so safe in liver disease but dose-reduced in moderate and contraindicated in severe renal impairment.

HOLD THIS

Naltrexone and acamprosate are the two first-line anti-craving agents after detoxification and disulfiram is the supervised, consented aversive reserve, a ranking BAP leads and the Indian Psychiatric Society, NICE and WHO all echo; match by drinking type and organ function (naltrexone the reward-blunting mu-antagonist for the reward drinker but never in an opioid user; acamprosate the NMDA-modulating abstinence-stabiliser for the relief drinker and the choice in liver disease; disulfiram the ALDH-blocking deterrent only for the motivated, supervised, non-cardiac, non-hepatic abstainer started at least 24 hours dry).

38 · Emerging anti-craving agents

Only three anti-craving drugs are first-line and licensed for alcohol dependence, and they sit in their own notes: naltrexone, acamprosate and disulfiram. This topic is the **second tier** behind them, the **emerging anti-craving** and off-label agents a clinician reaches for when the licensed three fail, are contraindicated, or when a comorbidity steers the choice. Four names carry the marks: **baclofen**, **topiramate**, **gabapentin** and **nalmefene**. This is a management/drug topic, so the yield is in the one-line mechanism, the dose, the line and the single signature niche or caution of each, not in a long description.

Why it matters clinically. Exams like these because each has one clean discriminator: baclofen is the **GABA-B agonist for the cirrhotic drinker**, topiramate is the **carbonic-anhydrase inhibitor** that dulls cognition, gabapentin is the **gabapentinoid for withdrawal-linked negative affect and insomnia**, and nalmefene is the **as-needed opioid antagonist** that reduces drinking without demanding abstinence. All four are off-label or non-first-line for alcohol in most guidelines; the reward and mesolimbic-dopamine anatomy they act on is developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and is not re-derived here.

30 to 80	300	18
BACLOFEN RELAPSE-PREVENTION DOSE (MG/DAY)	TOPIRAMATE TARGET CEILING (MG/DAY)	NALMEFENE AS-NEEDED DOSE (MG)

38.1 Baclofen: the GABA-B agonist for the drinker with liver disease

Mechanism and rationale. Baclofen is a selective GABA-B receptor agonist first marketed as a skeletal-muscle relaxant (Kaplan and Sadock 2024; Companion to Psychiatric Studies). Its off-label use in alcohol dependence rests on that GABA-B agonism alone; the guidelines state no craving mechanism for it (Maudsley Prescribing Guidelines). It carries no licence for this indication and the evidence is mixed, a recent meta-analysis failing to find a consistent positive effect on abstinence, so it stays a second-line off-label option (Maudsley Prescribing Guidelines).

The one niche. Baclofen's signature selling point is that it is *not hepatically metabolised*: it is renally cleared, so it can be given where alcohol-related liver disease makes naltrexone (hepatotoxic, contraindicated in acute hepatitis) unusable. It is a preferred anti-craving option in moderate-to-severe cirrhosis (BAP 2026; WFSBP rating it strength A specifically in cirrhotic liver disease). The dose is titrated slowly, starting **5 mg three times daily** and increasing by 5 to 10 mg/day every 3 days to a usual **30 to 80 mg/day** in divided doses (BAP 2026; IPS 2014).

The cautions. Sedation, confusion and affective instability are the monitoring flags, so BAP advises caution in comorbid mood disorder; and because abrupt cessation of a GABA-B agonist can precipitate a withdrawal state with seizures and delirium, it must never be stopped suddenly (BAP 2026).

GOOD TO REMEMBER

- **Baclofen (off-label, alcohol):** GABA-B receptor agonist that reduces craving; renally cleared, so the second-line anti-craving choice in the drinker with alcohol-related liver disease or cirrhosis where naltrexone is contraindicated; dose **30 to 80 mg/day** in divided doses (start 5 mg TDS, titrate every 3 days); watch sedation, confusion and affective instability and never stop abruptly (withdrawal seizures).

38.2 Topiramate: the anticonvulsant that raises GABA and blocks glutamate

Mechanism. Topiramate is an anticonvulsant with a dual action relevant to addiction: it *potentiates GABA-A* transmission and *antagonises the AMPA/kainate glutamate* receptor, and it is also a carbonic-anhydrase inhibitor (Kaplan and Sadock 2024). Damping down the hyperglutamatergic, GABA-deficient state that drives craving and heavy drinking is the rationale, and unlike the licensed three it can be started while a patient is still drinking (Kaplan and Sadock 2024; New Oxford Textbook).

Line and dose. Topiramate has the strongest evidence of the emerging agents; VA/DoD actually rates it strong-for and offers it first-line alongside naltrexone, while BAP, IPS and CANMAT keep it as an off-label second-line for moderate-to-severe alcohol use disorder (VA/DoD; BAP 2026). It is titrated slowly, target range **150 to 300 mg/day** to a ceiling of **300 mg/day** (New Oxford Textbook; Kaplan and Sadock 2024). Slow titration is not optional: it is what keeps the dose-limiting side effects tolerable.

The signature caution. Topiramate's memorable toxicity is *cognitive*, the so-called "dopey" or word-finding and memory impairment that patients dislike (its narrow therapeutic index for tolerability), plus paraesthesia, weight loss, metabolic acidosis and a raised risk of renal stones

and acute glaucoma from carbonic-anhydrase inhibition (Kaplan and Sadock 2024; BAP 2026). Monitor cognition and memory.

GOOD TO REMEMBER

- **Topiramate (off-label, alcohol):** anticonvulsant that potentiates GABA-A and blocks AMPA/kainate glutamate; second-line (first-line for VA/DoD) for moderate-to-severe alcohol use disorder, can start while still drinking; slow titration to **150 to 300 mg/day** (max 300); signature harm is cognitive impairment and word-finding difficulty, plus paraesthesia, weight loss and renal-stone/glaucoma risk, so monitor cognition and memory.

RULE **Match the emerging agent to the comorbidity.** Liver disease steers you to baclofen; craving with cognitive headroom to topiramate; alcohol-related insomnia or negative affect or a withdrawal history to gabapentin; a patient who will not commit to abstinence but wants to cut down to nalmefene.

38.3 Gabapentin: the gabapentinoid for withdrawal-linked craving and insomnia

Mechanism and niche. Off-label gabapentin binds the alpha-2-delta subunit of the voltage-gated calcium channel, reducing excitatory neurotransmitter release and calming the hyperexcitable, protracted post-withdrawal state (Kaplan and Sadock 2024). The whole case for **gabapentin for alcohol** is its niche: it is the pick for relapse prevention in patients with *alcohol-related insomnia, negative affect, or a documented history of alcohol withdrawal*, the group in whom the calming and sleep-restoring effect maps onto the symptom (BAP 2026).

Line and dose. Gabapentin is an off-label second-line agent for moderate-to-severe alcohol use disorder (BAP strength B; VA/DoD weak-for where first-line is contraindicated or ineffective); IPS also lists it, at **900 to 1800 mg/day** in divided doses, as an anticonvulsant adjunct where benzodiazepine monotherapy for withdrawal is inadequate or benzodiazepine misuse is a concern (IPS 2014; VA/DoD; BAP 2026).

The caution. Gabapentinoids carry their own *misuse and diversion* liability, so BAP explicitly weighs the risk of non-prescribed use, particularly in a population with substance use disorder; it is a reason to prefer it in a supervised or lower-risk patient (BAP 2026).

GOOD TO REMEMBER

- **Gabapentin (off-label, alcohol):** alpha-2-delta calcium-channel ligand; off-label second-line relapse-prevention agent whose niche is alcohol-related insomnia, negative affect or a history of alcohol withdrawal; dose **900 to 1800 mg/day** divided; signature caution is its own misuse and diversion liability in a substance-using population.

38.4 Nalmefene: the as-needed opioid antagonist to reduce drinking

Mechanism. Nalmefene is a 6-methylene analogue of naltrexone: a mu (MOR) and delta (DOR) opioid antagonist with partial agonist activity at the kappa (KOR) receptor, giving it a longer half-life and greater oral bioavailability than naltrexone (New Oxford Textbook; Goodman and Gilman). Like naltrexone it blocks the opioid-mediated reward of drinking (Stahl's Essential Psychopharmacology).

What makes it different, the "as-needed" model. Nalmefene's exam-defining feature is not its receptor profile but its *dosing paradigm*: it is taken **as-needed**, one **18 mg** tablet on each day drinking is anticipated (ideally 1 to 2 hours before the expected drinking), not as a daily maintenance drug (WFSBP; Maudsley Prescribing Guidelines). Its licensed goal is therefore *reduction of heavy drinking*, not abstinence, in alcohol-dependent patients who have a high drinking-risk level, no physical withdrawal, and who do not need immediate detoxification (WFSBP RG1; BAP 2026). NICE recommends it as an option for reducing alcohol consumption on this basis (Shorter Oxford Textbook; Maudsley Prescribing Guidelines).

The one shared contraindication. Being an opioid antagonist, nalmefene carries the same hard rule as naltrexone: it must be avoided in anyone using opioids, including opioid analgesics, because it will precipitate withdrawal and block analgesia (BAP 2026; Maudsley Prescribing Guidelines).

GOOD TO REMEMBER

- **Nalmefene (alcohol):** mu/delta antagonist and kappa partial agonist (a naltrexone analogue); taken **as-needed 18 mg** on anticipated drinking days (1 to 2 hours before), goal is *reduction of heavy drinking* not abstinence, for high-risk dependent drinkers without physical withdrawal; same opioid contraindication as naltrexone (avoid with any current opioid or analgesic-opioid use).

TRAP **Nalmefene is not naltrexone taken every day.** Its whole point is the as-needed, one-tablet-before-drinking model aimed at cutting down rather than abstaining; treating it as a daily maintenance antagonist, or missing that it shares naltrexone's opioid contraindication, both lose marks.

38.5 The four agents side by side

The discriminating table. The examinable content collapses to a mechanism, a dose, a line and a niche for each. Read the table down the "steer" column: that single clinical cue is what selects the agent in a vignette.

AGENT	MECHANISM	DOSE	LINE AND THE ONE STEER
Baclofen	GABA-B agonist	30 to 80 mg/day (start 5 mg TDS)	2nd-line off-label; the drinker with liver disease / cirrhosis (renally cleared)
Topiramate	GABA-A up, AMPA/kainate glutamate down; carbonic-anhydrase inhibitor	150 to 300 mg/day (max 300)	2nd-line off-label (1st-line VA/DoD); craving, can start while drinking; harms cognition
Gabapentin	alpha-2-delta calcium-channel ligand	900 to 1800 mg/day divided	2nd-line off-label; alcohol-related insomnia / negative affect / withdrawal history; misuse risk
Nalmefene	mu/delta antagonist, kappa partial agonist	18 mg as-needed on drinking days	reduce (not stop) drinking; high-risk, no withdrawal; avoid with opioids

The emerging anti-craving agents in one grid; the right-hand "steer" is the single cue that selects each in a vignette (BAP 2026; VA/DoD; WFSBP; IPS 2014).

INDIA

The emerging agents matter in India precisely because of the treatment gap and the licensing landscape. Alcohol-related liver disease is common in Indian de-addiction practice, and baclofen, being cheap, freely available and renally cleared, is a genuinely useful anti-craving choice where naltrexone's hepatotoxicity is a barrier; the IPS substance-use guideline lists it (30 to 80 mg/day) as a second-line option specifically for co-existing significant hepatic disease. Gabapentin is available and inexpensive and is used as an anticonvulsant adjunct in alcohol withdrawal, but its misuse liability is a real concern given the substance-using population and the broader diversion environment the Narcotic Drugs and Psychotropic Substances (NDPS) Act, 1985 tries to control. Topiramate is available generically. Nalmefene is *not* routinely available or established in Indian practice, so the licensed three plus baclofen carry most of the anti-craving work in the day care centre and de-addiction setting; the wider NDPS and medico-legal frame sits in the Mental health legislation and forensic psychiatry notes.

COMMON TRAP

Do not promote any of these four to first-line for alcohol out of the blue. In most guidelines (BAP, IPS, NICE) baclofen, topiramate and gabapentin are off-label second-line, reached only after or alongside the licensed three; the one defensible exception to name is VA/DoD, which offers topiramate first-line together with naltrexone. Nalmefene is licensed but for a different goal (reduced drinking, not abstinence), so it is not interchangeable with the abstinence-oriented three.

HOLD THIS

Behind the licensed three (naltrexone, acamprosate, disulfiram), the emerging anti-craving agents each own one cue: baclofen (GABA-B, 30 to 80 mg/day) for the cirrhotic drinker, topiramate (150 to 300 mg/day) for craving at the cost of cognition, gabapentin (900 to 1800 mg/day) for withdrawal-linked insomnia and negative affect, and nalmefene (18 mg as-needed) to cut down rather than quit.

Apply and consolidate

39 · Worked cases

This is the arc closer: four worked clinical cases that make you *reason* the substance-use material rather than recite it. Each one puts a decision in front of you that the earlier notes teach in the abstract, and forces the sequence, the drug, the dose and the safety step in the order an examiner (and a ward) demand. Work each case as a viva: state the recognition, name the discriminator, then commit to the first move with its number attached.

How to use these. The four cases map to the four commonest high-stakes decisions on this block: an escalating withdrawal that becomes **delirium tremens**; a **Wernicke** prophylaxis call in a drinker who came in for something else; an **opioid overdose** reversed with titrated naloxone and watched for re-narcotisation; and an **anti-craving** choice tailored to one patient. Every named syndrome closes with a criterion-anchored Good-to-remember and every named drug with a dose-anchored one, so the case teaches the fact it hangs on.

39.1 Case 1: escalating alcohol withdrawal that becomes delirium tremens

The vignette. A 44-year-old man with a decade of daily heavy drinking is admitted after a road-traffic injury and stops drinking abruptly. At hour 10 he is tremulous, sweating and anxious; by hour 60 he is disoriented in time and place, picking at insects he sees on the bedclothes, febrile, pulse 130, drenched. He does not know where he is. This is not anxiety and not "settling down after a drink": the clouded, fluctuating sensorium plus the autonomic storm makes it delirium tremens (Maudsley Prescribing Guidelines; Kaplan and Sadock 2024).

39.2 Case 1 reasoning: the CIWA-Ar guides the benzodiazepine while he can still report

Score first, dose to the score. While he was still orientable at hour 10 to 40, the right instrument was the CIWA-Ar: a symptom-triggered regimen medicates once the score crosses the trigger of about **8 to 10**, re-scores every one to two hours and gives a long-acting benzodiazepine (chlordiazepoxide, or diazepam) until the score settles, with **15 or more** mandating medication (the CIWA-Ar form is reproduced in the scales gallery). A score over **25** with fever or a fast pulse is the danger flag. Symptom-triggered dosing gives less total benzodiazepine and a shorter course than fixed-schedule dosing, and it is the assessment principle of alcohol withdrawal.

RULE **Score the withdrawal, then dose to the score.** Symptom-triggered CIWA-Ar-guided benzodiazepine (medicate at 8 to 10, treat hard at 15 or more) gives less drug and a shorter course than a fixed schedule, in the patient who can still report.

39.3 Case 1 reasoning: once he is delirious, titrate parenterally and abandon the score

The pivot at hour 60. A delirious patient cannot reliably report symptoms or take oral medication, so the CIWA-Ar becomes unreliable and dosing shifts to *clinical titration of a parenteral benzodiazepine* to a lightly sedated, arousable state. Escalate to intravenous lorazepam (about 1 to 2 mg per dose, repeated to effect) or intravenous diazepam, in a high-dependency or monitored bed (Maudsley Prescribing Guidelines; IPS 2014). Lorazepam is preferred where the liver is compromised, because it is glucuronidated with no active metabolite and does not accumulate. Alongside the benzodiazepine: correct potassium, magnesium and phosphate; monitor pulse, blood pressure and temperature; exclude infection, head injury and hepatic encephalopathy; and give parenteral thiamine before any glucose (Case 1 shares its supportive spine with Case 2). An antipsychotic is an adjunct for refractory agitation only, never monotherapy.

8 to 10	48 to 96 h	10 to 20
CIWA-AR TRIGGER TO START BENZODIAZEPINE	ONSET OF DELIRIUM TREMENS AFTER THE LAST DRINK	PER CENT MORTALITY OF DELIRIUM TREMENS UNTREATED

TRAP **Do not manage established delirium tremens by a score.** The CIWA-Ar depends on a patient who can report and orient; in the delirious patient it under-reads, so dose the parenteral benzodiazepine by clinical titration, not by the number.

GOOD TO REMEMBER

- **Delirium tremens (syndrome):** the criterion picture is clouded fluctuating consciousness plus disorientation plus a gross autonomic storm, with vivid visual and tactile hallucinations on top; onset 48 to 96 hours after the last drink; the discriminator from alcoholic hallucinosis is the *clouded* sensorium; the first move is to treat it as a medical emergency with generously titrated parenteral benzodiazepine and supportive care, and to give parenteral thiamine before any glucose.
- **Lorazepam (in delirium tremens):** the parenteral benzodiazepine of choice when the oral route is unreliable or the liver is compromised; glucuronidated, no active metabolite, so it does not accumulate; give IV/IM about 1 to 2 mg per dose repeated to a light arousable sedation; it controls the autonomic storm and prevents seizures.

39.4 Case 2: the Wernicke prophylaxis decision in a malnourished drinker admitted for something else

The vignette. A 51-year-old woman with long-standing alcohol dependence, visibly cachectic, is admitted with community-acquired pneumonia. She is not in florid withdrawal and has no eye signs. The intern writes up intravenous dextrose for her poor intake. The decision that matters here is not the pneumonia: it is whether, and in what order, she gets thiamine, because a carbohydrate load in a thiamine-depleted brain can precipitate acute Wernicke encephalopathy (NICE; WHO mhGAP 2016; IPS 2014).

39.5 Case 2 reasoning: parenteral thiamine before glucose, and treat on any one feature

The sequence and the doses. Give parenteral thiamine *before* the dextrose, always. For prophylaxis in a malnourished or withdrawing drinker, parenteral thiamine **100 mg** IM/IV daily for at least 3 to 5 days is standard (then oral). The reason to be aggressive is the exam trap: the

classic **Wernicke** triad of confusion, ophthalmoplegia (or nystagmus) and ataxia is complete in only about **10 per cent** of cases, so *any one* feature in a malnourished drinker mandates empirical high-dose treatment (Kaplan and Sadock 2024; NICE). If she develops any confusion, eye sign or ataxia, escalate at once to the emergency regimen, **500 mg IV three times daily** for 2 to 3 days then 250 mg daily for 5 days, before it hardens into the irreversible anterograde amnesia of Korsakoff syndrome (the amnestic mechanism sits in the Dementias and neurocognitive disorders notes and the Neuropsychiatry of systemic and neurological disease notes). Oral thiamine has poor, saturable absorption, so the acute treatment must be parenteral.

INDICATION	THIAMINE ROUTE AND REGIMEN
Prophylaxis (malnourished or withdrawing drinker)	**100 mg IM/IV daily for at least 3 to 5 days, then oral**
Before any IV glucose in a drinker	**Thiamine FIRST, glucose second (never the reverse)**
Suspected Wernicke (any one triad feature)	**500 mg IV three times daily for 2 to 3 days, then 250 mg daily for 5 days**

The thiamine decision tree for the malnourished drinker: parenteral, before glucose, and escalated on any single Wernicke feature (NICE; Kaplan and Sadock 2024).

TRAP **Never give IV glucose before thiamine in a drinker.** A glucose load in a thiamine-depleted patient can precipitate acute Wernicke encephalopathy; the order is thiamine first, always, and parenterally.

PEARL

The Wernicke prophylaxis decision is triggered by the *company the patient keeps*, not by eye signs. A cachectic drinker admitted for pneumonia, a fracture, hyperemesis or a GI bleed is a Wernicke risk the moment a drip goes up; the reason to prophylax is precisely that she is not yet showing the triad, and the ten-per-cent completeness figure means waiting for it is waiting too long.

GOOD TO REMEMBER

- **Wernicke encephalopathy (syndrome):** the criterion is the triad of confusion, ophthalmoplegia/nystagmus and ataxia, but the full triad is present in only about 10 per cent, so treat on any one feature; the discriminator from delirium tremens is eye signs and ataxia *without* the autonomic storm; the first step is high-dose IV thiamine (500 mg three times daily) at once, before it becomes irreversible Korsakoff.
- **Thiamine (vitamin B1):** give parenterally BEFORE any glucose in a malnourished or withdrawing drinker; withdrawal prophylaxis is 100 mg IM/IV daily for at least 3 to 5 days (then oral); suspected Wernicke is treated as an emergency with 500 mg IV three times daily for 2 to 3 days; oral absorption is poor and saturable, so acute treatment must be parenteral.

39.6 Case 3: opioid overdose reversed with titrated naloxone

The vignette. A 26-year-old man who uses heroin is brought in unresponsive, breathing four times a minute, cyanosed, with *pinpoint* pupils. This is the substance emergency that is genuinely time-critical: the triad of *coma, respiratory depression and miotic pupils* is opioid overdose, and the

immediate cause of death is respiratory failure (Kaplan and Sadock 2024). The first move is airway and ventilation, then the antidote.

39.7 Case 3 reasoning: titrate naloxone to breathing, not to full wakefulness, and watch for re-narcotisation

The antidote, titrated. Naloxone is a competitive opioid antagonist: give IM **0.4 to 2 mg**, repeated every 2 to 3 minutes up to about **10 mg**, or intranasal 4 mg per spray repeated after 2 to 3 minutes, alongside bag-mask ventilation (BAP 2026; WHO). Titrate to *adequate respiration*, not to a fully awake, sitting-up patient: over-reversal in a dependent user precipitates a violent, distressing acute withdrawal. The safety catch is **re-narcotisation**. Naloxone's half-life is shorter than that of heroin and much shorter than that of long-acting opioids like methadone, so as the naloxone wears off the patient can slide back into respiratory depression; observe for at least a few hours (longer for long-acting agents), and consider a naloxone infusion for methadone or sustained-release overdose.

0.4 to 2 mg	10 mg	4 mg
NALOXONE IM STARTING DOSE, REPEAT EVERY 2 TO 3 MIN	APPROXIMATE CEILING BEFORE DOUBTING THE OPIOID DIAGNOSIS	INTRANASAL NALOXONE PER SPRAY (TAKE-HOME KIT)

RULE **Titrate naloxone to breathing and expect it to wear off.** Aim for adequate respiration, not full wakefulness, and observe for re-narcotisation, because naloxone outlasts nobody, least of all a long-acting opioid.

TRAP **Opioid withdrawal is not an emergency; opioid overdose is.** Withdrawal is intensely unpleasant but rarely lethal, so do not treat it as an emergency; overdose is the pinpoint-pupil respiratory failure that naloxone reverses, and it kills within minutes.

GOOD TO REMEMBER

- **Opioid overdose (emergency):** the criterion triad is coma plus respiratory depression plus pinpoint (miotic) pupils; the first move is airway and ventilation, then titrated naloxone; the fallen-tolerance windows after detoxification or release from custody are the highest-risk period and the leading cause of death in opioid use disorder.
- **Naloxone (Indian brand Nexnal; the 0.4 mg/1 mL ampoule):** competitive opioid antagonist and the antidote to overdose; give IM 0.4 to 2 mg, repeat every 2 to 3 minutes to about 10 mg, or intranasal 4 mg per spray; titrate to respiration, not wakefulness; its short half-life means watch for re-narcotisation and re-dose or infuse; take-home kits with family rescue-breathing training are recommended for anyone with current or recent opioid use.

39.8 Case 4: choosing the anti-craving agent for a specific relapse-prevention plan

The vignette. A 38-year-old man has completed a medically assisted alcohol withdrawal and has been abstinent seven days. He is motivated, has compensated alcohol-related liver disease, lives with a supportive wife, and wants pharmacological help to stay dry. The task is not "prescribe an anti-craving drug"; it is to *match* the agent to this patient across naltrexone, acamprosate and disulfiram (IPS 2014; NICE 2011; Maudsley Prescribing Guidelines).

39.9 Case 4 reasoning: match mechanism and caution to the patient in front of you

Working the three agents. All three start only *after* withdrawal is complete, alongside a structured psychosocial intervention. Naltrexone (an opioid antagonist, oral 50 mg/day started at 25 mg, or the 380 mg monthly injection; Indian brands Nodict, Naltima) is the verified first-line, blunting the reward of drinking and reducing heavy-drinking days; but it is a poor fit if he is on any opioid analgesic, and its hepatic caution matters given his liver disease. Acamprosate (a glutamate/NMDA modulator, 666 mg three times daily = 1998 mg/day, reduced to 1332 mg/day if under 60 kg; Indian brand Acamprol) is renally cleared, so it is the cleaner choice in liver disease, works best to *maintain* an abstinence already achieved, and has the strongest evidence for holding total abstinence. Combining the two adds no benefit over either alone. Disulfiram (an aversive ALDH inhibitor, 250 to 500 mg/day; Indian brands Esperal, Dizone) works only when taken under supervision and is dangerous in significant hepatic or cardiac disease, so it is a supervised second-line here, not the drug to reach for first in a man with liver disease. For this motivated patient with compensated liver disease and a supervising spouse, the reasoned choice is *acamprosate* (renally safe, best abstinence-maintenance evidence), with a supervised disulfiram a considered second-line given his engaged wife.

AGENT (INDIAN BRAND)	MECHANISM	DOSE	BEST FIT / SIGNATURE CAUTION
Naltrexone (Nodict, Naltima)	Opioid (mu) antagonist; blunts reward of drinking	**Oral 50 mg/day (start 25 mg); or 380 mg IM monthly**	Verified first-line; reduces heavy-drinking days; avoid with opioid analgesics; hepatic caution
Acamprosate (Acamprol)	Glutamate/NMDA modulator; repairs withdrawal-driven hyperexcitability	**666 mg three times daily (1998 mg/day; 1332 if under 60 kg)**	Renally cleared, cleaner in liver disease; best evidence to *maintain* abstinence
Disulfiram (Esperal, Dizone)	Aldehyde-dehydrogenase inhibitor; aversive disulfiram-ethanol reaction	**250 to 500 mg/day (maintenance 250 mg/day)**	Needs supervision to work; contraindicated in significant hepatic or cardiac disease and in a still-drinking patient

The three anti-craving agents matched by mechanism, dose and caution; the choice is patient-specific, and in compensated liver disease acamprosate is the reasoned first move (IPS 2014; NICE 2011; Maudsley Prescribing Guidelines).

TRAP **Never start disulfiram in a still-drinking or cardiac patient, or naltrexone in a current opioid user.** Disulfiram plus alcohol is a deliberate toxic reaction, dangerous in cardiac disease; naltrexone in someone using opioids precipitates acute withdrawal.

GOOD TO REMEMBER

- **Naltrexone (Nodict, Naltima):** opioid antagonist, the verified first-line anti-craving agent in alcohol use disorder; oral 50 mg/day started at 25 mg, or 380 mg IM monthly; started after withdrawal is complete; reduces heavy-drinking days and cue-induced craving; avoid in current opioid users and use hepatic caution.
- **Acamprosate (Acamprol):** glutamate/NMDA modulator that repairs protracted withdrawal hyperexcitability; 666 mg three times daily (1998 mg/day, 1332 if under 60 kg); renally cleared, so the cleaner agent in liver disease; strongest evidence for *maintaining* an achieved abstinence; no punishment mechanism, so adherence-friendly.
- **Disulfiram (Esperal, Dizone):** aversive aldehyde-dehydrogenase inhibitor, 250 to 500 mg/day (maintenance 250 mg/day), producing the disulfiram-ethanol reaction; works only under supervision, so it fits a family-supervised model; contraindicated in significant hepatic or cardiac disease and in a patient who is still drinking.

INDIA

All four cases sit inside a heavy Indian treatment gap: most people with alcohol or opioid dependence never reach formal care, so delirium tremens and overdose reach general and emergency wards after an unsupervised, cost- or stigma-driven abrupt stop, exactly the patient who arrives at hour 60 in a full autonomic storm. Services concentrate in government de-addiction centres and the Drug De-addiction Programme units rather than general practice. The opioid emergencies run under the Narcotic Drugs and Psychotropic Substances (NDPS) Act, 1985 (developed in the Mental health legislation and forensic psychiatry notes). Naloxone is available as the 0.4 mg/1 mL ampoule and increasingly as take-home kits; buprenorphine (Indian brand Tidigesic; the buprenorphine-naloxone 4:1 combination as Suboxone or generics) is the workhorse of Indian opioid-agonist treatment precisely because methadone is restricted to licensed OST clinics, and the anti-craving agents are all cheaply available as Indian generics (Nodict, Acamprol, Esperal). The de-addiction context, not the abstract algorithm, is what these cases are really testing.

HOLD THIS

Recognise the syndrome, name the one discriminator, then commit to the numbered first move: parenteral benzodiazepine plus thiamine-before-glucose for delirium tremens, empirical high-dose thiamine on any one Wernicke feature, titrated naloxone to breathing for overdose, and an anti-craving agent matched to the patient (acamprosate when the liver is the constraint).

40 · Consolidation

This is the arc closer for the whole substance-use chapter, and its job is retrieval, not new teaching. Everything here has already been built earlier in the block; what this topic does is give you a small number of hooks that let you *pull the whole thing back* under exam pressure. The chapter opened on one distinction, harmful use versus the dependence syndrome, and seeded a master mnemonic there; here that mnemonic is paid off and stretched to cover the syndromes, the emergencies, the scales, the substitution agents and the anti-craving drugs. Use this topic the way a viva candidate uses the last ten minutes before the bell: cover the branches, name the number, commit to the first move.

How to work this closer. First rehearse the master mnemonic until the six dependence features fall out automatically, because that is the spine every stem hangs off. Then run the answer-free recall prompts cold, saying the answer aloud before you read on. Then walk the synthesis map branch by branch, covering each branch with your hand and reconstructing it. The four numbers that most often decide a mark, a scale cut-off, a thiamine dose and a withdrawal window, are gathered into one strip so you can drill them. The concept map that draws the whole chapter as one figure is flagged for central rendering (Fig 13.22).

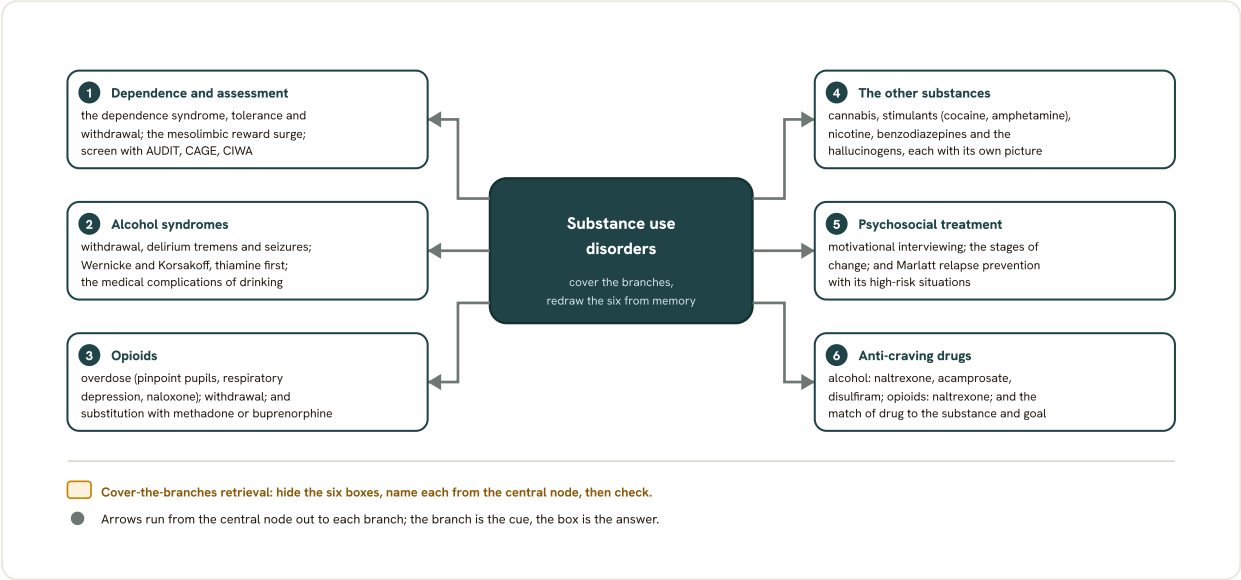


Fig 13.22 Chapter synthesis map: substance use disorders at a glance. Six branches radiate from the disorder at the centre: dependence and assessment with the reward neurobiology; the alcohol syndromes, emergencies and complications; opioid overdose, withdrawal and substitution; the other substances; the psychosocial treatments (motivational interviewing, the stages of change and Marlatt relapse prevention); and the anti-craving pharmacotherapy. Frame it for retrieval by covering the branches and redrawing all six from the central node.

40.1 The master mnemonic, paid off: the 3 C's + 3 unlocks the dependence syndrome

The payoff. The dependence-syndrome opener seeded the mnemonic **the 3 C's + 3**, and this is where it earns its keep as the single retrieval key for the chapter. The three C's are the behavioural core, compulsion (a strong desire to use), impaired *Control* over onset, level and termination, and *Continued* use despite clear harm. The plus-three are the reinforcing shell, tolerance, a physiological withdrawal state, and salience (primacy, the progressive neglect of other pleasures). That is the full six-feature ICD-10 dependence set; any **three** of the six clustering within **12 months** makes the diagnosis.

Why one mnemonic carries the chapter. The same six features regenerate the two nosologies and point at management. Collapse the three C's plus tolerance-and-withdrawal-as-one and salience, and you have the three central ICD-11 features (impaired control, increasing precedence, physiological features), of which **two** are needed. Recognise the "withdrawal" C and you are into the emergencies branch; recognise the "compulsion/craving" C and you are into the anti-craving branch. Count the units instead of the features and you have made the classic error the chapter warns against from the outset.

MNEMONIC

THE 3 C's + 3: Compulsion, impaired Control, Continued use despite harm; plus Tolerance, Withdrawal, Salience.

The three C's are the behavioural heart (compulsion, impaired control, persistence despite harm); the plus-three are the physiological-and-priority shell (tolerance, physiological withdrawal state, salience/primacy). Any three of the six, clustering within a 12-month period, are ICD-10 dependence. Fold them into three and you get the ICD-11 set (two of three needed).

RULE **Recall the mnemonic, then let it branch.** Start every substance stem by reciting the 3 C's + 3; the six features regenerate both nosologies, flag withdrawal risk, and route you to the right emergency, scale or drug.

TRAP **Reciting seven for ICD-10 dependence.** ICD-10 dependence has six features (threshold three); "seven criteria" is the DSM-IV dependence relic, and DSM-5 has eleven for a single substance use disorder (threshold two).

40.2 Active-recall prompt list: the syndromes (answer-free, say it before you read on)

Cover the answer column of your memory and answer each aloud. These prompts drill the recognition-and-discriminator layer that every clinical stem tests. The point is to force retrieval, not recognition, so do not peek at the topics; if you cannot answer one, that is exactly the branch to re-open.

Dependence vs harmful use

What single feature best discriminates dependence from harmful use, and do you count features or units?

ICD-10 vs ICD-11 dependence

How many of how many for each, and over what time frame?

Delirium tremens vs alcoholic hallucinosis

Which one clouds the sensorium, and which preserves clear consciousness?

Delirium tremens vs Wernicke encephalopathy

Which is an autonomic storm, and which is eye-signs-and-ataxia without the storm?

Wernicke vs Korsakoff

Which is the acute, reversible triad and which is the irreversible anterograde amnesia with confabulation?

Opioid vs sedative-hypnotic withdrawal

Which withdrawal is distressing but rarely fatal, and which can kill by seizures and delirium?

Tolerance and withdrawal vs the dependence syndrome

Why does physical dependence on a prescribed drug not by itself equal addiction?

40.3 Active-recall prompt list: the emergencies (name the recognition and the first move)

For each, state the recognition triad, the discriminator, and the very first management step with its number. These are the high-stakes, time-critical branches; the examiner wants the safety

step in the right order.

Delirium tremens
Onset window after the last drink? First move, and what guides the benzodiazepine once the patient is delirious?

Wernicke encephalopathy
What proportion show the full triad, so on how many features do you treat? Which comes first, thiamine or glucose?

Opioid overdose
The triad? The antidote, its starting dose, and what you titrate it to? What is re-narcotisation and how long do you watch?

Sedative-hypnotic (benzodiazepine) withdrawal
Why is a too-fast taper dangerous, and what is the safe substitution-and-taper principle?

Withdrawal seizure
In which withdrawals does it occur, and what is the class of drug that both treats and prevents it?

TRAP **Do not read opioid withdrawal as a medical emergency it is not.** Uncomplicated opioid withdrawal is intensely distressing but rarely life-threatening; sedative-hypnotic and severe alcohol withdrawal are the ones that kill by seizures and delirium.

40.4 Active-recall prompt list: the scales, the substitution and the anti-craving agents

The number branches. These prompts drill the cut-offs, induction doses and maintenance doses that are the pure-recall marks of the block. The scale *forms* live in the scales gallery; here you drill only what each is and its cut-off.

AUDIT, CAGE, DAST-10, ASSIST
State each screen's cut-off number and what it is for.

CIWA-Ar and COWS
The CIWA-Ar trigger to medicate, and the COWS threshold before a first buprenorphine dose?

SADQ and FTND
What does each grade (severity of what), and the score that flags severe/high?

Buprenorphine vs methadone induction
Which waits for objective withdrawal and why; which starts low and titrates slowly and why? Starting and maintenance doses of each?

Naltrexone, acamprosate, disulfiram
Mechanism, dose, and the one signature caution of each? Which needs an opioid-free window, and how long?

Nicotine replacement, varenicline, bupropion
First-line for the heavily dependent smoker, and the one contraindication of bupropion?

40.5 The whole-chapter synthesis map: cover a branch, reconstruct it

How to drill the map. The chapter is one tree with six branches growing off the master mnemonic. Read the branch heads, then cover the "reconstruct" column with your hand and

rebuild each branch from the head alone. When you can regenerate all six from the 3 C's + 3, the chapter is consolidated. The same six branches are drawn as a single concept figure for central rendering (Fig 13.22).

BRANCH (FROM THE 3 C'S + 3)	RECONSTRUCT: THE MUST-HOLD CONTENT
Diagnosis and nosology	Harmful use vs dependence; salience is the discriminator; ICD-10 three of six in 12 months; ICD-11 two of three central features; DSM-5 one disorder, eleven criteria (two or more), graded mild/moderate/severe.
Screening and assessment	AUDIT 8, CAGE 2, DAST-10 3, ASSIST 27 (alcohol high-risk); SADQ grades dependence severity (severe above 30); FTND grades nicotine dependence (high at 6 or more); the count-features-not-units rule.
Alcohol emergencies	Delirium tremens (clouded sensorium plus autonomic storm, 48 to 96 hours, symptom-triggered then titrated benzodiazepine); Wernicke (triad complete in about ten per cent, treat on any one feature, parenteral thiamine before glucose); Korsakoff (irreversible amnesia); alcoholic hallucinosis (clear sensorium).
Withdrawal management	Alcohol, score with CIWA-Ar and dose to the score with a long-acting benzodiazepine; sedative-hypnotic, substitute long-acting and taper slowly (never fast); opioid, distressing but rarely fatal, symptomatic relief plus a substitution decision.
Opioid substitution and overdose	Buprenorphine (partial agonist, wait for objective withdrawal, induct 2 to 8 mg, maintain 12 to 16 mg/day); methadone (full agonist, start low 20 mg, titrate slowly, maintain 60 to 120 mg/day); overdose reversed with titrated naloxone, watch for renarcotisation.
Anti-craving and psychosocial	Naltrexone 50 mg/day (opioid-free window first); acamprosate 666 mg three times daily (liver-safe); disulfiram 250 to 500 mg/day (aversive, supervised, after abstinence); nicotine replacement, varenicline, bupropion for tobacco; MI, brief intervention and relapse prevention wrap all of it.

The six chapter branches growing off the master mnemonic; cover the right column and rebuild each branch from its head (rendered centrally as Fig 13.22).

3 of 6 ICD-10 DEPENDENCE THRESHOLD, WITHIN 12 MONTHS	**8** AUDIT HAZARDOUS OR HARMFUL-USE CUT-OFF	**100 mg** PARENTERAL THIAMINE DAILY, WITHDRAWAL PROPHYLAXIS	**48 to 96 h** DELIRIUM TREMENS ONSET AFTER THE LAST DRINK

40.6 The four safety anchors that outrank everything else

If you hold nothing else, hold these. Four ordering-and-safety rules recur across the emergencies and the drugs, and getting any one of them wrong is the kind of error that loses

more than a mark. Parenteral thiamine goes in *before* glucose in any malnourished or withdrawing drinker, because a carbohydrate load in a thiamine-depleted brain can precipitate acute Wernicke. Naltrexone is never given to a current opioid user, because it precipitates withdrawal; you wait for a documented opioid-free window of **7 to 10 days**. Buprenorphine's first dose waits for objective withdrawal (a COWS of about **8 to 12**), because a partial agonist given too early precipitates withdrawal. And a benzodiazepine taper (or a sedative-hypnotic substitution taper) is never rushed, because a fast taper risks seizures and delirium.

The mirror-image traps. Each anchor has a classic wrong answer: giving glucose first, starting naltrexone in someone still using opioids, inducting buprenorphine before withdrawal appears, and tapering a benzodiazepine too fast. Reciting the anchor and its trap together is the most efficient way to make both stick.

COMMON TRAP

Two more high-yield errors to name and avoid: starting disulfiram in a still-drinking, intoxicated or cardiac patient (the disulfiram-ethanol reaction can be dangerous there), and managing established delirium tremens "by the score" (the CIWA-Ar under-reads in a patient who can no longer report, so you titrate a parenteral benzodiazepine clinically instead).

INDIA

The chapter's India thread ties into one strategic picture worth reconstructing whole. India carries a very large substance-use treatment gap: most people who meet dependence criteria never reach formal care, and services concentrate in government de-addiction centres and Drug De-addiction Programme (DDAP) units rather than in general practice, which is why the harmful-use end and non-specialist-delivered brief intervention carry so much weight (IPS 2014). The legal frame is the Narcotic Drugs and Psychotropic Substances Act, 1985 (the medico-legal detail sits in the Mental health legislation and forensic psychiatry notes), which is what makes agonist opioid-substitution prescribing licence-bound. Within that frame, buprenorphine, usually as the buprenorphine-naloxone 4:1 combination (Tidigesic for buprenorphine alone; Suboxone or Bunorph for the combination), is the accessible outpatient first-line for opioid maintenance because methadone is restricted to government OST clinics. The anti-craving agents that sit outside the NDPS scheduling, naltrexone (Naltima, Nodict), acamprosate (Acamprol) and disulfiram (Esperal, Dizone), are prescribable in any de-addiction setting, and disulfiram's family-supervised model fits Indian practice particularly well. Take-home naloxone (Nexnal) with family training is the highest-value overdose intervention against a heavy opioid burden.

PEARL

Every branch of this chapter routes back to one first question at the bedside: is this harmful use or dependence? That single call, made by counting the 3 C's + 3 rather than the units, decides whether the patient needs brief motivation-based intervention or the full apparatus of assisted withdrawal, relapse-prevention pharmacotherapy and long-term follow-up. Get the first question right and the rest of the tree is just retrieval.

HOLD THIS

The whole chapter grows off the 3 C's + 3 (Compulsion, impaired Control, Continued use despite harm, plus Tolerance, Withdrawal, Salience): count the features not the units, and the four safety anchors outrank everything, thiamine before glucose, no naltrexone in a current opioid user, no buprenorphine before objective withdrawal, and never a fast benzodiazepine taper.

GOOD TO REMEMBER

- **Dependence syndrome (the arc-closing criterion set):** three or more of the 3 C's + 3 (compulsion, impaired control, continued use despite harm, tolerance, withdrawal, salience) clustering within 12 months; the discriminator from harmful use is salience; the first move on recognising it is to assess withdrawal risk and the need for assisted withdrawal.
- **Delirium tremens (emergency recall anchor):** clouded, fluctuating sensorium plus an autonomic storm, 48 to 96 hours after the last drink; the discriminator from Wernicke is the autonomic storm, from alcoholic hallucinosis the clouded sensorium; first move is generously titrated parenteral benzodiazepine plus supportive care, thiamine before glucose.
- **Wernicke encephalopathy (emergency recall anchor):** the confusion-ophthalmoplegia-ataxia triad, complete in only about ten per cent, so treat on any one feature; parenteral thiamine before glucose, escalating to high-dose IV thiamine before it hardens into irreversible Korsakoff.
- **Thiamine (dose anchor):** 100 mg IM/IV daily for withdrawal prophylaxis, 500 mg IV three times daily for suspected Wernicke; always parenteral (oral absorption is saturable) and always before any glucose.
- **Buprenorphine (dose anchor):** partial mu agonist with a respiratory ceiling; first dose only once objective withdrawal appears (COWS about 8 to 12); induct 2 to 8 mg (usually 4 mg), maintain 12 to 16 mg/day; the Indian outpatient first-line as the 4:1 buprenorphine-naloxone combination.
- **Naloxone (dose anchor):** competitive opioid antagonist for overdose; 0.4 to 2 mg IM (4 mg intranasal), repeated every 2 to 3 minutes, titrated to adequate breathing not full arousal; watch for re-narcotisation because its half-life is shorter than the opioid it reverses.
- **Naltrexone (dose anchor):** mu-opioid antagonist, 50 mg/day orally (start 25); first-line anti-craving after alcohol detox; never in a current opioid user, and only after a 7 to 10 day opioid-free window (precipitated withdrawal).
- **Acamprosate (dose anchor):** glutamatergic NMDA-modulator, 666 mg three times daily (1998 mg/day over 60 kg, 1332 mg/day under); liver-safe, so the anti-craving agent of choice in alcohol-related liver disease; dose-reduce in moderate and avoid in severe renal impairment.
- **Disulfiram (dose anchor):** irreversible ALDH inhibitor and aversive deterrent, 250 to 500 mg/day, supervised and consented; started at least 24 hours after the last drink; never in a still-drinking, intoxicated, cardiac or significantly hepatically impaired patient.

Previously asked

Substance use is one of the most heavily examined territories in the paper, and it is tested at two levels at once: the individual substance (its intoxication, its withdrawal and its complications) and the treatment (the withdrawal protocol, the anti-craving or substitution agent, the psychosocial intervention and the relapse-prevention plan). The reliable pattern is that alcohol carries the most weight, that a single agent or a single scale can be asked as a standalone note, and that every long substance essay ends in a guideline-anchored management plan. The alcohol emergencies recur as diagnose-investigate-manage case questions, so the discrimination between delirium tremens, Wernicke encephalopathy and alcoholic hallucinosis must be exam-ready. The genuine

questions on record are grouped by band below. The reward-pathway anatomy and the dopamine circuit that these disorders act on are developed in the Neurochemistry, neuroendocrinology, neuroimaging and basic psychopharmacology notes; the motivational-interviewing and relapse-prevention technique is owned here but cross-referenced to the Psychotherapies, clinical assessment, MSE and nosology notes.

? HOW THIS TERRITORY IS ACTUALLY TESTED

Q **Alcohol withdrawal, the emergencies and the amnestic syndromes.** A "45 year old chronic alcoholic brought to casualty with fever, difficulty recognizing relatives and irrelevant speech" and a "30 year old alcoholic admitted following seizure with tremors, confusion, ataxia and next-day visual hallucinations" have both come as full 25-mark diagnose-investigate-manage case questions, and "Wernicke's-Korsakoff's psychosis", "Wernicke's encephalopathy" and "Korsakoff's Psychosis" recur as standalone 10-mark notes. Prepare the withdrawal spectrum and its benzodiazepine protocol, the delirium-tremens-versus-Wernicke-versus-alcoholic-hallucinosis differential, and the thiamine triad and doses (parenteral thiamine before glucose) in full. case question and short note, recurring

Q **Alcohol dependence, prognosis and the model of care.** "Discuss the model of care in management of Alcohol dependence syndrome", "Discuss alcohol dependence and its prognosis", "Enumerate various types of substance use and induced disorder and discuss management approaches in alcohol dependence syndrome" and "Discuss neuropsychiatric aspects of Alcoholism" (asked three times) have all come as essays. Prepare the dependence-syndrome concept, the assessment, the neuropsychiatric complications and the guideline-anchored management pathway, essay-length. essay, recurring

Q **The anti-craving and aversive agents.** "Antabuse (Disulfiram)", "Naltrexone" and "Acamprosate" have each been asked as standalone 10-mark notes, and "Relapse prevention in alcohol dependence" as a note that turns on agent selection. Prepare each agent with its mechanism, its indication, its dose and its signature caution (disulfiram in the still-drinking or cardiac patient, naltrexone in the opioid user), and the guideline-anchored comparison that chooses between them. short note, recurring

Q **Opioid, nicotine and the other-substance disorders.** "Management of Opioid Dependence", "Methadone", "Nicotine use disorder", "Management of Nicotine dependence", "Discuss Nicotine related psychiatric disorders and management in detail", "Discuss psychopathologies of cannabis use related disorders", "Cannabis dependence", "Cocaine dependence", "Benzodiazepine Dependence", "Mephedrone", "Caffeine induced disorders" and "Oral substitution therapy" are all on record. Prepare the by-substance intoxication and withdrawal picture and the treatment (opioid substitution and antagonist, the nicotine pharmacotherapy) for each named substance. essay and short note, recurring

Q **Psychosocial treatment, relapse prevention and the general frame.** "Alcoholics Anonymous" (asked three times), "Relapse prevention in alcohol dependence", "Discuss recent advances in management of substance use disorders", "Prevalence of substance abuse in adolescence", "Pathological Gambling" and the emergency-management case of a "23 year old male brought to psychiatric emergency after being arrested in a rave party" have all come. Prepare the twelve-step and self-help frame, the Marlatt relapse-prevention model, the stage-matched psychosocial interventions and the recent advances, and the acute substance emergency. essay and short note, recurring

Prepare this material to be assessed and treated, not just recited: the scale cut-offs (the CIWA-Ar and COWS thresholds, the AUDIT and CAGE), the dose-anchored good-to-remember boxes, the thiamine prophylaxis-versus-treatment figures, the substance-emergency differential and the guideline-anchored agent selection in these notes are built to the way the block is examined. The reward-pathway anatomy and the mesolimbic dopamine mechanics live in the Neurochemistry, neuroendocrinology, neuroimaging and basic psychopharmacology notes; the substance-induced psychotic disorder boundary lives in the Other psychotic disorders, delusional syndromes and catatonia notes; the wider delirium and emergency frame

lives in the Perinatal/women's mental health and emergency psychiatry notes; the NDPS and forensic frame lives in the Mental health legislation and forensic psychiatry notes; and the wider amnestic frame lives in the Dementias and neurocognitive disorders notes.

Quick review

THE WHOLE SUBJECT IN ONE TABLE: DEFINITIONS, SCREENS AND WITHDRAWAL SCALES	
HARMFUL USE VS DEPENDENCE	**Harmful use** (F1x.1) = demonstrable damage to physical/mental health; ICD-11 harmful pattern adds harm to others. **Dependence** (F1x.2) = capture, substance takes priority. Mutually exclusive in ICD-10. Discriminator: salience.
ICD-10 DEPENDENCE CRITERIA	Three or more of six within 12 months: desire/compulsion, impaired control, withdrawal, tolerance, salience, persistence despite harm. Threshold 3, six features. ("Seven" is the DSM-IV relic; DSM-5 = one SUD, eleven criteria, two or more.)
ICD-11 DEPENDENCE CRITERIA	Two or more of three: impaired control, precedence/salience, neuroadaptation (tolerance or withdrawal). Over 12 months, or if continuous use (daily) for at least 3 months. Hold: two of three.
SCREENING CUT-OFFS (FOUR NUMBERS)	**AUDIT** (10-item, 0-40): **8 or more** hazardous, refer above 15; AUDIT-C = first 3. **CAGE** (4-item): **2 or more**. **DAST-10**: **3 or more** (3-5 mod, 6-8 substantial, 9-10 severe). **ASSIST**: 0-3 / 4-26 / **27 or more** high (alcohol 0-10 / 11-26 / 27+). Positive screen triggers assessment, never diagnosis.
ALCOHOL WITHDRAWAL ON THE CLOCK	Tremor/autonomic overactivity at **6 to 12 hours**; hallucinosis (clear sensorium) 12 to 24 h; seizures ("rum fits") at **12 to 48 hours**, peak near the second day; delirium tremens at **48 to 72 hours** (up to 96). Early benzodiazepine cover prevents later seizures/delirium.
CIWA-AR (WITHDRAWAL SEVERITY)	Ten items (nine 0-7, orientation 0-4), max **67**. Under 10 mild, 8 to 15 moderate, **15 or more** needs pharmacotherapy; symptom-triggered dosing at about **8 to 10**. Do not use in established delirium tremens (titrate clinically).
SADQ (DEPENDENCE SEVERITY)	Twenty items, each 0-3, max **60**. 15 or less mild, 16 to 30 moderate, **above 30** severe (inpatient detox). SADQ before withdrawal sets starting dose/setting; CIWA-Ar during detox titrates each dose.
COWS (OPIOID WITHDRAWAL)	Eleven items. Bands: **5 to 12** mild, **13 to 24** moderate, **25 to 36** moderately severe, **above 36** severe; under 5 minimal. Buprenorphine induction threshold is COWS about **8 to 12**, not the mild band's 5.
THE EMERGENCIES, THEIR ONE DISCRIMINATOR, AND THE MAINTENANCE PHARMACOTHERAPY	
DELIRIUM TREMENS	Clouded fluctuating consciousness + disorientation + autonomic storm + vivid visual/tactile hallucinations; onset **48 to 96 hours**; about **5 per cent** of admissions; **10 to 20 per cent** mortality untreated. Discriminator: clouded sensorium. Parenteral benzodiazepine to light sedation, correct electrolytes; antipsychotic adjunct only.

THE EMERGENCIES, THEIR ONE DISCRIMINATOR, AND THE MAINTENANCE PHARMACOTHERAPY	
THE SUBSTANCE-EMERGENCY DIFFERENTIAL	One discriminator each. **DT**: clouded sensorium + autonomic storm. **Wernicke**: eye signs + ataxia, no storm; triad complete in only about **10 per cent**, treat on one feature (IV thiamine 500 mg three times daily). **Hallucinosis**: clear sensorium. **Opioid overdose**: pinpoint pupils + respiratory depression, naloxone. **Sedative withdrawal**: keyed to half-life (short-acting 12 to 24 h; long-acting peaks at 5 to 8 days).
THIAMINE AND NALOXONE	**Thiamine**: parenteral BEFORE glucose in a withdrawing drinker; prophylaxis **100 mg** daily 3 to 5 days, treatment **500 mg IV three times daily** 2 to 3 days if any Wernicke feature. **Naloxone**: opioid-overdose antidote, IM **0.4 to 2 mg** every 2 to 3 min up to about 10 mg (intranasal 4 mg); short half-life, watch re-narcotisation.
OST: BUPRENORPHINE	Partial mu-agonist, ceiling on respiratory depression (safer than methadone). Caution: precipitated withdrawal, so first dose waits for objective withdrawal (COWS about **8 to 12**). Induct **2 to 8 mg** (usually 4), maintenance **12 to 16 mg/day**. India first-line as buprenorphine-naloxone (4:1).
OST: METHADONE	Long-acting full mu-agonist, no ceiling. Cautions: overdose in first two weeks (accumulation) and QTc prolongation. Start **20 mg/day** (max 30), raise ~10 mg every few days; maintenance **60 to 120 mg/day** (below 60 raises dropout). India: licensed government/NACO clinics only.
NALTREXONE (ANTI-CRAVING)	Mu-antagonist, blunts reward (the reward drinker). Oral **50 mg/day** (start 25; 380 mg IM monthly); first-line after detox, BAP-preferred for high craving. Caution: never in current opioid use (precipitates withdrawal), needs a **7-to-10-day opioid-free window** + negative screen. Monitor LFTs.
ACAMPROSATE (ANTI-CRAVING)	Glutamate/NMDA modulator, stabilises abstinence (the relief drinker). **666 mg three times daily** (1998 mg/day over 60 kg; 1332 mg under 60 kg). Caution: renally cleared, so safe in liver disease but dose-reduced/contraindicated in renal impairment. Monitor renal function.
DISULFIRAM (AVERSIVE RESERVE)	Aldehyde-dehydrogenase inhibitor: acetaldehyde builds on drinking (flushing, headache, vomiting, tachycardia, hypotension). Not anti-craving; supervised consented deterrent. Oral **250 to 500 mg/day** (maintenance 250). Caution: never if still drinking (at least **24 hours** dry), never in cardiac/hepatic disease. Effect persists 7 to 14 days.

References

The substance-use content is grounded in the standard addiction-medicine and psychopharmacology sources (the source hierarchy below), with Kaplan and Sadock and the

Maudsley Prescribing Guidelines as the depth bar for the neurobiology, the withdrawal syndromes, the doses, the anti-craving and substitution pharmacology and the monitoring, and the management is guideline-first (the British Association for Psychopharmacology leading, with the Indian Psychiatric Society substance-use guidelines, NICE and WHO mhGAP). Every screening cut-off, withdrawal-scale threshold, detoxification regimen, anti-craving dose, first-line recommendation and medico-legal fact has been checked against these sources; anything that could not be confirmed was omitted and flagged rather than guessed. Each journal PMID here was verified against PubMed this build, matched on title, first author and year; identifiers that resolved to the wrong paper were corrected or dropped, and two candidate citations that could not be confidently resolved (a 1988 CIWA-Ar threshold co-citation and a 1993 SOCRATES paper) were dropped rather than listed. Books and guideline documents are cited by author, title and year without a PMID.

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PART VII

VII

Anxiety, OCD and Trauma-Related Disorders

Fear, obsession and the wound of trauma: the anxiety, obsessive-compulsive and stress-related disorders.

01 Anxiety disorders

02 Obsessive-compulsive and related disorders

03 Trauma and stressor-related disorders

04 Apply and consolidate

PAPER II

Anxiety, OCD and trauma-related disorders

Three sections . one complete notes document

This material gathers the anxiety, obsessive-compulsive and trauma-related disorders into one document, by syndrome and by treatment. The first band is **the anxiety disorders**: generalised anxiety disorder, panic disorder and Clark's cognitive model, agoraphobia, social anxiety disorder and the specific phobias, separation anxiety, the neurobiology of the fear circuit, the cognitive behaviour therapy of anxiety, and the differential diagnosis and medical mimics. The second band is **the obsessive-compulsive and related disorders**: obsessive-compulsive disorder and its symptom dimensions, the guideline-anchored management ladder, the Yale-Brown scale, the cortico-striato-thalamo-cortical circuit, clomipramine versus the serotonin reuptake inhibitors, exposure and response prevention, the treatment-resistant ladder to deep brain stimulation, and the related disorders from body dysmorphic disorder through hoarding, trichotillomania and excoriation to illness anxiety on the spectrum. The third band is **the trauma and stressor-related disorders**: post-traumatic stress disorder and its criteria, the evidence-based trauma-focused treatment, complex PTSD, the acute stress reaction and acute stress disorder, adjustment disorder, the neurobiology of fear conditioning, prolonged grief, and the attachment disorders of early neglect. The examinable skill is the safe, guideline-anchored diagnosis and treatment of each disorder: which disorder behind which fear, which scale and cut-off, which first-line agent for which anxiety disorder, the high-dose long-trial rule in obsessive-compulsive disorder, and the trauma-focused-psychotherapy-first algorithm in post-traumatic stress disorder.

HOW TO USE THESE NOTES

Read the three bands as one continuous account of how the anxiety, obsessive-compulsive and trauma-related disorders are diagnosed and treated. The **anxiety** band builds the frame: the individual anxiety disorders discriminated one from another, the fear-circuit neurobiology, the cognitive behaviour therapy owned here, and the medical mimics that must be excluded. The **obsessive-compulsive and related** band teaches obsessive-compulsive disorder in full, its cortico-striato-thalamo-cortical circuit, the Yale-Brown scale and the guideline-anchored management ladder (a high-dose serotonin reuptake inhibitor for a long trial, then clomipramine, then antipsychotic augmentation, then the refractory options), exposure and response prevention, and the related disorders across the spectrum. The **trauma and stressor** band teaches post-traumatic stress disorder and its trauma-focused treatment, complex PTSD and its distinction from a personality disorder, the acute stress and adjustment reactions, and the neurobiology of fear conditioning. Every management recommendation is guideline-anchored, led by the BAP guidelines with the Indian Psychiatric Society, NICE and CANMAT positions stated, on the where-to-treat, target-by-phase, modes-of-treatment spine; every named syndrome ends with a **Good to remember** box giving the criterion, the discriminator and the first step, and every named drug or psychotherapy ends with one giving the mechanism or principle, the signature caution and the one dose or first-line indication. Figures declare one axis and code it in colour: **petrol** marks structure and the neutral case, **coral** marks the trap or the danger, and **marigold** highlights the number to hold; the rating scales are reproduced as the actual instruments where the licence permits, credited to their sources, or typeset from their structure where it does not. Several boundaries are stated up front: the anxiolytic and hypnotic pharmacology is taught in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes and cross-referenced here; the deep antidepressant pharmacology in the Mood disorders: pharmacotherapy notes; the fear-circuit anatomy and receptor systems in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; deep brain stimulation and neurosurgery in the ECT and neurostimulation notes; the somatic-symptom and illness-anxiety boundary in the Somatic-symptom, sexual, impulse-control disorders and suicide notes; and the wider cognitive behaviour therapy technique in the Psychotherapies, clinical assessment, MSE and nosology notes. Exposure and response prevention, trauma-focused cognitive behaviour therapy, eye movement desensitisation and Clark's cognitive model of panic are owned and fully taught here. This is doctor-facing revision, so the full technical vocabulary is used, brand names lead with the Indian brand, and every dose, scale cut-off, criterion and first-line recommendation is verified against a source or omitted and flagged.

Anxiety disorders

1 · Generalised anxiety disorder

Almost every anxious patient a psychiatrist sees carries the same engine under the bonnet: worry that will not switch off. **Generalised anxiety disorder** (GAD) is the disorder of chronic, **free-floating anxiety** and **excessive worry**, an **apprehensive expectation** spread across many domains of life rather than fixed to one object or situation, which the person finds hard to control and which drags a train of somatic and psychic symptoms behind it. Examiners like GAD because

it sits at the crossroads of the whole anxiety block: it is the free-floating baseline against which panic (episodic), phobia (cued) and obsessive-compulsive disorder (intrusive and ritualised) are contrasted, it carries the two scales you must know cold (the GAD-7 and the Hamilton Anxiety Rating Scale), and its management is the template first-line story, **SSRI first-line** with **pregabalin** and **buspirone** as options and the benzodiazepine held back, that repeats across the anxiety disorders.



Fig 14.1 Anxiety disorders organise threat differently: diffuse future danger in generalised anxiety, abrupt bodily alarm in panic, social evaluation, specific objects or situations, and fear of difficult escape or unavailable help in agoraphobia.

Why it matters, and the chapter mnemonic. This topic seeds the master mnemonic for the whole anxiety block, **"WORRIED FEARS"**, unpacked in the mnemonic box below and paid off at consolidation. The amygdala and fear-circuit anatomy that underlies the sustained arousal is developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and is not re-derived here; the deep pharmacology of the SSRIs and SNRIs lives in the Mood disorders: pharmacotherapy notes, and the anxiolytic story of pregabalin, buspirone and the benzodiazepines (with dependence and withdrawal) in the

Dissociative, conversion and anxiolytic/hypnotic pharmacology notes. What this note owns is the diagnosis, the discrimination from normal worry and from the other anxiety disorders, the two scales and their cut-offs, and the guideline-anchored drug plan.

GENERALIZED ANXIETY DISORDER 7-ITEM SCALE (GAD-7)

Spitzer RL, Kroenke K, Williams JBW, Lowe B, 2006

Over the **last 2 weeks**, how often have you been bothered by the following problems? *(Use the scale to the right to indicate your answer.)*

Question	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious, or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid, as if something awful might happen	0	1	2	3

Add columns (total): Column totals summed give a total score of 0 to 21.

Score interpretation: 0-4 minimal anxiety; 5-9 mild anxiety; 10-14 moderate anxiety; 15-21 severe anxiety.

Clinical threshold: A score of 10 or greater is the common cut-off for probable generalized anxiety disorder (a cut-off of 8 or greater maximizes sensitivity and specificity).

If you checked off any problems, how **difficult** have these made it for you to do your work, take care of things at home, or get along with other people?

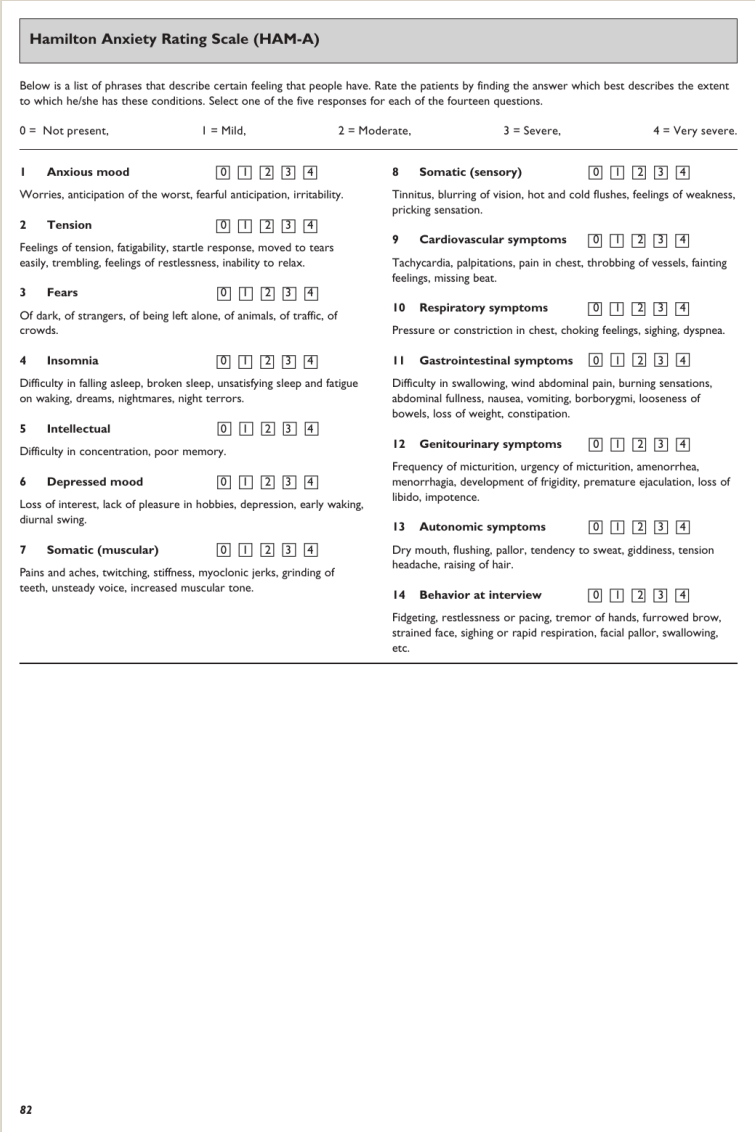
Not difficult at all □ Somewhat difficult □ Very difficult □ Extremely difficult □

Source: Spitzer RL, Kroenke K, Williams JBW, Lowe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med. 2006;166(10):1092-1097.

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The GAD-7: 7 self-report items, each scored 0 to 3 over the last two weeks (total 0 to 21); the bands are 0 to 4 minimal, 5 to 9 mild, 10 to 14 moderate, 15 to 21 severe, and a score of 10 or more is the common cut-off for probable generalised anxiety disorder.

GAD-7 (Spitzer, Kroenke, Williams and Lowe, 2006); developed with an educational grant from Pfizer, no permission required to reproduce; free non-commercial educational use.



Hamilton Anxiety Rating Scale (HAM-A)

Below is a list of phrases that describe certain feeling that people have. Rate the patients by finding the answer which best describes the extent to which he/she has these conditions. Select one of the five responses for each of the fourteen questions.

0 = Not present, 1 = Mild, 2 = Moderate, 3 = Severe, 4 = Very severe.

1 **Anxious mood** [0] [1] [2] [3] [4]
Worries, anticipation of the worst, fearful anticipation, irritability.

2 **Tension** [0] [1] [2] [3] [4]
Feelings of tension, fatigability, startle response, moved to tears easily, trembling, feelings of restlessness, inability to relax.

3 **Fears** [0] [1] [2] [3] [4]
Of dark, of strangers, of being left alone, of animals, of traffic, of crowds.

4 **Insomnia** [0] [1] [2] [3] [4]
Difficulty in falling asleep, broken sleep, unsatisfying sleep and fatigue on waking, dreams, nightmares, night terrors.

5 **Intellectual** [0] [1] [2] [3] [4]
Difficulty in concentration, poor memory.

6 **Depressed mood** [0] [1] [2] [3] [4]
Loss of interest, lack of pleasure in hobbies, depression, early waking, diurnal swing.

7 **Somatic (muscular)** [0] [1] [2] [3] [4]
Pains and aches, twitching, stiffness, myoclonic jerks, grinding of teeth, unsteady voice, increased muscular tone.

8 **Somatic (sensory)** [0] [1] [2] [3] [4]
Tinnitus, blurring of vision, hot and cold flushes, feelings of weakness, pricking sensation.

9 **Cardiovascular symptoms** [0] [1] [2] [3] [4]
Tachycardia, palpitations, pain in chest, throbbing of vessels, fainting feelings, missing beat.

10 **Respiratory symptoms** [0] [1] [2] [3] [4]
Pressure or constriction in chest, choking feelings, sighing, dyspnea.

11 **Gastrointestinal symptoms** [0] [1] [2] [3] [4]
Difficulty in swallowing, wind abdominal pain, burning sensations, abdominal fullness, nausea, vomiting, borborygmi, looseness of bowels, loss of weight, constipation.

12 **Genitourinary symptoms** [0] [1] [2] [3] [4]
Frequency of micturition, urgency of micturition, amenorrhea, menorrhagia, development of frigidity, premature ejaculation, loss of libido, impotence.

13 **Autonomic symptoms** [0] [1] [2] [3] [4]
Dry mouth, flushing, pallor, tendency to sweat, giddiness, tension headache, raising of hair.

14 **Behavior at interview** [0] [1] [2] [3] [4]
Fidgeting, restlessness or pacing, tremor of hands, furrowed brow, strained face, sighing or rapid respiration, facial pallor, swallowing, etc.

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The Hamilton Anxiety Rating Scale (HAM-A): 14 clinician-rated items covering psychic and somatic anxiety, each scored 0 to 4 (total 0 to 56); commonly below 17 is mild, 18 to 24 mild to moderate and 25 to 30 moderate to severe (the bands vary by source).

HAM-A (Hamilton, 1959); in the public domain.

Fig 14.2 The anxiety rating scales. The GAD-7 is the brief self-report screen for generalised anxiety, seven items each scored 0 to 3 for a total of 0 to 21, with 5, 10 and 15 marking mild, moderate and severe and a score of 10 or more the common threshold for probable generalised anxiety disorder. The Hamilton Anxiety Rating Scale is the clinician-rated severity measure, fourteen items spanning the psychic and the somatic symptoms of anxiety, each 0 to 4, for a total of 0 to 56. Both are shown here as their actual, freely reproducible forms; the GAD-7 keeps its original United States spelling.

1.1 The core concept: free-floating, excessive, hard-to-control worry

What "generalised" means. The defining quality is that the anxiety is *not tied to a specific trigger*. Unlike phobia (bound to a feared object) or panic disorder (episodic attacks), GAD is a persistent, diffuse free-floating anxiety, a general apprehensiveness "not restricted to any particular environmental circumstance" in the ICD-11 wording (ICD-11 CDDR). The cognitive core is excessive worry (apprehensive expectation) about multiple everyday domains, work, health, finances, the safety of family, minor chores, that is out of proportion to the actual likelihood or impact of the feared event.

The control criterion. The feature that separates GAD from the ordinary worry of a stressed but well person is that the patient *cannot control* the worry, cannot put it down to attend to the task in hand, and finds it pervasive, distressing and long-lasting. Everyday worry is manageable, focused and deferrable; GAD worry is uncontrollable, free-floating and self-perpetuating. This is the discriminator to lead with in any answer.

GOOD TO REMEMBER

- **Generalised anxiety disorder:** chronic, free-floating, excessive and uncontrollable worry (apprehensive expectation) spread across multiple life domains, not bound to a specific object or situation; the defining discriminator from normal worry is that it is excessive, pervasive and hard to control; the first diagnostic step is to exclude an organic mimic (hyperthyroidism, caffeine, substance withdrawal) before labelling it.

1.2 The symptom clusters: psychic worry plus a somatic tail

Psychic and somatic together. GAD is worry *with a body*. The psychic cluster is the apprehensive expectation itself, plus restlessness, feeling keyed up or on edge, difficulty concentrating or mind going blank, and irritability. The somatic cluster is dominated by **muscle tension** (with trembling, twitching, aches and soreness), fatigue and sleep disturbance, and a background of autonomic symptoms, sweating, nausea, gastrointestinal upset and an exaggerated startle. A teaching point examiners probe: overt autonomic hyperarousal (racing heart, breathlessness, dizziness) is *less* prominent in GAD than in panic disorder (Kaplan and Sadock 2024), because GAD is the sustained low-grade state rather than the acute surge.

Muscle tension is the signature somatic marker. Of the somatic features, muscle tension is the one most specific to GAD and the one most reliably present; it is the physical correlate of chronic vigilance and the symptom that best distinguishes GAD's body from the episodic autonomic storm of panic.

1.3 DSM-5-TR criteria: six months, three of six symptoms

The criteria to state cold. DSM-5-TR requires excessive anxiety and worry (apprehensive expectation), occurring more days than not for at least **6 months**, about a number of events or activities; the person finds it difficult to control the worry; and the anxiety and worry are associated with **three or more of six** symptoms, more days than not for the past 6 months (DSM-5-TR 2022). The six are: restlessness or feeling keyed up or on edge; being easily fatigued; difficulty concentrating or mind going blank; irritability; muscle tension; and sleep disturbance. The disturbance must cause clinically significant distress or impairment, must not be attributable to a substance or another medical condition, and must not be better explained by another mental disorder.

The paediatric relaxation. A high-yield discriminator: in children, *only one* of the six associated symptoms is required, not three, reflecting that the worry-plus-body picture is thinner in a developing child.

CRITERION	DSM-5-TR REQUIREMENT
A. Worry	**Excessive anxiety and worry (apprehensive expectation), more days than not for at least 6 months, about multiple events/activities**
B. Control	The individual finds it difficult to control the worry
C. Symptoms	**3 or more of 6: restlessness/keyed up, easily fatigued, poor concentration, irritability, muscle tension, sleep disturbance (only 1 required in children)**
D. Impairment	Clinically significant distress or social/occupational impairment
E. Not organic	Not due to a substance or another medical condition (e.g. hyperthyroidism)
F. Not better explained	Not better accounted for by another mental disorder (panic, social anxiety, OCD, PTSD, illness anxiety and others)

DSM-5-TR criteria for generalised anxiety disorder; the two numbers to hold are the 6-month duration and 3-of-6 symptom threshold (only 1 in children) (DSM-5-TR 2022).

1.4 ICD-11 CDDR: free-floating anxiety and "at least several months"

Where ICD-11 differs. The ICD-11 CDDR frames GAD as either general apprehensiveness "not restricted to any particular environmental circumstance (free-floating anxiety)" or excessive worry (apprehensive expectation) about negative events across several domains of everyday life, accompanied by additional symptoms such as muscle tension, restlessness, difficulty relaxing, difficulty concentrating, irritability and sympathetic autonomic overactivity (ICD-11 CDDR). Crucially, ICD-11 does *not* impose the DSM's fixed 6-month clock: it requires the symptoms to be **not transient and to persist for at least several months, more days than not**. This softer, more clinically flexible duration is the classic ICD-11-versus-DSM-5 discriminator to name in a comparison answer.

Onset and course. ICD-11 notes the typical age of onset is the early-to-mid thirties (later than most anxiety disorders), that severity fluctuates between threshold and subthreshold forms, and that full remission is uncommon, GAD is chronic and relapsing, which is exactly why the guidelines argue for long continuation.

RULE **Duration is the ICD/DSM fork.** DSM-5-TR fixes GAD at 6 months more days than not with 3 of 6 symptoms; ICD-11 asks only for "at least several months" and does not set a hard 6-month threshold, so quote the framework you are asked about.

GOOD TO REMEMBER

- **ICD-11 GAD:** free-floating general apprehensiveness or excessive multi-domain worry plus muscle tension/autonomic and cognitive symptoms, not transient, persisting for at least several months more days than not; the defining contrast with DSM-5-TR is the absence of a fixed 6-month rule; typical onset is the early-to-mid thirties and full remission is uncommon.

1.5 The differential: excluding organic mimics and the other anxiety disorders

Rule out the body first. Before diagnosing GAD, exclude an organic cause of chronic anxiety: hyperthyroidism, phaeochromocytoma, hypoglycaemia, cardiac arrhythmia, and above all caffeine and substance withdrawal (alcohol and benzodiazepine withdrawal both produce a GAD-like picture). A first presentation of "anxiety" in an older patient, or one with prominent physical signs, warrants thyroid function and a substance history rather than a straight-to-SSRI reflex.

Then separate it from its neighbours. GAD is the free-floating baseline; the specific anxiety disorders are carved out by the *focus* of the fear, panic disorder (fear of the attacks themselves), social anxiety disorder (fear of negative evaluation), OCD (contamination or other obsessions), PTSD (trauma reminders), illness anxiety disorder (fear of serious illness), separation anxiety (separation from attachment figures). DSM criterion F requires that GAD not be better explained by any of these. Depression is the commonest comorbidity and can be hard to separate: in a depressive episode the worry is coloured by hopelessness and worthlessness, whereas GAD worry is future-oriented apprehension.

COMMON TRAP

Do not label chronic anxiety as GAD without excluding a medical mimic. Hyperthyroidism, a caffeine habit, and alcohol or benzodiazepine withdrawal each reproduce restlessness, tremor, poor sleep and autonomic arousal; missing them means treating the wrong disorder. Thyroid function, a substance and caffeine history, and attention to withdrawal timing come before the prescription.

1.6 The GAD-7: the screening and severity scale to know cold

What it is. The GAD-7 (Generalised Anxiety Disorder-7) is a seven-item self-report scale of general worry and fear symptoms over the last 2 weeks, each item scored 0 to 3 on a Likert scale (not at all, several days, more than half the days, nearly every day), giving a total range of **0 to 21** (Spitzer et al 2006; Kaplan and Sadock 2024). It is the workhorse instrument of primary-care anxiety screening and of tracking treatment response, and it is reproduced in full on the accompanying scale plate.

The cut-offs. The suggested severity bands are **5, 10 and 15** for mild, moderate and severe anxiety respectively. The single most useful clinical threshold to memorise is a score of **10**, the usual cut-off for probable GAD and the point at which further assessment is warranted. A two-item short form, the GAD-2, is used as a rapid case-finding question; NICE recommends being alert to GAD and considering the GAD-2 to ask about anxiety and the ability to control worry (NICE 2011). A caveat examiners like: the GAD-7 asks about the last 2 weeks, whereas the DSM diagnosis needs symptoms over 6 months, so a high GAD-7 supports but does not by itself make the diagnosis.

GOOD TO REMEMBER

- **GAD-7:** seven self-rated items over 2 weeks, each 0 to 3, total 0 to 21; severity bands at 5/10/15 for mild/moderate/severe; a score of 10 is the standard clinical cut-off for probable GAD; the 2-item GAD-2 is the rapid screen; it measures 2-week severity and screens, it does not replace the 6-month DSM diagnosis.

1.7 The Hamilton Anxiety Rating Scale (HAM-A): the clinician-rated outcome measure

What it is. The Hamilton Anxiety Rating Scale (HAM-A, also HARS) is a *clinician-rated* scale of 14 items, each scored 0 to 4, covering both the psychic and the somatic components of anxiety, for a maximum total of **56** (Maudsley Deprescribing Guidelines). It is the standard anxiety-severity and treatment-outcome measure in trials, the scale against which drug effects in GAD are reported, and it too is set out on the accompanying scale plate. Where the GAD-7 is a quick self-report screen, the HAM-A is the fuller clinician instrument used to quantify change.

Reading it. The 14 items split into a psychic-anxiety factor (anxious mood, tension, fears, insomnia, cognitive difficulty, depressed mood) and a somatic-anxiety factor (muscular, sensory, cardiovascular, respiratory, gastrointestinal, genitourinary, autonomic), so the profile shows which arm of the disorder dominates. Commonly used severity bands place mild anxiety below the high-teens and increasing severity above the mid-twenties, though the exact numeric cut-points vary by source and are not standardised the way the GAD-7 bands are, so quote the structure (14 items, max 56) with confidence and the precise band figures with appropriate caution.

GOOD TO REMEMBER

- **HAM-A (HARS):** a clinician-rated 14-item scale, each item 0 to 4, maximum 56, splitting into psychic-anxiety and somatic-anxiety factors; it is the standard outcome measure in GAD drug trials (drug effects are reported as points reduced on the HAM-A); contrast with the GAD-7, which is self-rated, 7 items and used to screen.

10 GAD-7 CLINICAL CUT-OFF FOR PROBABLE GAD (BANDS AT 5/10/15)	**0 to 21** GAD-7 TOTAL SCORE RANGE (7 ITEMS, EACH 0 TO 3)	**56** HAM-A MAXIMUM (14 ITEMS, EACH 0 TO 4)	**6 months** DSM-5-TR DURATION; 3 OF 6 SYMPTOMS

1.8 Management: SSRI or SNRI first-line, across the guidelines

The BAP position. Lead with the British Association for Psychopharmacology: an SSRI is the first-line pharmacological treatment for GAD, the efficacious agents named being citalopram, escitalopram, paroxetine and sertraline; if an SSRI is unsuitable, an SNRI (duloxetine or venlafaxine) or pregabalin is the alternative initial treatment, and higher pregabalin doses may achieve greater response (BAP 2014). This is the verified **SSRI first-line** anchor and must not be contradicted.

What the other guidelines say. The picture is strikingly consistent. The Indian Psychiatric Society CPG names cognitive behavioural therapy as the first-line psychological treatment (the Indian Psychiatric Society 2020), sitting alongside the same pharmacology. NICE offers an SSRI if drug treatment is chosen, considering sertraline first as the most cost-effective option, then an alternative SSRI or an SNRI, and pregabalin only if SSRIs and SNRIs cannot be tolerated (NICE 2011). CANMAT lists SSRIs (escitalopram, paroxetine, sertraline), SNRIs (duloxetine, venlafaxine XR), agomelatine and pregabalin as first-line, with CBT as a first-line psychological treatment of comparable magnitude (CANMAT 2014). The WFSBP likewise puts an SSRI or SNRI first-line with CBT as first-line psychotherapy (WFSBP 2022). The convergence is the exam point: *SSRI or SNRI first-line everywhere*.

GUIDELINE	FIRST-LINE PHARMACOLOGY	KEY NOTE
BAP 2014	**SSRI (citalopram, escitalopram, paroxetine, sertraline)**	SNRI or pregabalin if SSRI unsuitable
Indian Psychiatric Society 2020	SSRI/SNRI, with CBT first-line psychological	CBT named as first-line therapy
NICE 2011	**SSRI, consider sertraline first (most cost-effective)**	Pregabalin only if SSRI/SNRI not tolerated
CANMAT 2014	SSRI, SNRI, agomelatine or pregabalin	CBT equal first-line to drugs

First-line pharmacotherapy for GAD across the major guidelines; the shared message is SSRI or SNRI first, with pregabalin as an option and CBT a co-equal first-line psychological treatment.

RULE **SSRI or SNRI is first-line for GAD, full stop.** BAP, NICE, CANMAT, WFSBP and the Indian Psychiatric Society all put an SSRI (or SNRI) first, with pregabalin and buspirone as options; CBT is the co-equal first-line psychological treatment.

1.9 The options and the second line: pregabalin, buspirone and the trial rules

Pregabalin. Pregabalin (Indian brands Pregeb, Pregastar) is a calcium-channel alpha-2-delta ligand with a genuinely anxiolytic effect and a relatively rapid onset. It is an alternative initial treatment when SSRIs are unsuitable (BAP 2014) and an augmentation option after non-response to an SSRI or SNRI. Its advantages are that it is renally cleared (useful in hepatic impairment) and fast-acting; its cautions are weight gain in about a fifth of long-term users, discontinuation symptoms on abrupt withdrawal, and a real potential for misuse, which is why NICE requires a drug-abuse history to be evaluated before prescribing (NICE 2011).

Buspirone. Buspirone (Indian brand Buspin) is a 5-HT1A partial agonist, efficacious in the acute treatment of GAD, non-sedating and non-dependence-forming, which makes it a useful option, particularly where a benzodiazepine is being avoided. Its limitations are a slow onset (a couple of weeks, so no use as a rescue drug) and no evidence for relapse prevention.

The adequate trial. A shared rule: allow up to **12 weeks** to judge efficacy, but recognise that absence of any benefit by **4 weeks** signals that response to unchanged treatment is unlikely (BAP 2014). SSRIs and SNRIs are often started at half the usual dose in GAD and titrated up, because early activation is common. When a patient responds, continuation of at least a further 6 to 18 months (BAP: up to 18 further months; NICE: at least a year) reduces relapse.

GOOD TO REMEMBER

- **Pregabalin (Pregeb, Pregastar):** an alpha-2-delta calcium-channel ligand; alternative first-line or augmentation option in GAD, relatively rapid-acting and renally cleared; signature cautions are weight gain, discontinuation symptoms and misuse potential (check a drug-abuse history first).
- **Buspirone (Buspin):** a 5-HT1A partial agonist; non-sedating, non-dependence-forming option for acute GAD; signature caution is its slow onset (about 2 weeks, so not a rescue agent) and no relapse-prevention evidence.

1.10 The benzodiazepine: not first-line, and not for the long term

The hard rule. A benzodiazepine is explicitly *not* a first-line treatment for GAD and must not be used long-term. BAP reserves benzodiazepines only after non-response to an SSRI, SNRI, pregabalin and buspirone, for persistent, severe, distressing, impairing anxiety where other treatments have failed (BAP 2014). NICE is blunter: do not offer a benzodiazepine for GAD except as a short-term measure during a crisis, and no more than 2 to 4 weeks (NICE 2011). The reason is the class's tolerance, dependence and withdrawal liability, the full pharmacology of which is developed in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes: a meta-analysis shows the HAM-A advantage of benzodiazepines over placebo shrinks from about 8 points at 1 week to almost nothing by 3 months (Maudsley Deprescribing Guidelines).

Propranolol. The beta-blocker propranolol (Indian brands Ciplar, Inderal) blunts the peripheral autonomic symptoms (tremor, palpitations) and is useful for *performance* anxiety, but it is not a treatment for GAD itself and is explicitly not recommended for its long-term management (MOH Singapore 2015).

TRAP **Never give a benzodiazepine as long-term monotherapy for GAD.** It is not first-line, is limited to short crisis use (2 to 4 weeks), and its apparent benefit fades within weeks as tolerance and dependence develop; the exam-fatal error is to write it up as the maintenance answer.

1.11 The India lens: the treatment gap and the benzodiazepine problem

Two genuine Indian realities. First, most people with GAD in India never reach formal care, part of the very large anxiety-disorder treatment gap; anxiety is under-recognised, somatised (patients present with physical complaints rather than "worry"), and under-treated. Second, and connected, is the entrenched over-prescription of benzodiazepines: in Indian general and primary care, a benzodiazepine (often alprazolam) is frequently the default and only "anxiety" prescription, given long-term against every guideline. The Indian Psychiatric Society CPGs exist precisely to correct this, an SSRI or SNRI first-line with CBT, the benzodiazepine reserved and time-limited, and the anxiolytic used only as a short bridge while the antidepressant takes effect (the Indian Psychiatric Society 2020).

Prescribing in Indian practice. The first-line agents are cheap and familiar as Indian brands: escitalopram (Nexito, Rexipra) and sertraline lead, with pregabalin (Pregeb, Pregastar) and buspirone (Buspin) as options and propranolol (Ciplar, Inderal) for the performance-anxiety niche. Starting the SSRI low and warning the patient about early activation, then holding the course to 12 weeks before judging failure, is the practical antidote to the "one alprazolam strip forever" pattern.

INDIA

The single highest-yield Indian point on this topic is the benzodiazepine over-prescription problem. Anxiety is common, somatised and under-recognised, and the treatment gap is wide; into that gap has flowed long-term benzodiazepine (typically alprazolam) prescribing that runs directly against the Indian Psychiatric Society CPG. The correct Indian answer mirrors the global one: an SSRI or SNRI first-line (Nexito or Rexipra escitalopram, sertraline) with CBT, pregabalin (Pregeb, Pregastar) or buspirone (Buspin) as options, and the benzodiazepine only as a short, time-limited bridge, never the maintenance treatment.

MNEMONIC

WORRIED FEARS

The chapter mnemonic, seeded here and paid off at consolidation. **WORRIED** holds the GAD picture: **W**orry (free-floating, uncontrollable), **O**n edge/restless, **R**umination and poor concentration, **R**elaxation impossible (muscle tension), **I**rritability, **E**asily fatigued, **D**isturbed sleep. **FEARS** holds the management: **F**irst-line SSRI/SNRI, **E**valuate for 12 weeks (4-week early-failure warning), **A**lternatives pregabalin and buspirone, **R**efer/CBT co-equal first-line, **S**hun the benzodiazepine as long-term monotherapy.

HOLD THIS

GAD is chronic, free-floating, uncontrollable worry across many domains, requiring 6 months and 3 of 6 symptoms in DSM-5-TR (only "several months" in ICD-11); the GAD-7 (self-rated, 0 to 21, cut-off 10) and HAM-A (clinician-rated, 14 items, max 56) are the scales; management is an SSRI or SNRI first-line (up to 12 weeks to judge), with pregabalin, buspirone and CBT as options, propranolol for performance anxiety, and the benzodiazepine never a long-term monotherapy.

2 · Panic disorder

Panic disorder is the disorder of the false alarm. A surge of autonomic terror arrives out of a calm sky, peaks in minutes, and the patient, feeling their heart pound and their breath shorten, concludes they are dying, suffocating or losing their mind. That misreading is the engine of the illness: the body's fear response is real, but the interpretation is catastrophic, and the fear of the next attack becomes a second illness layered on the first. Examiners test **panic disorder** on a tight set of exact points, the definition of a **panic attack** (an abrupt surge peaking within minutes, four or more of thirteen symptoms), the requirement of **recurrent** *unexpected* attacks plus a month of **anticipatory anxiety** or behaviour change, the medical mimics that must be excluded, and the management, where the one thing a wrong answer fails is starting an antidepressant without warning about early activation.

Why it matters clinically. This is a management/drug topic, so the marks sit in the drug, the dose, the line and the monitoring as much as in the phenomenology. Two facts anchor every answer. First, the diagnostic core is the *unexpected*, cued-by-nothing attack followed by persistent worry, which separates panic disorder from the situationally-bound attacks of the phobias. Second, the treatment core is that an SSRI is first-line but must be started low and slow with an

explicit warning, because these patients are exquisitely sensitive to the transient jitteriness of an antidepressant and will read it as another attack and stop the drug. The fear-circuit anatomy on which the alarm is built is developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes, the wider CBT model in the Psychotherapies, clinical assessment, MSE and nosology notes, and the deep SSRI pharmacology in the Mood disorders: pharmacotherapy notes; they are not re-derived here.

2.1 What a panic attack is: an abrupt surge that peaks within minutes

The unit of the disorder. A panic attack is an abrupt surge of intense fear or intense discomfort that reaches a peak *within minutes*, during which four or more of a list of thirteen physical and cognitive symptoms occur (DSM-5-TR 2022). The word to hold is *abrupt*: the surge can rise from a calm state or an already-anxious state, and it crescendos fast rather than building over hours. Fewer than four symptoms is a **limited-symptom attack**, which still counts clinically but not as a full attack.

The thirteen symptoms. The list divides into autonomic and cognitive. The autonomic and somatic symptoms are palpitations or pounding heart, sweating, trembling, shortness of breath or smothering, feelings of choking, chest pain, nausea or abdominal distress, dizziness or faintness, chills or heat sensations, and paraesthesiae. The cognitive symptoms are the three that give panic its dread: derealisation or depersonalisation, fear of losing control or "going crazy", and fear of dying (DSM-5-TR 2022). It is the cognitive triad that turns a burst of arousal into terror.

WORKED EXAMPLE

A 28-year-old software engineer is brought to casualty at midnight convinced he is having a heart attack: chest tightness, a racing heart, tingling in both hands, a sense that the room is unreal and that he is about to die. It began abruptly while he was watching television and peaked in about five minutes. ECG, troponin and examination are normal. This is a full panic attack (well over four symptoms, including the cognitive fear-of-dying and derealisation), arising unexpectedly from a calm state. If this is his third such attack and he now avoids being alone at night for fear of another, the diagnosis is panic disorder, not cardiac disease.

2.2 Recurrent unexpected attacks: the diagnostic spine

Recurrent and unexpected. **Panic disorder** requires **recurrent** *unexpected* panic attacks (Criterion A) (DSM-5-TR 2022). *Recurrent* means more than one; *unexpected* means the attack comes with no obvious cue at the time it occurs, as when a person is relaxing or is woken from sleep by a **nocturnal panic attack**. This is the single discriminator that examiners protect: an attack triggered reliably by a feared situation is an *expected* attack and points to a phobia, not to panic disorder. Roughly half of patients with panic disorder also have expected attacks, so the presence of expected attacks does not rule the diagnosis out, but at least some attacks must come out of the blue.

The one-month tail. Criterion B requires that at least one attack has been followed by a month or more of one or both of: persistent concern or worry about further attacks or their consequences (the **anticipatory anxiety**), or a significant maladaptive change in behaviour

because of the attacks, such as avoiding exercise or unfamiliar places (DSM-5-TR 2022). Without this month-long tail there are panic attacks but not the disorder.

RULE **Unexpected attack plus a month of worry.** Panic disorder needs *recurrent unexpected* panic attacks (out of the blue, not situationally cued) plus at least one month of anticipatory worry or maladaptive avoidance; a situationally-triggered attack is a phobia's attack, not this diagnosis.

2.3 Anticipatory anxiety, catastrophic misinterpretation and the panic cycle

The cognitive engine. The dominant cognitive model, Clark's, holds that **panic disorder** arises from the **catastrophic misinterpretation** of benign bodily sensations: a normal palpitation is read as an impending heart attack, breathlessness as suffocation, dizziness as impending collapse or madness (Tasman Psychiatry; New Oxford Textbook of Psychiatry). The misinterpretation amplifies the very sensations it fears, which are then read as further proof of catastrophe, closing a vicious loop, the **panic cycle**, that drives the attack to its peak. This is why interoceptive exposure, deliberately inducing the feared sensations, is a core ingredient of panic-focused CBT: it disconfirms the catastrophic prediction.

Anticipatory anxiety and phobic avoidance. Between attacks the patient is left with **anticipatory anxiety**, a persistent apprehensive dread of the next attack, and often with *fear of the fear* itself. This can generalise into agoraphobia, avoidance of situations from which escape would be difficult or help unavailable if an attack struck, so that a third illness (avoidance) stacks on the anticipatory anxiety and the attacks. The three layers, the attack, the anticipatory anxiety, and the avoidance, are what a full answer names.

PEARL

Panic disorder is really three problems in a stack: the *panic attack* (the false autonomic alarm), the *anticipatory anxiety* (fear of the next alarm, the "fear of fear"), and the *phobic avoidance* that can crystallise into agoraphobia. The catastrophic misinterpretation of body sensations is the hinge that converts a burst of arousal into terror and keeps the cycle turning. Treatment must reach all three layers, which is why an SSRI (dampens the attacks) plus CBT (breaks the misinterpretation and the avoidance) is the fullest answer.

2.4 The mimics you must exclude before you diagnose

Panic is a diagnosis of exclusion of the organic. Criterion C requires that the disturbance is not due to a substance or another medical condition, and Criterion D that it is not better explained by another mental disorder (DSM-5-TR 2022). The medical mimics to actively exclude are **hyperthyroidism**, **hyperparathyroidism**, **phaeochromocytoma**, vestibular dysfunction, seizure disorders, and cardiopulmonary conditions such as arrhythmias, supraventricular tachycardia, asthma and COPD (DSM-5-TR 2022). Substance causes, intoxication with stimulants (cocaine, amphetamines, caffeine) or cannabis and withdrawal from alcohol or barbiturates, must also be considered.

The red flags that push you toward the organic. First onset after 45 years, or atypical features during the attack, vertigo, loss of consciousness, loss of bladder or bowel control, slurred speech

or amnesia, should make you suspect a medical or substance cause rather than primary panic disorder (DSM-5-TR 2022). A first "panic attack" in an older patient is a cardiac or endocrine event until proven otherwise.

TRAP **Missing the organic mimic.** A panic attack is a diagnosis of exclusion: hyperthyroidism, phaeochromocytoma, hypoglycaemia, an arrhythmia or supraventricular tachycardia, and stimulant or caffeine excess all mimic it. First onset after 45, or vertigo, syncope, incontinence, slurred speech or amnesia during the attack, are red flags for a medical cause, do not label them panic.

2.5 ICD-11 and the criterion-anchored discriminators

ICD-11 CDDR. ICD-11 places panic disorder (6B01) among the anxiety and fear-related disorders and, like DSM-5-TR, requires recurrent unexpected panic attacks that are not restricted to a particular stimulus or situation, together with persistent concern about their recurrence or their significance, or behaviours intended to avoid recurrence (ICD-11 CDDR). The systems align on the essentials: it is the *unexpected, uncued* attack plus the persistent apprehension that defines the disorder.

The discriminator to state. If panic attacks occur *only* in a specific context, in social situations (social anxiety disorder), before phobic objects (specific phobia or agoraphobia), triggered by obsessions (OCD), by trauma reminders (PTSD), or by separation (separation anxiety disorder), then only that disorder is diagnosed and not panic disorder (DSM-5-TR 2022). Panic disorder is the diagnosis when the attacks are, at least in part, cued by nothing at all.

GOOD TO REMEMBER

- **Panic disorder (the syndrome):** the defining criterion is *recurrent unexpected* panic attacks (an abrupt surge peaking within minutes, four or more of thirteen autonomic and cognitive symptoms) followed by at least one month of persistent anticipatory worry about further attacks or a maladaptive behaviour change; the discriminator from the phobias is that at least some attacks are *uncued*, and the first step before diagnosis is to exclude the organic mimics (hyperthyroidism, phaeochromocytoma, arrhythmia, stimulant/caffeine excess), especially with first onset after 45 or atypical neurological features.

2.6 Management overview: SSRI first-line, CBT, and where the guidelines converge

Lead with BAP. The British Association for Psychopharmacology (BAP) makes an **SSRI** the first-line pharmacological treatment for panic disorder (escitalopram, citalopram, fluoxetine, fluvoxamine, paroxetine or sertraline), and cognitive behaviour therapy the first-line psychological treatment, noting that drug and psychological approaches have broadly similar efficacy; for partial or non-response it recommends combining cognitive therapy with an antidepressant, which is more effective than drug treatment alone and may protect better against relapse (BAP 2014). This is the verified first-line position and anchors any answer: an SSRI or CBT, chosen by availability and patient preference, with the combination reserved for the incomplete responder.

Then the other bodies. The Indian Psychiatric Society clinical practice guideline makes SSRIs or SNRIs the first-line agents for the long-term management of panic disorder and recommends

CBT (psychoeducation, self-monitoring, systematic exposure to panic-inducing cues, countering anxious beliefs, relapse prevention), adding that a combination of CBT and medication gives the best outcomes; in the elderly it prefers SSRIs as safer, avoiding TCAs and benzodiazepines because of anticholinergic effects, orthostatic hypotension, ECG changes and paradoxical reactions (IPS 2017). NICE offers an SSRI licensed for panic (escitalopram, sertraline, citalopram, paroxetine) or venlafaxine as the first pharmacological option, offers CBT of 7 to 14 hours over four months as first-line, and explicitly says *do not* prescribe benzodiazepines, sedating antihistamines or antipsychotics for panic disorder (NICE 2011). CANMAT likewise places an SSRI or venlafaxine XR and CBT (with interoceptive and situational exposure) as first-line (CANMAT 2014). WFSBP grades the SSRIs and venlafaxine as first-line (Recommendation Grade 1) at **20 to 60 mg/day** (WFSBP 2008).

GUIDELINE	FIRST-LINE PHARMACOLOGY	PSYCHOTHERAPY	BENZODIAZEPINE STANCE
BAP 2014	SSRI (escitalopram, citalopram, fluoxetine, fluvoxamine, paroxetine, sertraline)	CBT first-line; combine with antidepressant for partial/non-response	Not first-line
Indian Psychiatric Society 2017	SSRI or SNRI first-line for long-term management	CBT; CBT plus medication gives best outcomes	Short-acting oral, only for the acute attack with reassurance
NICE 2011	SSRI licensed for panic (escitalopram, sertraline, citalopram, paroxetine) or venlafaxine	CBT 7 to 14 hours over 4 months, first-line	**Do not prescribe (worse long-term outcome)**
CANMAT 2014	SSRI or venlafaxine XR, first-line	CBT with interoceptive and situational exposure, first-line	Second-line only
WFSBP 2008	SSRI or venlafaxine, first-line, 20 to 60 mg/day	CBT alone or combined with medication	Reserve for treatment-resistant, no substance-use history

Guideline-level management of panic disorder; BAP-led, then the Indian Psychiatric Society, NICE, CANMAT and WFSBP, all converging on SSRI/SNRI plus CBT first-line and benzodiazepines out of the first line (verified from the drug-guideline supplement).

2.7 Starting the SSRI: start low, go slow, and warn about early activation

The single most examinable prescribing point. An **ssri panic** start must be at a *low* dose, lower than the usual antidepressant starting dose, and titrated slowly, because patients with panic disorder are unusually sensitive to the transient over-stimulation an antidepressant produces in the first days and weeks, the jitteriness syndrome of restlessness, insomnia, agitation and a paradoxical worsening of anxiety (Pohl et al., in Tasman Psychiatry; Maudsley Prescribing Guidelines; Stahl). Left unwarned, the patient reads this early activation as another panic attack, concludes the drug is harming them, and stops it. The instruction to memorise is therefore: *start low, go slow, and warn the patient in advance* that they may feel briefly more jittery before they feel better, that this is expected and self-limiting, and that it is not a sign of harm.

How this looks in practice. Begin, for example, sertraline at 25 mg/day rather than 50, or escitalopram at 5 mg/day, titrating upward after several days once early activation has settled; a short course of a benzodiazepine may be co-prescribed to cover the activation window in selected patients, then withdrawn (WFSBP 2008; MOH_SG 2015). The therapeutic effect is delayed, several weeks, so the patient must also be told the drug is not a rescue medication for an attack in progress but a preventive taken daily (NICE 2011).

TRAP **Starting the SSRI at a full dose with no warning.** Panic patients are hypersensitive to early SSRI activation (the jitteriness syndrome); a normal starting dose can trigger restlessness and a paradoxical surge of anxiety that the patient reads as another attack and stops the drug. Start at half the usual dose, titrate slowly, and warn in advance that a brief jittery phase is expected and self-limiting.

2.8 Dose, duration and stopping: the numbers to hold

Target dose and trial length. Once started low, the SSRI is titrated to the effective antidepressant range; WFSBP puts the first-line SSRI and venlafaxine range at **20 to 60 mg/day** (citalopram-equivalent), and panic disorder, like the other anxiety disorders, often needs the *upper* part of the range and an adequate trial before response is judged (WFSBP 2008; NICE 2011). NICE frames the antidepressant trial around a **12-week** course: if there is no improvement after a 12-week course of an SSRI, and only then, imipramine or clomipramine may be considered off-label as the next step (NICE 2011).

Continuation and the taper. After response, drug treatment is continued for *at least six months*, and when stopping the dose is reduced gradually over an extended period, a minimum of three months, to avoid discontinuation symptoms (BAP 2014). The relapse rate on abrupt withdrawal is high, so the slow taper is part of the treatment, not an afterthought. Patients should be told of both the delayed onset and the discontinuation risk from the outset, and monitored with a brief self-report panic-severity questionnaire (NICE 2011).

STEP	ACTION	SOURCE
Start	**SSRI at half the usual dose (e.g. sertraline 25 mg/day, escitalopram 5 mg/day); warn about early activation**	Maudsley; Stahl
Titrate	Up to the effective range, 20 to 60 mg/day, often the upper end	WFSBP 2008
Judge response	**Adequate trial; if no improvement after a 12-week course, consider imipramine or clomipramine (off-label)**	NICE 2011
Continue	At least six months after response	BAP 2014
Stop	**Taper gradually over a minimum of three months**	BAP 2014

The SSRI course in panic disorder: start low and warn, titrate to range, judge at 12 weeks, continue at least six months, taper over at least three (BAP 2014; NICE 2011; WFSBP 2008).

GOOD TO REMEMBER

- **SSRI in panic disorder (fluoxetine, sertraline, fluvoxamine, paroxetine, escitalopram; the antidepressant brand list applies):** the first-line agent across BAP, IPS, NICE, CANMAT and WFSBP; mechanism is serotonergic dampening of the fear circuit, the signature caution is early *activation* (the jitteriness syndrome), so *start at half the usual dose, titrate slowly and warn the patient in advance*; effective range 20 to 60 mg/day, judge response over a 12-week course, continue at least six months, and taper over a minimum of three months to avoid discontinuation.

2.9 CBT for panic: interoceptive exposure and the Clark model in practice

What panic-focused CBT does. CBT is first-line and, delivered as a structured 7-to-14-hour course over about four months, targets each layer of the disorder (NICE 2011; BAP 2014). Its ingredients are psychoeducation about the panic cycle, *interoceptive exposure* (deliberately inducing the feared bodily sensations, for example by hyperventilating or spinning, to disconfirm the catastrophic prediction), in-vivo exposure for any agoraphobic avoidance, and cognitive restructuring of the **catastrophic misinterpretation** at the heart of Clark's model (NICE 2011). Because it directly dismantles the misinterpretation and the avoidance, CBT tends to protect against relapse better than medication stopped early.

Where it sits against the drug. Drug and CBT have broadly similar acute efficacy; the fullest answer offers either as first-line and combines them for the partial responder (BAP 2014). The general CBT model and the wider exposure principle are developed in the Psychotherapies, clinical assessment, MSE and nosology notes.

GOOD TO REMEMBER

- **CBT for panic (the psychotherapy):** first-line, 7 to 14 hours over about four months; its defining active ingredient is *interoceptive exposure*, deliberately provoking the feared bodily sensations to disconfirm the catastrophic misinterpretation of Clark's model, plus cognitive restructuring and in-vivo exposure for agoraphobic avoidance; it has similar acute efficacy to an SSRI and better relapse protection, and combining CBT with an antidepressant is the recommended step for a partial responder.

2.10 The benzodiazepine: reserved, time-limited, never the first line

The reserved role. Every guideline pushes the benzodiazepine out of the first line. NICE says outright *do not* prescribe benzodiazepines for panic disorder, because they are associated with a worse long-term outcome (NICE 2011). CANMAT places them second-line, WFSBP reserves them for treatment-resistant cases with no substance-use history, and WHO permits them only for severe acute symptoms and only very short-term, 3 to 7 days (CANMAT 2014; WFSBP 2008; WHO mhGAP 2023). The Indian Psychiatric Society allows a short-acting, orally-dissolving benzodiazepine with reassurance for the *acute panic attack itself*, and MOH Singapore permits adding one to an antidepressant short-term to cover the early activation window, tapering it off within four weeks (IPS 2017; MOH_SG 2015). The through-line: a benzodiazepine is a bridge for the acute attack or the activation window, never the maintenance treatment and never a monotherapy.

Why the caution is genuine. The risks are dependence, tolerance, cognitive dulling, rebound anxiety and inter-dose panic, and a worse long-term course, which is why the drug is time-limited and tapered. The wider anxiolytic pharmacology, benzodiazepines, buspirone, pregabalin, the z-drugs, dependence and withdrawal, is developed in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes.

INDIA

Panic disorder sits inside a large, mostly untreated Indian anxiety burden, most sufferers never reach formal care, and it collides with the country's benzodiazepine over-prescription problem: alprazolam and clonazepam are dispensed freely, often long-term, as a first move for "ghabrahat" and palpitations, which is exactly what every guideline warns against. The Indian Psychiatric Society CPG is unambiguous, an SSRI or SNRI is first-line for long-term management and the benzodiazepine is only a short-acting, orally-dissolving bridge for the acute attack. Indian brands are cheap and available, sertraline (Serta, Zosert, Daxid), escitalopram (Nexito, Cipralex), paroxetine (Paxidep) and fluoxetine (Fludac); the correct Indian answer is a low-started, well-explained SSRI plus CBT, not a chronic benzodiazepine. A neat exam pearl: the lactate provocation (sodium lactate infusion) test can precipitate an attack in about 70% of panic-disorder patients, a classic Indian-textbook association.

TRAP **The chronic benzodiazepine.** A benzodiazepine as ongoing monotherapy for panic disorder is the classic error: it worsens the long-term outcome, breeds dependence and inter-dose rebound panic. It is at most a short-acting bridge for the acute attack or the SSRI activation window, tapered within a few weeks, never the maintenance treatment.

4 of 13	1 month	12 weeks	6 months
SYMPTOMS NEEDED FOR A FULL PANIC ATTACK (FEWER IS A LIMITED-SYMPTOM ATTACK)	OF ANTICIPATORY WORRY OR BEHAVIOUR CHANGE REQUIRED (CRITERION B)	SSRI COURSE BEFORE JUDGING NON-RESPONSE AND CONSIDERING A TCA	MINIMUM CONTINUATION AFTER RESPONSE; TAPER OVER AT LEAST 3 MONTHS

HOLD THIS

Panic disorder is recurrent *unexpected* panic attacks (an abrupt surge peaking within minutes, four or more of thirteen symptoms) plus at least a month of anticipatory worry, driven by catastrophic misinterpretation of body sensations, and treated first-line with an SSRI started at half the usual dose with an explicit warning about early activation plus CBT with interoceptive exposure; the benzodiazepine is reserved, time-limited and never a monotherapy.

3 · Clark cognitive model of panic

David M. **Clark**'s **cognitive model of panic** (1986) is the single most examined psychological model in the anxiety chapter, because it does two things at once: it explains why a panic attack feels like a heart attack, and it hands the clinician the exact lever that **cognitive behaviour therapy** pulls to abolish it. The claim is deceptively simple. Panic disorder arises not from the bodily sensations of arousal themselves, which everyone gets, but from the **catastrophic misinterpretation** of those benign sensations as an imminent physical or mental disaster. A racing heart is read as *"I am having a heart attack"*, breathlessness as *"I am suffocating"*, dizziness as

"I am about to collapse or go mad". That misreading feeds a self-amplifying loop that Clark drew as a **vicious cycle** (shown in the accompanying figure), and it is the loop, not any one symptom, that the model asks you to memorise.

Why it matters. The model is the reason panic disorder is one of the most treatable conditions in psychiatry: break the misinterpretation and the cycle collapses. It supplies the discriminator examiners want (panic disorder is a disorder of *interpretation*, not of the autonomic nervous system) and it maps one-to-one onto the CBT protocol that BAP, NICE and CANMAT all place first-line. The wider CBT technique, the general cognitive model and the exposure principle belong to the Psychotherapies, clinical assessment, MSE and nosology notes; this topic owns Clark's disorder-specific loop, the safety behaviours that keep it turning, and how CBT dismantles each link.

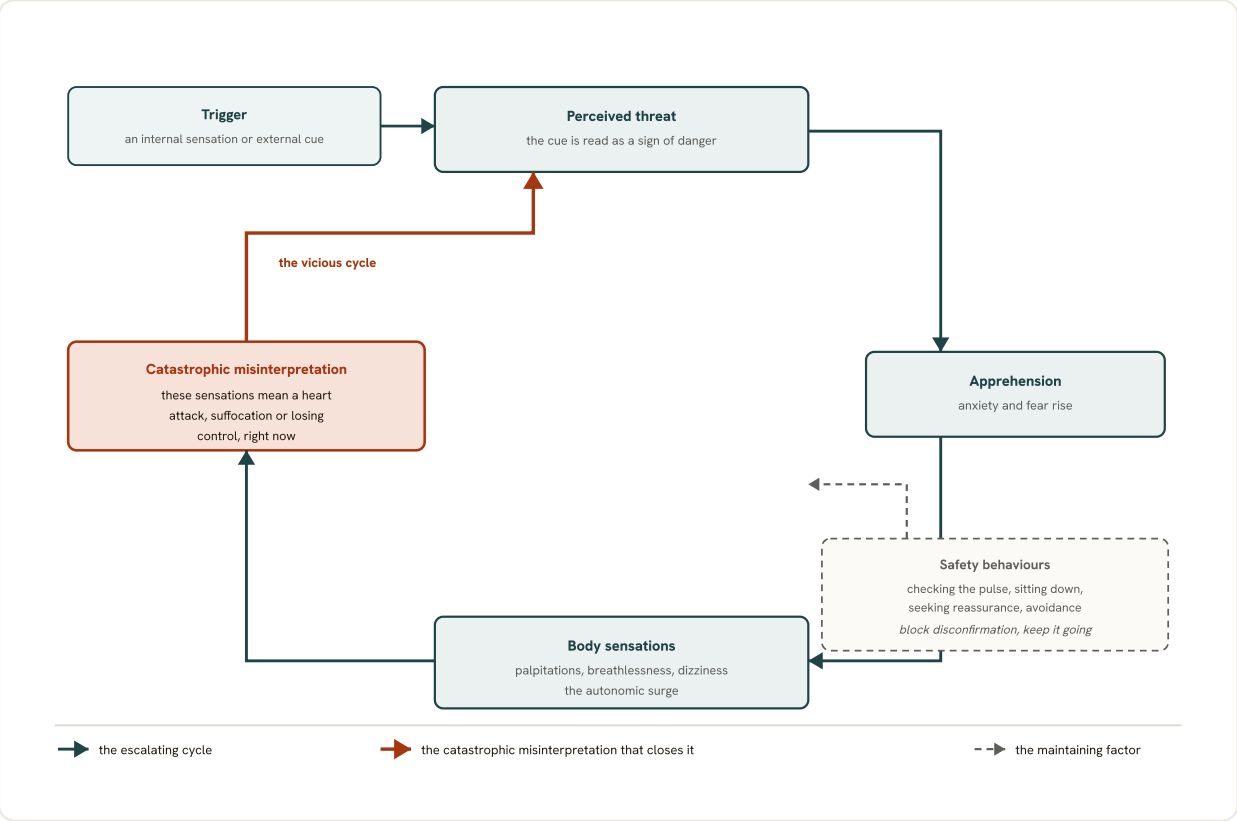


Fig 14.3 Clark's cognitive model of panic. A trigger, most often an ordinary bodily sensation, is read as a sign of threat; the apprehension that follows amplifies the autonomic body sensations, which are then catastrophically misinterpreted as an imminent heart attack, suffocation or loss of control, and that misinterpretation feeds straight back into the perceived threat, closing a vicious cycle that escalates to a full panic attack in minutes. Safety behaviours, checking the pulse, sitting down, seeking reassurance and avoidance, feel protective but block the disconfirmation that would break the cycle, so they maintain the disorder. Cognitive behaviour therapy works by targeting the misinterpretation and dropping the safety behaviours, and the wider technique is taught in the Psychotherapies, clinical assessment, MSE and nosology notes.

3.1 The core claim: catastrophic misinterpretation of benign bodily sensations

The single idea. According to Clark, a panic attack occurs when an individual interprets normal or benign **bodily sensations** as evidence of an immediate catastrophe (Clark 1986, 1988, 1996; Tasman Psychiatry). The sensations are ordinary products of arousal, exercise, caffeine, a missed meal, or a fleeting emotion; what is pathological is the meaning imposed on them. **The evidence that seals it.** When panic is provoked experimentally (for example by lactate infusion or carbon-

dioxide inhalation), panic-disorder patients and healthy controls report the *same* physical sensations, yet only the patients who make a catastrophic interpretation go on to a full attack (Sanderson and Rego; Tasman Psychiatry). The bodily signal is shared; the disorder lives in the appraisal. **Why "catastrophic".** The misinterpretation is not merely negative but specifically catastrophic and *imminent*, forecasting death, collapse, loss of control or insanity within seconds, which is what drives the terror out of proportion to the trigger.

RULE **The interpretation, not the sensation, is the disorder.** Everyone gets palpitations; only the person who reads them as "heart attack" panics. Treatment targets the appraisal.

3.2 The vicious cycle: the loop you must be able to draw

The five links. Clark's loop runs: a *trigger* (internal, such as a bodily sensation or intrusive thought, or external, such as a crowded shop) leads to the *perceived threat*, which produces *apprehension or fear*, which drives further *bodily sensations* of autonomic arousal, which are then subjected to *catastrophic misinterpretation*, which feeds straight back into perceived threat, tightening the spiral until a full attack crests (the accompanying figure lays out the loop). **Why it is self-amplifying.** Each turn recruits more arousal: the thought "I am dying" is itself a fresh threat, so the sympathetic surge grows, the sensations intensify, and the interpretation looks ever more confirmed. This positive-feedback quality is the reason a panic attack escalates from first flutter to peak terror within about **10 minutes** and then, once the loop can no longer amplify, spontaneously subsides. **The internal trigger point.** Crucially the trigger is often internal and invisible to bystanders, which is why panic attacks appear to come "out of the blue"; the patient has misread a benign internal cue, not responded to an external danger.

TRAP **Do not confuse the trigger with the cause.** The out-of-the-blue attack is not causeless; it is an internal bodily sensation, misread, that the patient did not consciously register as the trigger.

3.3 Safety behaviours: why the belief never disconfirms itself

What they are. Safety behaviours are actions the patient performs to avert the feared catastrophe: gripping the trolley or a companion's arm to avoid collapsing, sitting down and breathing deeply to avoid a "heart attack", carrying water or medication, scanning for exits, or avoiding exercise and caffeine (Anxiety and Panic Therapist Guide, Treatments that Work). **Why they are pathogenic.** They feel protective but are the engine of chronicity, because they prevent *disconfirmation*: the patient survives the attack, attributes the survival to the safety behaviour rather than to the harmlessness of the sensations, and so the catastrophic belief is never tested and never falsified ("I only survived because I sat down"). **The link to avoidance and agoraphobia.** The same logic scales up: avoiding the supermarket, the bus or being alone are macro-level safety behaviours that entrench agoraphobic avoidance, so that the belief "these sensations are dangerous" is protected across a widening range of situations (the phobic-avoidance detail sits with the panic disorder and agoraphobia topics).

PEARL

Safety behaviours are the reason reassurance and self-monitoring apps often make panic worse, not better. A pulse oximeter, a "check my heart" habit, or a benzodiazepine kept in the pocket "just in case" all become safety behaviours: they hand the patient a fresh reason the catastrophe was averted, so the belief is preserved rather than disproved. The therapeutic move is to *drop* the safety behaviour and let the sensation prove itself harmless.

3.4 How CBT breaks the cycle

The three levers. Cognitive behaviour therapy for panic maps exactly onto the loop and attacks it at three points (Clark; BAP, Baldwin et al.; NICE). *Cognitive restructuring* identifies and challenges the catastrophic misinterpretation, replacing "palpitations mean a heart attack" with an accurate, non-catastrophic account of arousal. *Interoceptive exposure* deliberately induces the feared sensations (hyperventilating to voluntary breathlessness and dizziness, spinning to induce vertigo, running on the spot to raise the heart rate) so the patient experiences the sensation, makes no misinterpretation, and learns experientially that it is harmless. *Dropping safety behaviours and situational (in-vivo) exposure* remove the props so the belief is finally tested and disconfirmed. **The behavioural experiment.** The pivotal technique is the behavioural experiment: the patient predicts the catastrophe ("if I don't sit down I will faint"), then hyperventilates without the safety behaviour, and observes that the catastrophe does not occur, which corrects the belief far more powerfully than argument. **Dose and place.** CBT for panic is first-line, delivered in the optimal range of **7 to 14 hours** total, typically weekly over about **4 months** (NICE; BAP). The general CBT and exposure technique is developed in the Psychotherapies, clinical assessment, MSE and nosology notes.

WORKED EXAMPLE

A 28-year-old woman has recurrent attacks that begin with a pounding heart she reads as "I'm having a heart attack." In the session the therapist has her hyperventilate for two minutes; her heart races and she feels dizzy, exactly her attack, but with the prediction "I will collapse" written down first. She does not collapse. Repeated across sessions, with her hand off the wall (a dropped safety behaviour), the sensation stops meaning catastrophe. The catastrophic misinterpretation is disconfirmed at its source, and the vicious cycle has nowhere to turn.

3.5 Where the model sits in management, and the benzodiazepine trap

First-line, and why. Because the model is so directly testable, CBT built on Clark's framework is a first-line treatment for panic disorder with or without agoraphobia, on a par with an SSRI (BAP; NICE; CANMAT places CBT first-line psychologically). Where medication is used, an SSRI licensed for panic (escitalopram, sertraline, paroxetine or citalopram) or venlafaxine is first-line; a patient starting an SSRI must be warned about early activation and a transient worsening of anxiety, because in Clark's terms the initial jitteriness supplies fresh bodily sensations to misinterpret. **The benzodiazepine trap.** NICE explicitly says *do not prescribe benzodiazepines* for panic disorder: they are associated with a worse long-term outcome, and, read through Clark's

model, they act as a chemical safety behaviour that blocks the disconfirming learning CBT depends on. This matters acutely in the Indian setting.

INDIA

Panic disorder in India is routinely met with a benzodiazepine, often alprazolam, prescribed long-term in primary care and by non-specialists, against every guideline. Clark's model gives the sharpest argument against the habit: the tablet-in-the-pocket becomes a safety behaviour that preserves the very belief driving the disorder, so symptomatic relief today buys chronicity tomorrow, on top of the well-documented dependence problem. The Indian Psychiatric Society clinical practice guidelines for anxiety disorders reserve benzodiazepines for short-term use and place SSRIs and CBT first; against the wide anxiety treatment gap, teaching the panic cycle to the patient is itself a low-cost, transferable intervention that does not require a psychologist on site.

TRAP **The prescribed benzodiazepine is a safety behaviour.** Giving alprazolam "to carry just in case" relieves the attack but preserves the catastrophic belief, blocking the disconfirmation CBT needs and inviting dependence.

7 to 14	4	1986
HOURS OF CBT FOR PANIC, THE FIRST-LINE DOSE (NICE, BAP)	MONTHS, THE TYPICAL CBT DELIVERY WINDOW	CLARK'S FOUNDATIONAL COGNITIVE-MODEL PAPER

GOOD TO REMEMBER

- **Clark cognitive model of panic:** panic disorder is the *catastrophic misinterpretation of benign bodily sensations* as imminent physical or mental catastrophe; the loop is trigger, perceived threat, apprehension, bodily sensations, catastrophic misinterpretation, back to perceived threat.
- **The maintaining mechanism:** safety behaviours (and avoidance) prevent disconfirmation, so the catastrophic belief is never tested and the disorder becomes chronic.
- **The discriminator:** the disorder is one of *interpretation*, not of the autonomic nervous system; provoked sensations are identical in patients and controls, only the misinterpretation predicts an attack.

GOOD TO REMEMBER

- **CBT for panic (Clark protocol):** first-line, 7 to 14 hours over about 4 months; three levers are cognitive restructuring of the misinterpretation, interoceptive exposure to the feared sensations, and dropping safety behaviours with in-vivo exposure, driven by behavioural experiments.
- **Signature caution:** a benzodiazepine (and any "just in case" prop) acts as a safety behaviour that blocks the disconfirming learning, so it is not first-line and NICE advises against it in panic disorder.

HOLD THIS

Panic disorder is the catastrophic misinterpretation of benign bodily sensations, sustained by safety behaviours that stop the belief being disconfirmed; CBT (7 to 14 hours) breaks the vicious cycle by restructuring the misinterpretation, exposing the patient to the sensations, and removing the safety behaviours so the catastrophe is finally proven not to happen.

4 · Agoraphobia

Agoraphobia is not, despite its name, a simple **fear of public places**. It is a fear of *being trapped*: of finding oneself in a situation from which escape would be difficult or embarrassing, or in which help would not be available, should a panic attack or some other incapacitating or humiliating bodily event strike. The Greek *agora* was the marketplace, and the marketplace still captures the clinical picture, the crowd, the queue, the bus, the open square, but the driving cognition is about escape and rescue, not about the place itself. The patient reorganises life around this fear until, at its most severe, they are completely homebound. Examiners test **agoraphobia** on a tight set of exact points: the two-or-more-of-five situations of Criterion A, the *escape/help-unavailable* cognition of Criterion B that separates it from a specific phobia, its modern status as a diagnosis in its own right independent of panic disorder, and the treatment, where the single load-bearing fact is that *graded in-vivo exposure* is the core of care.

Why it matters clinically. This is a hybrid topic, so the marks sit both in the criterion-anchored discrimination and in the exposure-based management. Two facts anchor every answer. First, the diagnostic core is the cluster of at least two of five feared situations plus the specific cognition that escape or help would be impossible, which is exactly what separates agoraphobia from the single-situation specific phobia and from the socially-evaluative fear of social anxiety disorder. Second, both ICD-11 and DSM-5-TR now diagnose **agoraphobia** as a stand-alone disorder, *irrespective of the presence of panic disorder*, a deliberate break from the older nesting of "panic disorder with agoraphobia". The fear-circuit anatomy on which the alarm is built is developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes, and the general CBT model and the wider exposure principle in the Psychotherapies, clinical assessment, MSE and nosology notes; they are not re-derived here.

4.1 What agoraphobia actually is: fear of being trapped, not fear of the place

The core fear. The essential feature is marked fear or anxiety triggered by the real or anticipated exposure to a range of situations, feared *because the person believes that escape might be difficult or that help might be unavailable* if panic-like or other incapacitating or embarrassing symptoms were to occur (DSM-5-TR 2022; ICD-11 CDDR). The place is incidental; the dread is of being stuck in it. "Panic-like symptoms" means any of the thirteen panic-attack symptoms (dizziness, faintness, fear of dying and the rest), and "other incapacitating or embarrassing symptoms" covers vomiting, incontinence, and, in older adults, a fear of falling.

What the avoidance looks like. The behaviour that follows is avoidance: the person actively rearranges their life to prevent contact with the feared situations, takes a job near home to avoid the bus, has food delivered to avoid the shop, insists on a companion, or sits near the exit at the cinema as a *safety behaviour*. Avoidance can be behavioural or cognitive (using distraction to endure), and at its most severe the person becomes entirely housebound, dependent on others for basic needs (DSM-5-TR 2022).

WORKED EXAMPLE

A 34-year-old woman has, over eight months, stopped taking the bus, stopped going to the crowded weekly market, and will now enter a shop only if her sister comes with her; she has not left the house alone in weeks. She describes no fear of the bus or the market as such, but a dread that she will "feel faint and trapped with no way out and no one to help". There is no current panic disorder, though she had a handful of panic attacks a year ago. Two or more of the five agoraphobic situations are feared (public transport, crowds, being outside the home alone), the cognition is the escape/help-unavailable one, the avoidance is marked and companion-dependent, and it has lasted well beyond six months. This is agoraphobia, diagnosable in its own right, panic disorder or not.

4.2 Criterion A: two or more of the five situations

The five situations. The diagnosis requires marked fear or anxiety about *two or more* of five situation clusters (DSM-5-TR 2022): (1) using **public transportation** (buses, trains, ships, planes); (2) being in **open spaces** (car parks, marketplaces, bridges); (3) being in **enclosed places** (shops, theatres, cinemas); (4) **standing in line or being in a crowd**; and (5) **being outside of the home alone**. The examples are not exhaustive, and the "two or more" threshold is the number examiners protect, because it is precisely what lifts the picture out of specific phobia.

Consistency and proportion. The fear must be evoked *nearly every time* the person meets the situation (Criterion C), must be actively avoided or endured with intense distress or need a companion (Criterion D), and must be out of proportion to the actual danger and to the sociocultural context (Criterion E) (DSM-5-TR 2022). That last clause matters cross-culturally: where it is socioculturally expected that a woman does not leave the house alone, that avoidance is not, by itself, agoraphobia.

CRITERION	REQUIREMENT
A	Marked fear/anxiety about two or more of five situations (public transport, open spaces, enclosed places, crowds/queues, outside home alone)
B	**Feared because escape may be difficult or help unavailable if panic-like or incapacitating/embarrassing symptoms occur**
C	The situations almost always provoke fear or anxiety
D	Actively avoided, need a companion, or endured with intense fear
E	Out of proportion to actual danger and sociocultural context
F	**Persistent, typically six months or more**
G	Clinically significant distress or impairment

The DSM-5-TR criteria for agoraphobia; the two-of-five rule (A) and the escape/help-unavailable cognition (B) are the load-bearing discriminators (DSM-5-TR 2022).

4.3 Criterion B: the escape-or-help cognition that defines it

The discriminating thought. Criterion B is what makes agoraphobia agoraphobia: the situations are feared *because of thoughts that escape might be difficult or help might not be available* in the event of developing panic-like symptoms or other incapacitating or embarrassing symptoms (DSM-5-TR 2022; ICD-11 CDDR). This single cognition is the examiner's favourite discriminator. If the situation is feared for another reason, fear the plane will crash, fear the dog will bite, then it is a *specific phobia*, not agoraphobia. If it is feared because of negative social evaluation, it is *social anxiety disorder*. The **exposure agoraphobia** treatment that follows is built directly on disconfirming this escape-or-help prediction.

Where the fear centres. ICD-11 puts it crisply: fear or anxiety in agoraphobia centres on *imminent perceived dangerous outcomes*, panic attacks, symptoms of panic, incapacitation, or embarrassing physical symptoms, that are anticipated to occur in multiple situations where obtaining help or escaping might be difficult (ICD-11 CDDR). It is worth establishing the specific feared outcome (a panic attack versus incontinence versus falling), because that shapes the exposure plan.

RULE **Two of five, feared for escape not for the object.** Agoraphobia = fear/avoidance of two or more of the five situations, feared *because escape or rescue would be impossible* if something dreadful happened in the body; that Criterion-B cognition, not the place, is the diagnosis.

4.4 The nosological shift: agoraphobia as a stand-alone diagnosis

Independent of panic. The examinable modern point is that both classifications now diagnose agoraphobia *independent of panic disorder*. DSM-5-TR states it outright: agoraphobia is diagnosed irrespective of the presence of panic disorder, and if a presentation meets criteria for both, *both* diagnoses are assigned (DSM-5-TR 2022). ICD-11 (6B02) similarly lists agoraphobia as its own category within the anxiety and fear-related disorders, with a "with panic attacks" specifier rather than a subordination to panic disorder (ICD-11 CDDR). This retired the old DSM-IV construct of "panic disorder with agoraphobia" and the notion that agoraphobia could not exist without a panic history.

The panic relationship in numbers. The link is real but not obligatory: the proportion of agoraphobia cases with panic attacks or panic disorder preceding onset ranges from about 30% in community samples to more than 50% in clinical samples, and agoraphobia without any preceding panic runs a mean age at onset of 25 to 29 years (DSM-5-TR 2022). Many patients avoid so completely that they no longer have attacks at all, which is exactly why tying the diagnosis to current panic was untenable.

PEARL

The single most exam-worthy fact about agoraphobia in ICD-11 and DSM-5-TR is that it is now a *free-standing* diagnosis, no longer a mere appendage of panic disorder. Where a patient meets both sets of criteria, code *both* (panic disorder *and* agoraphobia), not the old composite "panic disorder with agoraphobia". Heritability is high (about 61%), the highest and most phobia-specific of the phobias, another favourite one-liner.

4.5 Differential diagnosis: the boundaries an answer must draw

Against specific phobia. If only *one* agoraphobic situation is feared, diagnose specific phobia, situational type; two or more warrant agoraphobia (DSM-5-TR 2022). And if the situation is feared because of direct harm from the object (the plane crashing) rather than the escape/help cognition, it is again specific phobia.

Against the others. In *social anxiety disorder* the fear is of negative evaluation, so a fear confined to social scrutiny is social anxiety, not agoraphobia. In *PTSD* the person deliberately avoids trauma reminders, whereas in agoraphobia situations are avoided for fear of imminent bodily catastrophe with no escape (ICD-11 CDDR). In *separation anxiety disorder* the fear is of being apart from an attachment figure. And the organic and depressive mimics that colour every anxiety presentation, thyroid disease, arrhythmia, and secondary depression, are excluded as for panic disorder.

GOOD TO REMEMBER

- **Agoraphobia (the syndrome):** the defining criterion is marked fear/avoidance of *two or more of five* situations (public transport, open spaces, enclosed places, crowds or queues, being outside the home alone), feared specifically *because escape would be difficult or help unavailable* should panic-like or incapacitating/embarrassing symptoms strike (Criterion B); it must be persistent (six months or more) and out of proportion to sociocultural context; the discriminators are one-situation-only or object-directed fear (specific phobia), evaluative fear (social anxiety), trauma-reminder avoidance (PTSD); and, in the exam-critical shift, it is now diagnosed *independent of panic disorder*, with both coded if both are present.

4.6 Management overview: exposure-based CBT is the core

The treatment principle. The management of agoraphobia is, first and above all, *psychological and exposure-based*. CANMAT recommends cognitive behavioural therapy that uses *combined strategies including situational exposure* as first-line, noting that combined techniques outperform single techniques on agoraphobia measures (CANMAT 2014). NICE frames agoraphobia within panic-focused CBT: offer CBT for panic disorder *with or without agoraphobia* as first-line, delivered over about 7 to 14 hours across four months, with *in-vivo exposure for agoraphobic avoidance* as an explicit ingredient (NICE 2011). Where formal face-to-face therapy is impractical, minimal-intervention formats (self-help books, telephone or video delivery, internet-based CBT) are effective and cost-effective alternatives (CANMAT 2014).

Where drugs sit. Because agoraphobia so often travels with panic, the pharmacological backbone is the panic backbone: an SSRI is the first-line agent for the anxiety/panic component (the antidepressant class shared across the anxiety disorders, fluoxetine, sertraline, fluvoxamine, paroxetine, escitalopram), started low and titrated, with the tricyclics clomipramine (Anafranil) or imipramine as second-line agents that have meta-analytic efficacy for both panic and agoraphobia (CANMAT 2014). Medication is combined with exposure where agoraphobia is severe or rapidly worsening, or where CBT alone is likely to be insufficient (comorbid moderate-to-severe depression, frequent severe panic, or suicidal ideation) (CANMAT 2014).

LINE	TREATMENT	SOURCE
First-line	CBT with combined situational (in-vivo) exposure and cognitive restructuring	CANMAT 2014; NICE 2011
First-line (drug)	SSRI for the panic/anxiety component (start low, titrate, warn about early activation)	NICE 2011; BAP 2014
Second-line (drug)	**Clomipramine or imipramine (efficacy for both panic and agoraphobia)**	CANMAT 2014
Access alternative	Low-intensity or internet-based CBT, guided self-help	CANMAT 2014
Severe/rapid	Combined pharmacotherapy plus psychotherapy	CANMAT 2014

Guideline-level management of agoraphobia; exposure-based CBT is first-line, the SSRI carries the panic component, and the tricyclics clomipramine and imipramine are second-line (CANMAT 2014; NICE 2011).

4.7 Graded in-vivo exposure: how the core treatment actually works

What exposure agoraphobia treatment does. Graded in-vivo exposure is the active ingredient. The patient and therapist build a hierarchy of feared situations from least to most distressing (standing at the front door, walking to the gate, a short bus ride, the crowded market) and the patient enters them *repeatedly and in a graded way*, remaining until the anxiety falls, so that the escape-or-help catastrophe (Criterion B) fails to materialise and is disconfirmed (CANMAT 2014; NICE 2011). The exposures must be *real and in-vivo*, prolonged, and repeated across settings; the safety behaviours (the companion, the exit seat, the water bottle) are progressively dropped, because it is only exposure *without* the safety crutch that fully extinguishes the fear.

For those who decline formal therapy. For patients with persistent agoraphobic distress or avoidance who fear or decline formal CBT, the guideline is still exposure: provide instruction and support to engage in *graded exposure exercises* on their own or with minimal facilitation (CANMAT 2014). Where in-vivo entry is genuinely impractical, virtual-reality or interoceptive exposure can substitute or supplement, and where panic drives the avoidance, interoceptive exposure (deliberately inducing the feared body sensations) is added, as in panic-focused CBT.

TRAP **Exposure with the safety behaviours left in.** Sending a patient into the feared situation while they keep the companion, the exit seat and the escape route intact teaches nothing, the catastrophe is never disconfirmed. Grade the hierarchy, keep exposures prolonged and repeated, and *systematically drop the safety behaviours*; and never let avoidance itself go unaddressed while only prescribing a drug.

4.8 The Indian frame: the treatment gap, the benzodiazepine problem, and the IPS line

Genuine Indian context. Agoraphobia sits inside a large, mostly untreated anxiety burden in India: the anxiety, OCD and PTSD treatment gap means most sufferers never reach formal psychological care, and structured exposure-based CBT, the very treatment that is first-line, is scarce outside a handful of centres. Into that gap falls India's **benzodiazepine over-prescription**

problem: alprazolam and clonazepam are dispensed freely and often long-term for "ghabrahat", panic and phobic avoidance, which is precisely the wrong move, a benzodiazepine suppresses the very anxiety the patient needs to feel and habituate to during exposure, and can actively blunt the therapeutic effect of exposure work. The Indian Psychiatric Society CPGs keep the line clean: an SSRI or SNRI for the panic/anxiety component and CBT with systematic exposure as the treatment, not a chronic anxiolytic (IPS 2017). Indian brands are cheap and available: sertraline (Serta, Zosert, Daxid), escitalopram (Nexito, Cipralex), paroxetine (Paxidep), fluoxetine (Fludac), and clomipramine (Anafranil) for the second line. The correct Indian answer is graded in-vivo exposure plus a low-started, well-explained SSRI, never a standing benzodiazepine.

GOOD TO REMEMBER

- **Graded in-vivo exposure (the psychotherapy):** the first-line, core treatment of agoraphobia; its mechanism is repeated, graded, prolonged entry into the feared situations so the escape-or-help catastrophe of Criterion B is disconfirmed and the fear extinguishes; the signature caution is that *safety behaviours must be dropped* and a concurrent benzodiazepine avoided (both prevent habituation); combined CBT (exposure plus cognitive restructuring) outperforms single techniques, with the SSRI carrying the panic component and clomipramine or imipramine as the second-line drug.

2 of 5	6 months	7 to 14 h	61%
SITUATIONS FEARED, REQUIRED FOR CRITERION A	MINIMUM DURATION FOR THE DIAGNOSIS (CRITERION F)	CBT WITH IN-VIVO EXPOSURE OVER ABOUT 4 MONTHS (NICE)	HERITABILITY, THE MOST PHOBIA-SPECIFIC OF THE PHOBIAS

HOLD THIS

Agoraphobia is fear and avoidance of two or more of five situations (public transport, open spaces, enclosed places, crowds or queues, being outside the home alone), feared *because escape would be difficult or help unavailable* if a panic-like or incapacitating symptom struck; it is now diagnosed independent of panic disorder (code both if both present), and its first-line treatment is graded in-vivo exposure within CBT, with an SSRI for the panic component and the benzodiazepine kept firmly out.

5 · Social anxiety disorder

Social anxiety disorder (still widely called **social phobia**) is the disorder of a marked, persistent **fear of scrutiny** and of negative evaluation in social situations. Where generalised anxiety disorder is free-floating and panic is episodic and cued-by-nothing, this fear is *bound to the social gaze*: the patient dreads acting in a way, or showing anxiety symptoms, that others will judge as humiliating, embarrassing or offensive, and so avoids or endures with dread the very situations, conversations, meetings, eating in front of others, public speaking, in which that scrutiny might fall on them. Examiners like it because it carries a clean, high-yield distinction, the **generalised** subtype versus the **performance-only** specifier, and because its management is the anxiety-block template with one signature twist: the beta-blocker for discrete **performance anxiety**.

Why it matters, and how this note is framed. This is a hybrid topic: it teaches the diagnosis and its discrimination, then the guideline-anchored drug and psychotherapy plan. The core

discriminator to lead with is the *object* of the fear, negative evaluation by others, which is what separates social anxiety disorder from specific phobia (feared object), agoraphobia (fear that escape is impossible or help unavailable) and separation anxiety (fear of separation from an attachment figure). The amygdala and fear-circuit substrate is developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the deep SSRI pharmacology in the Mood disorders: pharmacotherapy notes; the general CBT and exposure model in the Psychotherapies, clinical assessment, MSE and nosology notes; and the benzodiazepine, pregabalin and buspirone story in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes. What this note owns is the phenomenology, the subtype split, the criteria, the LSAS, and the management.

5.1 The core concept: fear of scrutiny and of negative evaluation

The essential feature. The heart of the disorder is a marked, intense fear or anxiety about one or more social situations in which the individual is exposed to *possible scrutiny by others* (DSM-5-TR 2022). The dreaded outcome is not the situation itself but the judgement it invites: the person is concerned they will act in a way, or show visible anxiety, blushing, trembling, sweating, stumbling over words, that will be negatively evaluated as humiliating, embarrassing, or leading to rejection or offence. This fear of negative evaluation is the cognitive engine, and naming it is what earns the marks.

The three feared arenas. The scrutiny is dreaded across three kinds of situation: social *interactions* (having a conversation, meeting unfamiliar people), being *observed* (eating or drinking in front of others), and *performing* before others (giving a speech). Blushing is described as the hallmark physical response of the disorder (Kaplan and Sadock 2024). A useful clinical texture: some patients avoid public toilets when others are present (paruresis, "shy bladder"), and self-medication with alcohol before a social event is common.

GOOD TO REMEMBER

- **Social anxiety disorder (social phobia):** a marked, persistent fear of one or more social situations involving possible scrutiny, driven by the fear of negative evaluation (that one will be judged humiliating, embarrassing, weak or offensive); the defining discriminator from the other anxiety disorders is that the feared object is *the judgement of others*; blushing is the hallmark physical sign, and the first diagnostic step is to establish that the fear is of negative evaluation and out of proportion to the actual social threat.

5.2 Generalised versus performance-only: the subtype split to know cold

The one specifier DSM-5-TR keeps. DSM-5-TR replaced the old "generalised" subtype with a single specifier, *performance only*: the fear is **restricted to speaking or performing in public** (DSM-5-TR 2022). By default, without the specifier, the fear spans a broad range of social and interactional situations, the **generalised** picture, which is more chronic, more impairing and more comorbid. The **performance-only** group, by contrast, do not fear or avoid non-performance social situations; their impairment falls in professional lives that demand public performance, musicians, dancers, athletes, and in roles requiring regular public speaking.

Why the split drives treatment. The distinction is not cosmetic: it steers the prescription. Generalised social anxiety needs a serotonergic antidepressant and CBT. Discrete **performance anxiety** can be covered situationally, as needed, with a beta-blocker taken before the feared performance, an option that has no place in the generalised form. This is exactly why the subtype question is examinable.

FEATURE	GENERALISED (DEFAULT)	PERFORMANCE-ONLY SPECIFIER
Situations feared	**Broad: interactions, observation and performance**	Restricted to speaking/performing in public
Non-performance social situations	Feared and avoided	**Not feared or avoided**
Typical impairment	Pervasive; more chronic and comorbid	Focused on public-performance roles
First-line treatment	SSRI (or SNRI) plus CBT	**Situational beta-blocker for the discrete event**

The generalised picture versus the DSM-5-TR performance-only specifier; the split is high-yield because it changes the drug (serotonergic antidepressant versus as-needed beta-blocker).

RULE **Subtype sets the drug.** Generalised social anxiety disorder is treated with an SSRI (or SNRI) plus CBT; the discrete performance-only picture can be covered situationally with a beta-blocker before the event, which has no role in the generalised form.

5.3 DSM-5-TR criteria: marked fear, negative evaluation, six months

The criteria to state cleanly. DSM-5-TR requires (A) marked fear or anxiety about one or more social situations involving possible scrutiny; (B) the individual fears they will act, or show anxiety symptoms, that will be negatively evaluated; (C) the situations almost always provoke fear or anxiety; (D) they are avoided or endured with intense fear; (E) the fear is out of proportion to the actual threat and to the sociocultural context; (F) it is persistent, **typically lasting 6 months or more**; (G) it causes clinically significant distress or impairment; (H) it is not attributable to a substance or another medical condition; and (I) it is not better explained by another mental disorder (DSM-5-TR 2022). The specifier is *performance only*.

The paediatric qualifier. In children the anxiety must occur in *peer settings* and not only during interactions with adults, and the fear may be expressed by crying, tantrums, freezing, clinging or failing to speak. That "peer settings" caveat is a favourite discriminator.

CRITERION	DSM-5-TR REQUIREMENT
A. Fear	**Marked fear/anxiety about social situation(s) with possible scrutiny (interaction, observation, performance)**
B. Feared outcome	**Fear of acting or showing anxiety that will be negatively evaluated (humiliating, embarrassing, rejecting, offensive)**

CRITERION	DSM-5-TR REQUIREMENT
C. Consistency	The situations almost always provoke fear or anxiety (in children, may show as crying/tantrums/freezing)
D. Avoidance	Situations avoided or endured with intense fear or anxiety
E. Proportion	Out of proportion to the actual threat and to the sociocultural context
F. Duration	**Persistent, typically 6 months or more**
G. Impairment	Clinically significant distress or social/occupational impairment
H. Not organic	Not due to a substance or another medical condition
I. Not better explained	Not better explained by panic disorder, body dysmorphic disorder, autism spectrum disorder and others
Specifier	**Performance only: fear restricted to speaking or performing in public**

DSM-5-TR criteria for social anxiety disorder; the numbers to hold are the 6-month typical duration and the single performance-only specifier (DSM-5-TR 2022).

5.4 ICD-11 CDDR: marked and excessive fear, "at least several months"

Where ICD-11 frames it. ICD-11 (6B04) requires marked and excessive fear or anxiety that occurs *consistently* in one or more social situations, social interaction, being observed, or performing, with the concern that one will act, or show anxiety symptoms, that will be negatively evaluated (humiliating, embarrassing, leading to rejection or offence); the situations are consistently avoided or endured with intense fear; the symptoms are not transient and persist for **at least several months**; and they cause significant distress or impairment (ICD-11 CDDR). As across the anxiety block, ICD-11 does *not* impose the DSM's fixed 6-month clock, asking instead for "at least several months", the classic ICD-versus-DSM contrast to name.

The ICD-11 specifier. ICD-11 offers a "with panic attacks" qualifier rather than a performance-only one, so if you are asked about the performance-only distinction, that is a DSM-5-TR construct; ICD-11 codes the panic-attack overlay instead.

TRAP **Do not miss the medical and psychiatric mimics.** Blushing, tremor and palpitations before scrutiny can equally be hyperthyroidism, a phaeochromocytoma or excess caffeine; and fear of being looked at can be body dysmorphic disorder (fear centred on a perceived defect) or the social withdrawal of autism, not social anxiety, so exclude the organic mimic and check that the fear is genuinely of *negative evaluation*.

GOOD TO REMEMBER

- **ICD-11 social anxiety disorder (6B04):** marked, excessive, consistent fear of social situations with concern about negative evaluation, consistent avoidance, persisting at least several months, with distress or impairment; the defining contrast with DSM-5-TR is the absence of a fixed 6-month rule and a "with panic attacks" specifier in place of DSM's performance-only one.

5.5 The Liebowitz Social Anxiety Scale (LSAS): the severity instrument

What it is. The Liebowitz Social Anxiety Scale (**lsas**), developed by Michael Liebowitz in 1987, is the standard instrument for assessing social anxiety. It is a **24-item** scale that rates both *fear* and *avoidance* across 24 social and performance situations, each dimension scored **0 to 3**, splitting into a social-interaction subscale and a performance subscale (AIIMS Clinical Methods 2024; Kaplan and Sadock 2024). It exists in clinician-administered and self-rated forms; it is copyright-protected, so permission is needed to use it, and it is set out on the accompanying scale plate rather than reproduced here.

How it is used. The LSAS is the workhorse outcome measure in social anxiety trials, drug effects are reported as points reduced on the LSAS, and it is what tracks response over a treatment course. For quick case-finding, NICE instead recommends the 3-item Mini-Social Phobia Inventory (Mini-SPIN) or two screening questions, referring for full assessment if positive (NICE 2013). The through-line: Mini-SPIN to screen, LSAS to grade severity and follow response.

GOOD TO REMEMBER

- **LSAS (Liebowitz 1987):** a 24-item scale rating fear and avoidance across 24 situations, each 0 to 3, with social-interaction and performance subscales; it is the standard severity and outcome measure in social anxiety disorder (drug effects are reported as LSAS point reductions); contrast with the 3-item Mini-SPIN, which is the rapid screen.

5.6 Management: SSRI first-line and CBT, across the guidelines

Lead with BAP. The British Association for Psychopharmacology (BAP) makes an SSRI the first-line pharmacological treatment for social anxiety disorder, the efficacious agents named being escitalopram, fluoxetine, fluvoxamine, paroxetine and sertraline; it also offers cognitive behavioural therapy (cognitive therapy plus exposure) as an efficacious acute treatment of broadly similar efficacy to pharmacotherapy, and names the SNRI venlafaxine, the MAOI phenelzine and the RIMA moclobemide as alternative antidepressants (BAP 2014). This is the verified **SSRI first-line** anchor and must not be contradicted. BAP adds a pointed negative: *do not* prescribe atenolol or buspirone for generalised social anxiety disorder, as neither is efficacious (BAP 2014).

Then the other bodies. The convergence is striking. NICE puts individual CBT specifically developed for social anxiety disorder (the Clark and Wells or Heimberg model) as the *first-line* treatment for adults, and offers an SSRI (escitalopram or sertraline) if the adult declines psychological therapy and prefers medication, with an alternative SSRI (fluvoxamine or paroxetine) or the SNRI venlafaxine at the next step, and a MAOI (phenelzine or moclobemide) after that (NICE 2013). CANMAT lists first-line agents as escitalopram, fluvoxamine (including

CR), paroxetine (including CR), sertraline, venlafaxine XR or pregabalin, with CBT (cognitive restructuring plus exposure) as the gold-standard first-line psychotherapy (CANMAT 2014). The Indian Psychiatric Society does publish CPGs across the anxiety disorders and champions SSRI-plus-CBT for the anxiety block, but a dedicated social-anxiety-disorder recommendation could not be confirmed in the verified supplement, so its precise position is flagged under gaps rather than asserted here. The shared exam message: *SSRI first-line and CBT everywhere*.

GUIDELINE	FIRST-LINE	KEY NOTE
BAP 2014	**SSRI (escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline); CBT**	Do not use atenolol or buspirone for generalised SAD
NICE 2013	**Individual CBT (Clark & Wells / Heimberg); SSRI (escitalopram or sertraline) if medication preferred**	Do not routinely offer benzodiazepines/TCAs/antipsychotics
CANMAT 2014	SSRI/venlafaxine XR/pregabalin; CBT first-line	Beta-blockers not for generalised SAD; may help discrete performance
Indian Psychiatric Society	SSRI/SNRI with CBT (anxiety-block position)	Dedicated SAD recommendation unconfirmed (see gaps)

First-line treatment for social anxiety disorder; the shared message is an SSRI (or SNRI) plus CBT, with the beta-blocker reserved for discrete performance situations only.

RULE **SSRI plus CBT is first-line for social anxiety disorder.** BAP names an SSRI (escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline) first-line with CBT of similar efficacy; NICE puts disorder-specific CBT first and an SSRI if medication is preferred; CANMAT agrees. Venlafaxine, phenelzine and moclobemide are the antidepressant alternatives.

GOOD TO REMEMBER

- **SSRI in social anxiety disorder:** the mechanism is serotonergic (serotonin reuptake blockade with downstream receptor adaptation); it is first-line for the generalised disorder (escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline per BAP), needs an adequate trial before response is judged, and, once effective, is continued for at least a further 6 months because social anxiety disorder is chronic with high symptom re-emergence on stopping.

5.7 Propranolol for discrete performance anxiety, and what NOT to use

The one situational role. For discrete **performance anxiety**, a beta-blocker taken before the feared event is a recognised as-needed option. Propranolol (Indian brands Ciplar, Inderal), a non-selective beta-adrenergic blocker, is long-established as useful particularly for the performance situation, because it damps the peripheral autonomic symptoms, hand tremor and tachycardia, that the performer both feels and fears will be seen (Kaplan and Sadock 2024). The critical caveat: it has *no* effect on anticipatory anxiety or on the generalised disorder, so its use is strictly the discrete, foreseeable performance, taken before going on.

The important negatives. The beta-blocker is explicitly *not* a treatment for generalised social anxiety disorder: BAP says do not prescribe atenolol for it, and CANMAT lists propranolol and

atenolol among agents not recommended for the generalised disorder while conceding beta-blockers "may still help discrete performance situations" (BAP 2014; CANMAT 2014). Buspirone, too, is not efficacious as monotherapy for generalised social anxiety disorder (BAP 2014). And the benzodiazepine is not first-line and should not be a maintenance treatment: NICE says do not routinely offer benzodiazepines (alongside TCAs, anticonvulsants and antipsychotics) for social anxiety disorder in adults (NICE 2013).

WORKED EXAMPLE

A 24-year-old violinist has crippling tremor and a pounding heart only in the minutes before a solo recital; away from the stage she is socially at ease and has no other feared situations. This is the performance-only picture. The correct move is a beta-blocker, propranolol taken before the performance, to blunt the tremor and tachycardia she fears will be visible; it will not touch anticipatory dread and is not a daily treatment. Contrast a 30-year-old who avoids conversations, meetings, eating out and phone calls across his whole life, the generalised disorder, where the answer is an SSRI plus CBT, and a beta-blocker would be the wrong tool.

GOOD TO REMEMBER

- **Propranolol (Ciplar, Inderal) for performance anxiety:** a non-selective beta-blocker that damps the peripheral autonomic signs (tremor, tachycardia) of discrete performance anxiety when taken before the event; the signature caution is that it does nothing for anticipatory anxiety or for generalised social anxiety disorder, for which it is not recommended; check for asthma and bradycardia before prescribing.

5.8 CBT: the first-line psychotherapy and the partial-response rule

What disorder-specific CBT does. CBT is the first-line psychological treatment; NICE specifies *individual* CBT developed for social anxiety disorder, following the Clark and Wells or the Heimberg model, over group CBT, which it found less clinically and cost effective (NICE 2013). Its ingredients are cognitive restructuring of the fear of negative evaluation and the self-focused, distorted self-image, plus graded exposure to feared social situations, and it targets the safety behaviours (over-rehearsing, avoiding eye contact, gripping the glass) that maintain the belief that catastrophe was only just averted. Delivered well, it produces durable benefit that can outlast medication.

The partial-response rule. A clean examinable step: for an adult whose symptoms have only *partially* responded to an SSRI after **10 to 12 weeks**, NICE says add individual CBT to the SSRI; for a partial response to CBT, consider adding a pharmacological intervention (NICE 2013). So the initial trial length before judging partial response is 10 to 12 weeks, and the response to incomplete benefit is to combine, not to abandon.

GOOD TO REMEMBER

- **CBT for social anxiety disorder:** the principle is cognitive restructuring of the fear of negative evaluation plus graded exposure and the dropping of safety behaviours (Clark and Wells or Heimberg model); it is first-line and individual is preferred over group (NICE); the signature rule is that partial response to an SSRI at 10 to 12 weeks is managed by *adding* CBT, not switching away.

INDIA

Social anxiety disorder sits inside India's large, mostly untreated anxiety burden, most sufferers never reach formal care, and it is easily mistaken for "shyness" or a personality trait and left undiagnosed for years. It also collides with the country's benzodiazepine over-prescription problem: alprazolam and clonazepam are dispensed freely, often long-term, for "nervousness" before social or performance situations, which is exactly what NICE and BAP warn against, the benzodiazepine is not first-line and not a maintenance treatment. The correct Indian answer is a low-cost, widely available SSRI plus CBT for the generalised disorder, sertraline (Serta, Zosert, Daxid), escitalopram (Nexito, Cipralex), paroxetine (Paxidep) or fluoxetine (Fludac), with propranolol (Ciplar, Inderal) reserved for the discrete performer. The Indian Psychiatric Society CPGs anchor the SSRI-plus-CBT approach for the anxiety disorders; a dedicated social-anxiety-disorder recommendation could not be confirmed in the verified supplement and is flagged rather than invented.

24	6 months	10 to 12 weeks
LSAS ITEMS (FEAR + AVOIDANCE, EACH RATED 0 TO 3)	DSM-5-TR TYPICAL DURATION FOR SOCIAL ANXIETY DISORDER	SSRI TRIAL BEFORE ADDING CBT FOR PARTIAL RESPONSE (NICE)

HOLD THIS

Social anxiety disorder is fear of negative evaluation under scrutiny: SSRI (escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline) plus CBT first-line for the generalised disorder, propranolol before the event for discrete performance anxiety only, and never a benzodiazepine as maintenance.

6 · Specific phobias

The **specific phobia** is the purest of the anxiety disorders: a fear that is not free-floating, not episodic and not social, but bound tight to one circumscribed object or situation, so that the anxiety switches on the moment the thing is met and switches off the moment it is gone. It is also the commonest anxiety disorder in the community and the anxiety disorder examiners most like to test as a discrimination exercise, because the whole diagnosis turns on a single feature, the **circumscribed phobic stimulus**, and because it carries two facts that appear nowhere else in the anxiety block: the diphasic vasovagal response of the **blood-injection-injury** subtype, and the **applied-tension technique** that is its bespoke treatment.

Why it matters, and what this note owns. Specific phobia is the disorder against which the other anxiety disorders are carved, GAD is diffuse, panic is episodic and unexpected, social anxiety fears evaluation, agoraphobia fears escape being difficult, whereas specific phobia is cued and only cued. What this note owns is the subtype classification (with the fainting subtype and its coping skill), the DSM-5-TR and ICD-11 criteria, and the exposure-based treatment that is the treatment of choice. The general CBT model and the wider exposure principle behind all of this are developed in the Psychotherapies, clinical assessment, MSE and nosology notes and are not re-derived here; the amygdala and fear-circuit anatomy that lights up to a phobic stimulus lives in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

6.1 The core concept: a cued, circumscribed, out-of-proportion fear

The defining quality. The essence of a specific phobia is that the fear is *circumscribed* to a particular object or situation, the phobic stimulus, and is out of proportion to the actual danger it poses (DSM-5-TR 2022; ICD-11 CDDR). Unlike the other anxiety disorders, no specific dysfunctional cognition defines it: the person is simply and immediately afraid of the thing itself. The fear is evoked *nearly every time* the stimulus is met (it is reliable and cued, not "out of the blue"), it comes on immediately rather than being delayed, and it drives active avoidance, or, where the situation cannot be avoided, endurance with intense distress.

The old name. The specific phobia was called simple phobia in earlier classifications (DSM-III-R and ICD-10 "simple phobia"), and the terms are interchangeable in exam answers; "specific" replaced "simple" to signal the tie to a specific stimulus rather than any simplicity of the condition.

GOOD TO REMEMBER

- **Specific phobia (simple phobia):** a marked, out-of-proportion fear cued reliably and immediately by one circumscribed object or situation, leading to active avoidance or distressed endurance; the defining discriminator is that the fear is *bound to the stimulus* (cued and only cued), with no defining cognition, which separates it from the diffuse worry of GAD, the unexpected attacks of panic, and the evaluation fear of social anxiety.

6.2 The five subtypes: animal, natural environment, blood-injection-injury, situational, other

The DSM-5-TR specifiers. Specific phobia is coded by the type of phobic stimulus, and DSM-5-TR recognises five families (DSM-5-TR 2022): **animal** (spiders, insects, dogs), **natural environment** (heights, storms, water, darkness), **blood-injection-injury** (blood, needles, invasive medical or dental procedures, injury), **situational** (aeroplanes, lifts, enclosed places, driving), and **other** (situations that might lead to choking or vomiting; in children, loud sounds or costumed characters). When more than one stimulus is feared, each is coded separately, and this is the rule rather than the exception: the average patient with specific phobia fears three objects or situations, and roughly three-quarters fear more than one.

The classic eponyms. The Greek-derived names are worth recognising: acrophobia (heights), zoophobia (animals), claustrophobia (enclosed spaces), algophobia (pain), xenophobia (strangers), and, of the fainting subtype, the fear of blood, injection and injury. The list of named phobias is virtually endless, but the exam-relevant work is done by the five subtypes, not the eponyms.

SUBTYPE	TYPICAL STIMULI	AUTONOMIC SIGNATURE AND PEARL
Animal	Spiders, insects, dogs, snakes	Sympathetic arousal; earliest onset, more common in younger children and in females
Natural environment	Heights, storms, water, darkness	Sympathetic arousal; younger onset for water/weather
Blood-injection-injury	Blood, needles, injury, medical/dental procedures	**Diphasic vasovagal response with fainting; the only subtype with equal sex ratio and a familial pattern; treat with applied tension**
Situational	Aeroplanes, lifts, enclosed places, driving	Sympathetic arousal; older onset (flying, heights); overlaps with panic/agoraphobia
Other	Choking, vomiting; in children loud sounds, costumed figures	Heterogeneous residual category

The five DSM-5-TR specific-phobia subtypes; the one that carries all the special facts is blood-injection-injury (DSM-5-TR 2022). ICD-11 6B03 sets no subtype specifiers, its only specifier being "with panic attacks".

GOOD TO REMEMBER

- **Subtypes:** animal, natural environment, blood-injection-injury, situational and other; the average patient fears three stimuli and each is coded separately; the blood-injection-injury subtype is the exam favourite because it alone shows the diphasic vasovagal faint, has an equal sex ratio, runs in families, and is treated with applied tension rather than exposure alone.

6.3 The blood-injection-injury subtype: the diphasic vasovagal response

Why it is unique. Every other phobia produces plain sympathetic arousal, a racing heart and rising blood pressure that stay up until escape. The blood-injection-injury subtype does something different and diagnostic: it produces a **diphasic** (biphasic) autonomic response. There is a brief initial acceleration of heart rate and a rise in blood pressure, followed by an abrupt *deceleration* of heart rate and a *fall* in blood pressure, a vasovagal reflex that commonly ends in fainting (vasovagal syncope) at the sight of blood, a needle or an injury (DSM-5-TR 2022). This is the one anxiety presentation in which the patient does not run but falls: the fainting is the presenting feature and the reason the person avoids donating blood, having dental work, or attending for injections.

The other quirks. Two more facts hang off this subtype and are heavily tested. First, sex ratio: whereas specific phobias overall run about 2:1 female-to-male, the blood-injection-injury subtype affects men and women roughly equally (ICD-11 CDDR). Second, it has the strongest familial pattern of the phobias, a heritable tendency to the vasovagal faint. Recognising the diphasic pattern matters clinically because the ordinary phobia instruction, "relax", would lower blood pressure further and precipitate the faint the patient fears.

RULE **Blood-injection-injury faints; the rest run.** Only the blood-injection-injury subtype shows the diphasic vasovagal response (a brief pressor phase then a bradycardic hypotensive drop to syncope); every other subtype shows sustained sympathetic arousal, so recognising the faint identifies the subtype and dictates applied tension rather than relaxation.

GOOD TO REMEMBER

- **Blood-injection-injury phobia:** the criterion-defining feature is the diphasic vasovagal response, an initial brief rise in heart rate and blood pressure followed by a vagally mediated fall in both, ending in fainting at the sight of blood/needles/injury; it uniquely has an equal sex ratio and the strongest familial loading, and it is the one subtype where relaxation is contraindicated and applied tension is the treatment of choice.

6.4 Applied tension: the bespoke treatment for the fainting subtype

What it is. Applied tension is the coping skill developed by Lars-Goran Ost and colleagues specifically for the blood-injection-injury subtype (Ost, Sterner and Fellenius 1989). The patient is taught to repeatedly *tense* the large muscle groups of the arms, legs and trunk for about 10 to 15 seconds, release to normal (not to relaxation) for 20 to 30 seconds, and repeat five times, applying the technique at the first sign of the pressure drop when confronting the phobic stimulus. The tensing raises blood pressure, counteracts the vasovagal fall, and thereby prevents the faint that maintains the avoidance.

Why it beats plain exposure here. Ost concluded that applied tension should be the treatment of choice for blood phobia, and a dismantling study showed that tension alone was almost as effective as full applied tension (tension plus exposure), while exposure alone was considerably less effective (Craske, Antony and Barlow 2006). The teaching point is that in this one subtype the coping skill, keeping the blood pressure up, matters more than habituation, which is exactly why the generic "relax during exposure" instruction is wrong here.

COMMON TRAP

Do not teach relaxation to a blood-injection-injury phobic. Relaxation lowers blood pressure and, in a patient whose problem is a vasovagal pressure drop to syncope, it precipitates the very faint being treated. The correct skill is applied tension (repeated large-muscle tensing to raise blood pressure), not relaxation; confusing the two is the classic exam and clinical error for this subtype.

GOOD TO REMEMBER

- **Applied tension (Ost):** the treatment of choice for the blood-injection-injury subtype; repeated tensing of large muscle groups (about 10 to 15 seconds on, 20 to 30 seconds off, five cycles) raises blood pressure and aborts the vasovagal faint; the mechanism is counteracting the pressure drop, not habituation, so it is used *instead of* relaxation and is combined with graded exposure to the feared stimulus.

6.5 DSM-5-TR criteria: marked fear, immediate, avoided, out of proportion, six months

The criteria to state cold. DSM-5-TR requires a marked fear or anxiety about a specific object or situation (Criterion A); the phobic stimulus almost always provokes immediate fear or anxiety (B);

the stimulus is actively avoided or endured with intense fear (C); the fear is out of proportion to the actual danger and the sociocultural context (D); the fear, anxiety or avoidance is persistent, typically **6 months or more** (E); it causes clinically significant distress or impairment (F); and it is not better explained by another mental disorder (G) (DSM-5-TR 2022). In children the fear may present as crying, tantrums, freezing or clinging, and the child need not recognise the fear as excessive.

The two discriminators inside the criteria. Criterion B ("almost always" and "immediate") is what separates a true phobia from an occasional situational nerviness: the person who is anxious on only one flight in five does not qualify. Criterion D moves the judgement of "out of proportion" to the clinician, taking cultural context into account (a fear of the dark may be reasonable where night-time assault is common).

CRITERION	DSM-5-TR REQUIREMENT
A. Marked fear	**Marked fear/anxiety about a specific object or situation (in children: crying, tantrums, freezing, clinging)**
B. Immediate/reliable	**The phobic stimulus almost always provokes immediate fear or anxiety**
C. Avoidance	Actively avoided, or endured with intense fear or anxiety
D. Out of proportion	Fear out of proportion to actual danger and to sociocultural context (clinician judges)
E. Duration	**Persistent, typically 6 months or more**
F. Impairment	Clinically significant distress or functional impairment
G. Not better explained	Not better explained by another disorder (agoraphobia, OCD, PTSD, separation anxiety, social anxiety)

DSM-5-TR criteria for specific phobia; the numbers to hold are the 6-month duration and the "almost always / immediate" reliability of Criterion B (DSM-5-TR 2022).

GOOD TO REMEMBER

- **Specific phobia (DSM-5-TR):** marked fear of a circumscribed stimulus that almost always and immediately provokes anxiety (Criterion B), is avoided or endured with distress, is out of proportion to the real danger, persists 6 months or more, and impairs functioning; the first diagnostic step is to confirm the fear is *cued and reliable* and then to exclude that it is better explained by agoraphobia, OCD, PTSD, separation or social anxiety (Criterion G).

6.6 ICD-11 CDDR and the differential: what to exclude

Where ICD-11 sits. The ICD-11 CDDR essential features mirror DSM closely: marked and excessive fear or anxiety that consistently occurs on exposure or anticipated exposure to one or more specific objects or situations, out of proportion to the actual danger; the stimulus is actively avoided or endured with intense fear; the pattern is not transient, persisting for at least **several**

months; it is not better accounted for by another disorder; and it causes significant distress or impairment (ICD-11 CDDR). As across the anxiety block, ICD-11 uses the softer "at least several months" rather than DSM's fixed 6-month clock.

The differential. The work is in Criterion G. If the avoided situations are feared because escape would be difficult or help unavailable in a panic, it is agoraphobia. If the fear is of contamination or driven by an obsession, it is OCD, not a phobia (the hand-washer who avoids door handles has OCD). If the avoidance is of trauma reminders, it is PTSD. If it is fear of scrutiny and negative evaluation, it is social anxiety disorder. If it is fear of separation from an attachment figure, it is separation anxiety. And medical mimics of situational fear (for example genuine cardiac or vestibular disease presenting as fear of exertion or heights) are excluded first.

GOOD TO REMEMBER

- **ICD-11 specific phobia:** marked, excessive, out-of-proportion fear consistently cued by one or more specific stimuli, actively avoided or endured with intense fear, not transient (at least several months), with distress or impairment; the discriminator from its neighbours is the *reason* for the fear, of the stimulus itself in phobia, versus escape difficulty (agoraphobia), obsessions (OCD), trauma reminders (PTSD), evaluation (social anxiety) or separation (separation anxiety).

6.7 Epidemiology and course: the commonest anxiety disorder, earliest onset

The numbers. Specific phobia is the most prevalent anxiety disorder, with a 12-month community prevalence of about **8 to 12 per cent** in the United States (around 6 per cent in Europe, lower at 2 to 4 per cent in Asian, African and Latin American surveys) (DSM-5-TR 2022). It is roughly **twice as common in women** as in men across most subtypes, the exception being blood-injection-injury, which is equal. Onset is early, most commonly in childhood between 7 and 10 years of age, and specific phobias that persist from childhood rarely remit spontaneously.

Course and comorbidity. Animal and natural-environment phobias tend to the earliest onset; situational phobias such as flying and heights begin later. Patients report high lifetime rates of co-occurring depressive and other anxiety disorders, and in most cases the specific phobia comes *first* and precedes the other disorder, which is why it is a useful early marker.

8 to 12%	6 months	2:1	7 to 10 yrs
12-MONTH US PREVALENCE, THE COMMONEST ANXIETY DISORDER	DSM-5-TR MINIMUM DURATION (ICD-11: SEVERAL MONTHS)	FEMALE-TO-MALE RATIO (EQUAL IN BLOOD-INJECTION-INJURY)	TYPICAL AGE OF ONSET

6.8 Treatment: graded in-vivo exposure is the treatment of choice

Behavioural first, not drugs. The treatment of choice for specific phobia is *exposure-based* behaviour therapy, not medication; meta-analyses show very large effect sizes that are stable for at least a year (Craske, Antony and Barlow 2006). The workhorse is graded in-vivo exposure: the patient builds an **exposure hierarchy** (feared tasks rated 0 to 100 for anxiety, ordered from least to most provoking) and then repeatedly, systematically confronts the real phobic stimulus, starting low and climbing the ladder, until the feared catastrophe fails to occur and new, non-fearful learning takes hold. Modern practice reframes the goal not as staying until fear declines

but as staying long enough to *learn* that the feared outcome does not happen and that anxiety can be tolerated (inhibitory-learning model).

How fast it works. Specific phobia is unusually treatable: animal and blood phobias often respond to a single, prolonged session of exposure lasting two to three hours (Ost). No routine drug is indicated; a short-acting benzodiazepine or beta-blocker is at most an occasional aid for a discrete one-off exposure (for example a single flight) and is never the treatment, because it undermines the corrective learning that exposure depends on.

TRAP **Do not reach for a drug (or a benzodiazepine) as the treatment for a specific phobia.** The evidence-based treatment is graded in-vivo exposure; medication is not first-line, and a benzodiazepine taken to get through exposure blunts the fear-extinction learning that makes exposure work, so it undermines the very treatment.

GOOD TO REMEMBER

- **Graded in-vivo exposure:** the treatment of choice for specific phobia; the principle is repeated, systematic confrontation with the real phobic stimulus up a rated exposure hierarchy until the feared outcome is disconfirmed and anxiety is tolerated (inhibitory learning); it can work in a single 2 to 3 hour session for animal and blood phobias, and drugs are not first-line.

6.9 Systematic desensitisation and flooding: the two ends of the exposure spectrum

Systematic desensitisation. Systematic desensitisation is Joseph Wolpe's original method (Psychotherapy by Reciprocal Inhibition, 1958): the patient is taught deep muscle relaxation, an anxiety hierarchy is constructed, and the phobic stimuli are then paired, one graded step at a time, with the incompatible relaxation response, usually imaginally at first. Wolpe's mechanism was **reciprocal inhibition** (counter-conditioning): the relaxation response inhibits the anxiety response so the stimulus can be faced without fear. It is *gradual* and pairs each step with relaxation. Note the practical implication for the fainting subtype: because desensitisation uses relaxation, blood-injection-injury phobia is instead paired with applied tension.

Flooding. Flooding is the opposite pole: the patient is exposed to the most feared stimulus at full intensity from the outset, with no hierarchy and no graded climb, and stays in the situation until the anxiety, which cannot be sustained indefinitely, extinguishes. It is faster but more distressing and less tolerable, so graded exposure and desensitisation are generally preferred. The three methods sit on one spectrum, gradual-with-relaxation (systematic desensitisation), gradual real-life (graded in-vivo exposure), and all-at-once (flooding), and share the single active ingredient of exposure with prevention of avoidance.

MNEMONIC

SAFE-D

The specific-phobia essentials. **S**pecific circumscribed stimulus (cued, immediate, Criterion B); **A**void or endure with distress; **F**ive subtypes (animal, natural environment, blood-injection-injury, situational, other); **E**xposure is the treatment (graded in-vivo, systematic desensitisation, flooding); **D**iphasic vasovagal faint marks blood-injection-injury, treated with applied tension.

GOOD TO REMEMBER

- **Systematic desensitisation (Wolpe):** graded exposure up an anxiety hierarchy paired with deep relaxation; mechanism is reciprocal inhibition (relaxation inhibits anxiety); signature caution is that its reliance on relaxation makes it unsuitable, as-is, for the blood-injection-injury subtype, where applied tension replaces relaxation.
- **Flooding:** ungraded exposure to the most feared stimulus at full intensity from the outset until anxiety extinguishes; faster than graded methods but poorly tolerated, so it is not first-choice; the active ingredient it shares with all exposure is sustained contact with prevention of avoidance.

6.10 The India lens: a common, treatable disorder lost in the treatment gap

The genuine Indian point. Specific phobia is common, it presents early, and it is one of the most treatable conditions in psychiatry, a few sessions of exposure can resolve a fear that has constrained a life for decades. Yet in India it sits squarely inside the anxiety treatment gap: most people with a phobia never reach care, the fear is normalised or somatised, and when they do present the reflex prescription in general and primary care is a benzodiazepine (typically alprazolam), which is neither first-line nor a treatment for phobia at all and only undermines the exposure learning that would actually help. The correct Indian answer mirrors the global one: graded in-vivo exposure is the treatment, applied tension for the fainting subtype, and the benzodiazepine is at most a rare, single-exposure aid, never the plan. Where a drug is genuinely considered a beta-blocker such as propranolol (Indian brands Ciplar, Inderal) can blunt peripheral autonomic symptoms for a discrete situational exposure, but it too is an adjunct, not the treatment.

INDIA

The highest-yield Indian point is that specific phobia is common, early-onset and highly treatable with a short course of exposure, yet it is routinely lost in the anxiety treatment gap and met, when it does present, with a long-term benzodiazepine (usually alprazolam) that runs against the Indian Psychiatric Society CPG stance on anxiety and actively undermines the exposure-based learning that cures phobia. The right answer stays behavioural: graded in-vivo exposure and systematic desensitisation, applied tension for the blood-injection-injury faint, propranolol (Ciplar, Inderal) at most as an autonomic adjunct for a one-off situational exposure, and the benzodiazepine reserved and time-limited if used at all.

HOLD THIS

Specific (simple) phobia is a cued, out-of-proportion fear of one circumscribed stimulus that almost always and immediately provokes anxiety (DSM-5-TR: 6 months; ICD-11: several months), classified in DSM-5-TR into five subtypes (animal, natural environment, blood-injection-injury, situational, other); its treatment is exposure-based behaviour therapy, graded in-vivo exposure first, with systematic desensitisation (Wolpe, reciprocal inhibition) and flooding on the same spectrum, and the blood-injection-injury subtype alone shows the diphasic vasovagal faint and is treated with applied tension, never relaxation.

7 · Separation anxiety disorder

A childhood diagnosis that grew up. **Separation anxiety disorder** is the excessive, developmentally inappropriate fear of separation from an **attachment figure**. The single highest-yield fact for the exam is a nosological one: both the ICD-11 and the DSM-5 now list it as a **lifespan anxiety** disorder inside the anxiety and fear-related grouping, no longer walled off in the childhood-onset chapter. Examiners test the placement change, the criterion-anchored definition, and the boundary with normal developmental separation anxiety.

Keep the discrimination sharp. The apprehension is focused specifically on **separation from an attachment figure** (a parent in a child; a spouse, partner or one's own child in an adult), which is what sets it apart from panic disorder, agoraphobia and generalised anxiety. Treatment mirrors the wider anxiety toolkit, so the management detail lives in the neighbouring topics; this note is deliberately brief and criterion-led.

7.1 Definition and the core fear

Attachment-focused, not situation-focused. The disorder is characterised by marked, excessive and developmentally inappropriate fear or anxiety about separation from those to whom the person is emotionally bonded, with catastrophic beliefs about what separation will bring (harm, illness, an untoward event, never being reunited). Attachment figures are usually parents in children and a spouse, romantic partner or one's own children in adults.

7.2 The ICD-11 placement change (the exam hook)

Out of the childhood chapter, into anxiety. In DSM-IV and ICD-10, separation anxiety sat among disorders first diagnosed in infancy, childhood or adolescence (ICD-10 F93.0, "separation anxiety disorder of childhood"). The **icd-11 placement** moves it to code 6B05 within anxiety and fear-related disorders, and DSM-5 places it among the anxiety disorders. The reclassification reflects that the disorder can begin, or persist, in adulthood.

7.3 Lifespan reframe: no upper age bar

Adults get the diagnosis too. Unlike earlier editions, DSM-5 dropped the requirement for onset before 18 years and recognises that some adults report onset after 18. This is the substantive change behind the "lifespan" framing: an adult with excessive fear of being apart from a spouse or child, meeting criteria, is diagnosed here rather than being forced into a residual category.

7.4 The symptom set and threshold

Three of eight. DSM-5-TR requires at least three of eight symptoms: recurrent excessive distress on anticipated or actual separation; worry about losing the attachment figure or about harm to them; worry that an untoward event will cause separation; reluctance or refusal to leave home, school or work; fear of being alone; reluctance or refusal to sleep away from the attachment figure; nightmares about separation; and physical complaints (nausea, stomach ache, headache) on separation.

AXIS	DSM-5-TR	ICD-11 (6B05)
Chapter	**Anxiety disorders (not childhood chapter)**	**Anxiety and fear-related disorders**
Age scope	No onset-before-18 rule; adults included	Lifespan; adult onset recognised
Symptom threshold	**At least 3 of 8**	Marked fear plus characteristic features
Duration, children/adolescents	At least 4 weeks	Not transient (at least several months)
Duration, adults	**At least 6 months (typically)**	At least several months
Impairment	Distress or functional impairment	Distress or functional impairment

The two systems agree on substance; DSM-5-TR carries the explicit symptom count and duration thresholds most often examined.

7.5 Duration criterion

Four weeks in the young, six months in adults. DSM-5-TR asks for symptoms lasting at least **4 weeks** in children and adolescents and typically at least **6 months** in adults, the longer adult window added to avoid over-diagnosing transient fears (for example after a bereavement or a move). ICD-11 phrases this as symptoms that are "not transient," persisting for at least several months.

7.6 Boundary with normal developmental separation anxiety

Normal is time-limited and age-expected. Developmentally normal separation anxiety appears around **6 months** and declines between two and three years of age; it is a healthy marker of attachment. The disorder is diagnosed only when the fear is out of proportion to the child's developmental level, persists across repeated separations, and produces genuine distress or impairment (school refusal, inability to sleep alone, somatic complaints on parting).

RULE **Focus of fear decides the diagnosis.** If the apprehension is specifically about separation from an attachment figure, it is separation anxiety disorder, whatever the patient's age.

TRAP **Do not treat it as childhood-only.** Reflexively excluding the diagnosis in an adult (or over-calling normal toddler clinginess as a disorder) are the two classic errors since the placement change.

WORKED EXAMPLE

A 34-year-old woman cannot let her husband travel for work; she rings him repeatedly, is convinced he will be harmed while apart, cannot fall asleep until he is home, and has skipped her own commitments to stay near him for the past eight months. The apprehension is separation-focused, adult-onset, and beyond six months with clear impairment. This is separation anxiety disorder, not generalised anxiety, whose worry would be diffuse rather than pinned to one attachment figure.

INDIA

Anxiety disorders carry a large untreated **treatment gap** in India, and much of what does reach treatment is met with benzodiazepines: the **benzodiazepine over-prescription** problem is well recognised, with clonazepam and alprazolam handed out as first-line and long-term anxiolytics against guidance. The **IPS Clinical Practice Guidelines** and the international consensus are unambiguous that an SSRI (available here under brands such as sertraline, escitalopram and fluoxetine), with CBT or exposure, is first-line for the anxiety disorders, and that a benzodiazepine is neither first-line nor for long-term use. Separation anxiety disorder, presenting through a clingy child brought for "school refusal" or an adult brought by an exasperated spouse, is easily missed or sedated rather than diagnosed.

3 of 8	4 wk	6 mo
DSM-5-TR SYMPTOM THRESHOLD	MINIMUM DURATION IN CHILDREN	TYPICAL MINIMUM DURATION IN ADULTS

MNEMONIC

A-P-A-R-T

Attachment-figure fear is the core; **P**lacement now under anxiety in ICD-11 and DSM-5; **A**dults included (lifespan, no age bar); **R**equires three of eight symptoms; **T**ime threshold four weeks in children, about six months in adults.

PEARL

School refusal is a presentation, not a diagnosis. Separation anxiety disorder is one of its commonest drivers in younger children; social anxiety disorder takes over as the leading cause into adolescence.

GOOD TO REMEMBER

- **Separation anxiety disorder:** defining criterion is excessive, developmentally inappropriate fear focused specifically on separation from an attachment figure, at least three of eight symptoms, four weeks in children and about six months in adults; first step is to check the fear is separation-focused and to place it, correctly, as a lifespan anxiety disorder in ICD-11 (6B05) and DSM-5, no longer a childhood-only diagnosis.

HOLD THIS

Separation anxiety disorder is now a lifespan anxiety disorder: ICD-11 and DSM-5 moved it out of the childhood chapter, dropped the onset-before-18 rule, and it is defined by attachment-figure-focused fear meeting three of eight symptoms.

For the shared anxiolytic pharmacology and the benzodiazepine dependence problem, see the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes; for SSRI dosing and adverse effects, the Mood disorders: pharmacotherapy notes; for the general CBT and exposure model, the Psychotherapies, clinical assessment, MSE and nosology notes; and for the childhood

attachment disorders that sit nearby, the Child behavioural, emotional and other disorders notes and the Child psychiatry: assessment, treatment, services and protection notes.

8 · The neurobiology of anxiety

The **neurobiology of anxiety** is the machinery of a survival system that has become a symptom. Fear is an adaptive, fast, hard-wired response to a present threat; anxiety is its slower, sustained, anticipatory cousin, aimed at a threat that is diffuse, future or imagined. Both run on the same core circuit, a threat-detection network built around the **amygdala**, wired to fire the body's alarm before the thinking cortex has finished deliberating, and normally reined back in by the prefrontal cortex and hippocampus. When the alarm fires too readily, extinguishes too poorly, or is regulated too weakly, the survival system becomes an anxiety disorder. Examiners test this topic as the anatomy of a loop and the chemistry that tunes it: know the amygdala-centred **fear circuit**, its two sensory roads, its outputs to the hypothalamus, the brainstem and the periaqueductal grey, its cortical and hippocampal brakes, and the three transmitter systems, GABA, serotonin and noradrenaline, that the anxiolytic drugs act on.

Why it matters clinically. Every drug that works in the anxiety disorders acts somewhere on this circuit, so the neurobiology is not decoration, it is the rationale for the treatment. A benzodiazepine calms anxiety because it potentiates **gaba** inhibition across the amygdala and its targets; an SSRI works because **serotonin anxiety** pathways from the raphe tune the fear circuit over weeks; propranolol blunts performance anxiety by blocking the peripheral noradrenergic surge that the **locus coeruleus** drives. Two ideas anchor the whole answer. First, the amygdala is the hub: it evaluates threat and organises the fear response, and it is normally held in check by the prefrontal cortex, so anxiety disorders are, in circuit terms, an over-active amygdala under-regulated by a weak cortical brake. Second, the circuit has a fast, crude, subcortical route and a slow, accurate, cortical route, so the alarm can fire before you consciously know why. The pathway anatomy and receptor systems are developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; this topic applies that anatomy to the **fear circuitry** of clinical anxiety and refers to the accompanying figure for the map.

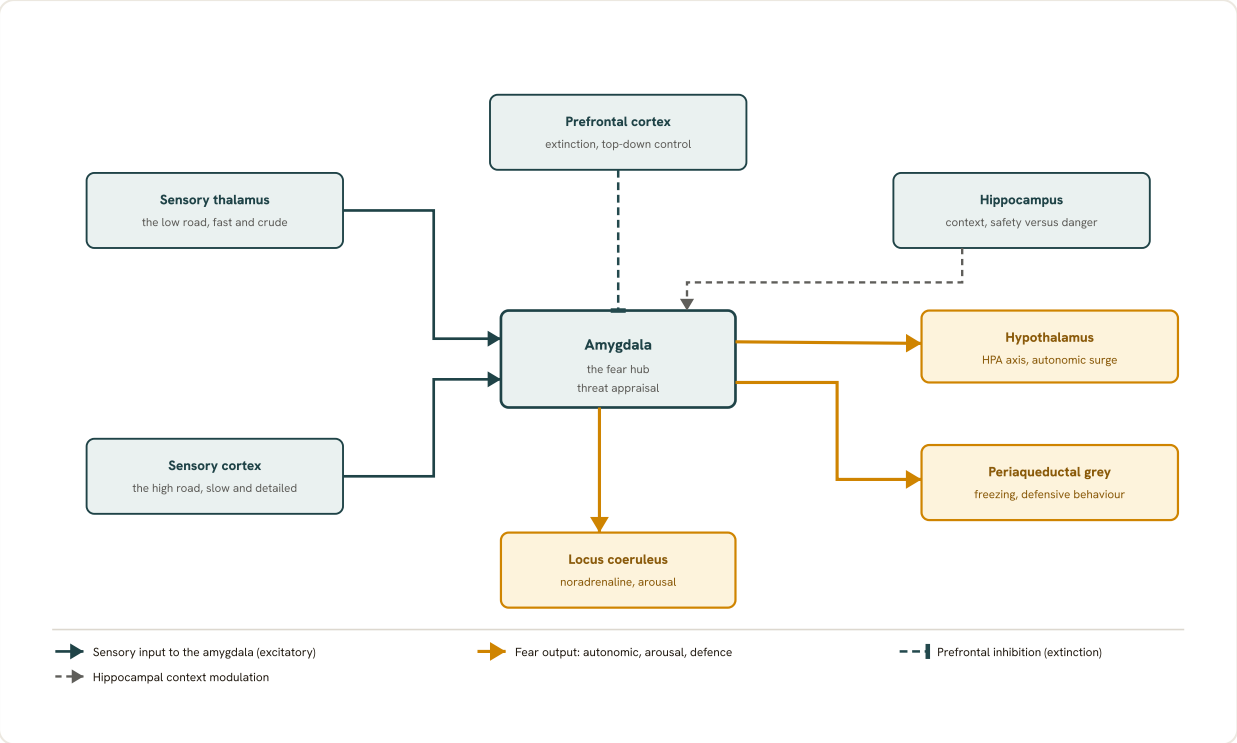


Fig 14.4 The fear circuit. The amygdala is the hub of the fear response: it receives a fast, crude input from the sensory thalamus (the low road) and a slower, detailed input from the sensory cortex (the high road), and it drives the fear state through the hypothalamus (the HPA axis and the autonomic surge), the periaqueductal grey (freezing and defensive behaviour) and the locus coeruleus (noradrenergic arousal). The prefrontal cortex exerts top-down inhibition, the basis of fear extinction, and the hippocampus supplies the context that separates safety from danger. A hyperresponsive amygdala with weak prefrontal control is the core lesion across the anxiety disorders. The receptor systems and the pathway anatomy are taught in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

8.1 Fear versus anxiety: the same circuit, two timescales

The distinction to open with. *Fear* is the response to a present, identifiable threat, phasic, fast, and organised largely by the central nucleus of the amygdala; *anxiety* is the response to a potential, diffuse or future threat, sustained, slower to build and slower to settle, and organised more by the bed nucleus of the stria terminalis (BNST), the amygdala's "extended" partner (Kaplan & Sadock CTP 2024). The BNST mediates the longer-duration apprehension elicited by less explicit or poorly-defined cues and contexts, which is why it is called the substrate of sustained anxiety rather than acute fear. Holding this apart matters because the clinical disorders are diseases of the anxiety end, a threat-detection system left switched on when no discrete threat is present.

One machine, one vulnerability. Because fear and anxiety share the amygdala hub, a system tuned to over-respond will produce both the acute false alarm (a panic attack) and the chronic apprehensive tension (generalised worry) in the same patient, which is why the anxiety disorders cluster and co-occur.

8.2 The amygdala as the hub: the lateral nucleus takes the input

The sensory gateway. The amygdala is an almond-shaped cluster of subnuclei (the amygdaloid complex) in the medial temporal lobe, and it is the pivot of the fear circuit. Its **lateral nucleus** (LA) is the primary sensory interface: it receives incoming sensory information from both the

sensory thalamus and the sensory cortex, and single LA neurons respond to auditory, visual and somatic stimuli, with the conditioned stimulus (the cue) and the unconditioned stimulus (the threat) converging there (Kaplan & Sadock CTP 2024). The LA is where a neutral cue first acquires threat value through **fear conditioning**, a form of synaptic plasticity (long-term potentiation) in the amygdala.

Distribution inside the complex. From the LA the signal is distributed to the basal and accessory basal nuclei and to the central nucleus (CE); the direct LA-to-CE projection can by itself drive conditioning to a simple cue, while the LA-to-basal projections build the longer-term fear memory (Kaplan & Sadock CTP 2024). The CE is the output nucleus, the amygdala's motor for the fear response.

PEARL

Think of the amygdala as a two-door hub. The *lateral nucleus* is the *in-door*, where thalamic and cortical sensory streams arrive and a cue is tagged as dangerous. The *central nucleus* is the *out-door*, from which the fear response is broadcast to the hypothalamus, brainstem and periaqueductal grey. Everything else, the fast road, the slow road, the cortical brake, is wiring around those two doors.

8.3 LeDoux's two roads: the low road and the high road

The fast, crude subcortical route. Joseph LeDoux mapped two parallel inputs to the amygdala. The *low road* runs from the sensory **thalamus** directly to the lateral amygdala, bypassing the cortex; it is fast and imprecise, a "quick and dirty" pathway that supports rapid conditioning to simple stimuli and permits an unconscious fear response before the stimulus is consciously identified (Kaplan & Sadock CTP 2024). Lesions of the auditory cortex do not prevent conditioning to a single tone, which is the experimental signature of the low road.

The slow, accurate cortical route. The *high road* runs from the sensory thalamus to the primary sensory and association **cortex** and then to the lateral amygdala; it is slower but detailed, and it is required for conditioned responding to more complex sensory stimuli and for the higher cognitive appraisal of the threat (Kaplan & Sadock CTP 2024). The two roads together explain the lived experience of fear: you flinch at the coiled shape on the path (low road) a fraction of a second before the cortex tells you it is a garden hose (high road).

WORKED EXAMPLE

A patient with a phobia of snakes freezes and gasps at a curved stick glimpsed in long grass, then within a second recognises it as a stick and feels foolish. The freeze-and-gasp is the low road, the sensory thalamus firing the amygdala directly and triggering the fear response before identification. The relief a moment later is the high road, cortical processing correcting the appraisal. In an anxiety disorder the low road is set too sensitive and the high-road correction is too weak or too slow to abort the alarm.

8.4 The output: central nucleus to hypothalamus, brainstem and periaqueductal grey

The three efferent targets to name. The central nucleus (CE) is the interface between the amygdala and the body's fear response, projecting to the medulla, midbrain and **hypothalamus** to drive the autonomic, endocrine and behavioural components (Kaplan & Sadock CTP 2024). Three CE outputs are the high-yield trio. To the *hypothalamus*, specifically the paraventricular nucleus (PVN), the amygdala drives release of corticotropin-releasing hormone and thereby the HPA-axis stress response; the projection is bisynaptic and GABAergic. To the **locus coeruleus** in the brainstem, the amygdala drives the noradrenergic surge that produces tachycardia, hypertension and hypervigilance. To the periaqueductal grey (PAG) in the midbrain, it drives the somatic and behavioural defence responses, freezing and avoidance (Gorman's neuroanatomical hypothesis, in Tasman Psychiatry).

Sustained anxiety takes the BNST branch. Both the CE and the BNST can directly activate the hypothalamus and brainstem; the BNST branch mediates the longer, context-driven anxiety states while the CE drives the phasic fear response (Kaplan & Sadock CTP 2024). Lesioning a specific CE efferent produces a selective deficit, PAG lesions blunt the somatobehavioural response, lateral hypothalamic lesions blunt the cardiovascular one, which is why the fear response is described as a set of parallel outputs from a single hub.

MNEMONIC

HELP the amygdala expresses fear: Hypothalamus, brainstem/LC, PAG

The central nucleus fires fear through its efferents: **H**ypothalamic PVN (CRH and the HPA stress axis), the brainstem **L**ocus coeruleus (noradrenaline, tachycardia, hypervigilance) and the **P**eriaqueductal grey (freezing and avoidance). Naming these three CE outputs is the fastest way to earn the "fear expression" marks.

8.5 The prefrontal brake and hippocampal context: how the alarm is switched off

The cortical brake. The medial and orbital prefrontal cortex (PFC) modulates the amygdala through extensive reciprocal projections and is the substrate of *fear regulation* and *extinction*, the learned reduction of a fear response once a cue is no longer dangerous (Kaplan & Sadock CTP 2024). The ventromedial PFC (the infralimbic region in the rat) drives extinction: it acts through the amygdala's GABAergic intercalated cells to inhibit central-nucleus output, so a strong vmPFC brake means a fear that can be extinguished. A weak vmPFC brake, or an over-driving dorsal anterior cingulate, means fear that persists, which is the circuit signature of the anxiety disorders and of PTSD.

Hippocampal context. The hippocampus supplies the *context* of the fear memory, whether the cue is dangerous *here and now* or only in the original setting, and it is central to contextual fear conditioning and to distinguishing a safe context from a dangerous one (Kaplan & Sadock CTP 2024). When hippocampal contextual gating fails, fear generalises to safe situations, the over-generalisation that characterises PTSD and generalised anxiety.

RULE **Over-active amygdala, under-active prefrontal brake.** The core circuit lesion of the anxiety disorders is an amygdala that fires too readily on threat and a ventromedial prefrontal cortex that regulates and extinguishes that fear too weakly; the hippocampus normally fixes the fear to its correct context, and when it fails, fear over-generalises to safe situations.

8.6 The GABA system: the brain's brake and the benzodiazepine target

Inhibition across the circuit. **gaba** (gamma-aminobutyric acid) is the principal inhibitory transmitter of the brain and the physiological brake on the fear circuit: GABAergic interneurons within the amygdala, the GABAergic intercalated cells through which the vmPFC inhibits CE output, and GABAergic tone throughout the limbic system all restrain the alarm (Kaplan & Sadock CTP 2024). A deficiency or reduced sensitivity of GABA-A signalling is a leading model of pathological anxiety.

Why the benzodiazepine works, and its ceiling. The benzodiazepine binds an allosteric site on the GABA-A receptor and potentiates GABA's action, increasing the frequency of chloride-channel opening, so it acutely amplifies the brake and calms anxiety within minutes. That immediacy is exactly why it is over-used and why it is *not* a first-line maintenance treatment: it does not correct the circuit, it only sedates it, and chronic use brings tolerance, dependence and rebound anxiety. The detailed anxiolytic pharmacology (benzodiazepines, buspirone, pregabalin, the z-drugs, dependence and withdrawal) is developed in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes.

GOOD TO REMEMBER

- **GABA and the benzodiazepine (the transmitter and its drug):** GABA is the brain's chief inhibitory transmitter and the physiological brake on the amygdala and fear circuit; the benzodiazepine potentiates GABA at an allosteric GABA-A site (increasing chloride-channel opening frequency), giving a fast anxiolytic effect, the signature caution is that it sedates rather than corrects the circuit, so tolerance, dependence and rebound anxiety follow chronic use and it is never a first-line maintenance drug for an anxiety disorder.

8.7 The serotonin system: the slow tuner and the SSRI target

Raphe modulation of the fear circuit. **serotonin anxiety** pathways ascend from the dorsal raphe nucleus of the brainstem to the amygdala, prefrontal cortex, hippocampus and hypothalamus, where serotonin tonically modulates the excitability of the fear circuit (Kaplan & Sadock CTP 2024; New Oxford Textbook of Psychiatry). The relationship is complex rather than simply inhibitory, but the clinical fact is that enhancing serotonergic transmission dampens pathological anxiety over weeks, and the postsynaptic 5-HT1A receptor is a key mediator (the partial agonist buspirone acts here).

Why the SSRI is first-line and slow. The SSRI raises synaptic serotonin at once, but the anxiolytic benefit is delayed by several weeks, the lag reflecting adaptive receptor changes and a re-tuning of the circuit rather than acute inhibition. This delayed, circuit-remodelling action is precisely why the SSRI corrects where the benzodiazepine only sedates, and why the SSRI (and SNRI) is first-line across the anxiety disorders and PTSD. The deep antidepressant pharmacology

(the SSRIs, SNRIs, clomipramine, doses, adverse effects, interactions) is developed in the Mood disorders: pharmacotherapy notes.

TRAP **Expecting the SSRI to work like a benzodiazepine.** The serotonergic anxiolytic effect is delayed by weeks and can transiently *worsen* anxiety in the first days (early activation); reaching for a benzodiazepine because "the SSRI is not working yet", or stopping the SSRI too early, is the classic error, warn the patient about the lag and the early jitteriness from the outset.

GOOD TO REMEMBER

- **Serotonin and the SSRI (the transmitter and its drug):** serotonin ascends from the dorsal raphe to tune the amygdala, prefrontal cortex and hippocampus (the 5-HT1A receptor a key mediator); the SSRI raises synaptic serotonin at once but re-tunes the fear circuit only over several weeks, the signature caution is the delayed onset with early activation, and the principle is that it *corrects* the circuit where a benzodiazepine only sedates, which is why the SSRI/SNRI is first-line for the anxiety disorders and PTSD.

8.8 The noradrenaline system: the locus coeruleus and the alarm's amplifier

The brainstem alarm centre. The **locus coeruleus** (LC) is the principal noradrenergic nucleus of the brain, in the pons, and it is the amplifier of the fear response: activation of the LC raises noradrenaline throughout the forebrain and drives the peripheral autonomic surge, tachycardia, raised blood pressure, sweating and hyperarousal, that the patient feels as the physical face of anxiety (Kaplan & Sadock CTP 2024; Tasman Psychiatry). The amygdala's central nucleus projects to the LC, and the LC in turn feeds arousal back into the circuit, a positive loop that panic disorder in particular exploits.

The pharmacological proof. The noradrenergic model is not merely theoretical: yohimbine, an alpha-2 antagonist that increases LC firing and noradrenaline release, provokes panic in vulnerable patients, while clonidine, an alpha-2 agonist that suppresses the LC, reduces arousal (Tasman Psychiatry). Clinically the same physiology explains why propranolol (Ciplar, Inderal), a beta-blocker, blunts the peripheral tremor and tachycardia of *performance* anxiety, and why prazosin (Minipress, Prazopress), an alpha-1 antagonist, dampens the noradrenergic hyperarousal that drives the nightmares of PTSD.

GOOD TO REMEMBER

- **Noradrenaline and the locus coeruleus (the transmitter and its nucleus):** the LC is the pontine noradrenergic alarm centre that amplifies the amygdala's fear output into the peripheral autonomic surge (tachycardia, hypertension, hyperarousal); yohimbine (alpha-2 antagonist) provokes panic and clonidine (alpha-2 agonist) suppresses it, the clinical corollary is that propranolol blunts the peripheral surge of performance anxiety and prazosin dampens the noradrenergic hyperarousal behind PTSD nightmares.

8.9 Putting the circuit together: how the transmitters map onto the anatomy

One picture, three dials. The fear circuit is one anatomical loop with three chemical dials. GABA is the inhibitory brake wired through the amygdala and the prefrontal intercalated cells; serotonin is the slow tuner descending from the raphe onto the whole circuit; noradrenaline from

the locus coeruleus is the amplifier of the output. An anxiety disorder is, in this scheme, too little brake, mis-tuning of the serotonergic set-point, and too much amplifier, on a hub (the amygdala) that is over-reactive and a cortex (vmPFC) that regulates it too weakly. Every anxiolytic drug is best understood as adjusting one of these dials.

NODE / SYSTEM	ROLE IN THE FEAR CIRCUIT	CLINICAL / DRUG CORRELATE
Lateral nucleus of amygdala (LA)	Sensory in-door; thalamic + cortical input converge; site of fear conditioning (LTP)	Over-sensitive threat detection in anxiety disorders
Central nucleus of amygdala (CE)	**Out-door; organises the fear response via efferents**	Lesion abolishes conditioned fear expression
Low road (thalamo-amygdala)	Fast, crude, pre-conscious alarm; bypasses cortex (LeDoux)	Explains reflex fear before identification
High road (thalamo-cortico-amygdala)	Slow, accurate cortical appraisal of threat (LeDoux)	Weak or slow high-road correction sustains the alarm
Hypothalamus (PVN)	**CE efferent; CRH release, HPA stress axis**	Neuroendocrine stress response
Locus coeruleus	CE efferent; noradrenaline, autonomic surge, hyperarousal	**Yohimbine provokes, propranolol/prazosin blunt**
Periaqueductal grey (PAG)	CE efferent; freezing and defensive avoidance behaviour	Somatobehavioural fear output
Ventromedial PFC	**The brake; drives extinction via GABAergic intercalated cells**	Weak brake = fear that will not extinguish (PTSD)
Hippocampus	Supplies context of the fear memory	Failure = fear over-generalises to safe settings
GABA	Inhibitory brake across the circuit	Benzodiazepine target (fast, sedating)
Serotonin (raphe)	Slow tonic tuner of the whole circuit; 5-HT1A	SSRI target (slow, corrective, first-line)
Noradrenaline (LC)	Amplifier of the fear output	Beta-blocker / prazosin / clonidine target

The amygdala-centred fear circuit node by node, mapped to its transmitter systems and drug correlates; the accompanying figure draws the same loop as a map (input roads, amygdala hub, efferent targets, cortical and hippocampal brakes). Grounded in Kaplan & Sadock CTP 2024 and Tasman Psychiatry.

8.10 Definitions to fix the vocabulary

Amygdala

Almond-shaped medial-temporal complex of subnuclei; the hub that evaluates threat and organises the fear response.

Lateral nucleus (LA)

The amygdala's sensory in-door; thalamic and cortical input converge here and cues acquire threat value.

Central nucleus (CE)

The amygdala's output nucleus; its efferents to hypothalamus, LC and PAG express the fear response.

Low road

LeDoux's fast thalamo-amygdala route that bypasses the cortex; pre-conscious, crude, quick.

High road

LeDoux's slower thalamo-cortico-amygdala route; accurate cortical appraisal of the threat.

BNST

Bed nucleus of the stria terminalis; the "extended amygdala" that mediates sustained, context-driven anxiety rather than phasic fear.

Extinction

Learned reduction of a conditioned fear once the cue is no longer dangerous; driven by the ventromedial PFC.

INDIA

India carries a large, largely untreated anxiety burden: the great majority of people with an anxiety, OCD or PTSD disorder never reach formal care, a treatment gap widened by stigma, scarcity of psychiatrists and the framing of anxiety as physical "ghabrahat" or "gas". Into that gap steps the country's **benzodiazepine over-prescription** problem: alprazolam and clonazepam are dispensed freely, often long-term and as a first move, by general practitioners and over the counter, which is exactly the wrong dial to turn on this circuit, the sedating brake that breeds dependence rather than the corrective serotonergic re-tuning. The neurobiology gives the corrective the Indian Psychiatric Society CPG endorses: an SSRI or SNRI is first-line for the anxiety disorders because it re-tunes the fear circuit, with the benzodiazepine reserved as a short bridge only. The relevant Indian brands are cheap and available, escitalopram (Nexito, Cipralex), sertraline (Serta, Zosert, Daxid), fluoxetine (Fludac) and paroxetine (Paxidep) for the serotonergic drugs, propranolol (Ciplar, Inderal) for the noradrenergic blunting of performance anxiety, and prazosin (Minipress, Prazopress) for PTSD nightmares; the correct answer treats the circuit, not merely the symptom.

2	3	3
SENSORY ROADS TO THE AMYGDALA (LEDOUX'S FAST LOW ROAD, SLOW HIGH ROAD)	CENTRAL-NUCLEUS EFFERENT TARGETS TO NAME (HYPOTHALAMUS, LOCUS COERULEUS, PAG)	TRANSMITTER DIALS ON THE CIRCUIT (GABA BRAKE, SEROTONIN TUNER, NORADRENALINE AMPLIFIER)

HOLD THIS

The fear circuit is an amygdala hub fed by LeDoux's fast subcortical low road and slow cortical high road, expressing fear through the central nucleus onto the hypothalamus, locus coeruleus and periaqueductal grey, and normally braked by the ventromedial prefrontal cortex and contextualised by the hippocampus; anxiety is that circuit over-reactive and under-regulated, tuned by three dials, the GABA brake (benzodiazepine target), the serotonergic tuner (SSRI target, slow and corrective) and the noradrenergic amplifier from the locus coeruleus (beta-blocker and prazosin target).

9 · Cognitive behaviour therapy for anxiety

Cognitive behaviour therapy for anxiety is the psychological treatment that the whole anxiety block leans on: across generalised anxiety disorder, panic, social anxiety and the phobias, every major guideline names **cbt for anxiety** as a first-line option of broadly similar efficacy to drug treatment. This note owns the disorder-specific CBT model, the cognitive model of anxiety, **cognitive restructuring**, the **behavioural experiment**, and the three classes of exposure, including **interoceptive exposure**, with the safety-behaviour idea running through all of them; the wider CBT technique (the general cognitive model, the wider exposure principle) is cross-referenced to the Psychotherapies, clinical assessment, MSE and nosology notes.



Fig 14.5 Exposure therapy repeatedly approaches feared-but-safe cues while reducing avoidance and safety behaviours, allowing new inhibitory safety learning to compete with the older threat association.

Why it matters, and how this note is framed. Examiners reward the candidate who can do two things: state the *cognitive model* of anxiety (that it is the appraisal of a situation, not the situation itself, that drives the fear, and that avoidance and safety behaviours keep the belief alive by preventing disconfirmation), and name the *techniques* with their disorder-specific twist,

interoceptive exposure for the "fear of fear" in panic, dropping safety behaviours and shifting attention outward in social anxiety, exposure and response prevention for OCD (owned separately in the OCD notes). The single sharpest fact to hold is that CBT works by *disconfirming a catastrophic prediction* through direct experience, which is exactly what a behavioural experiment is engineered to do.

9.1 The cognitive model of anxiety: appraisal, not the event, drives the fear

The basic assumption. The cognitive model holds that people's beliefs and appraisals of events are at least as important as the events themselves in determining their emotional reactions; problematic anxiety is frequently the product of unrealistic, unhelpful beliefs about the world, the self and others (Kaplan and Sadock 2024). The classic sequence is *thoughts and beliefs lead to emotions and behaviours*, Aaron Beck's belief-disconfirmation model, so the therapeutic target is the faulty appraisal, not the feared object directly. In anxiety specifically, the appraisals share a family resemblance: probability overestimation (the feared outcome is far more likely than it is) and catastrophic thinking (its consequences would be unbearable), plus all-or-nothing thinking, overgeneralisation and selective attention to confirming evidence.

How maintenance works. The disorder is held in place by a vicious cycle: an ambiguous cue is appraised as threatening, which raises anxiety and arousal, which is itself read as further evidence of danger, and the person then *avoids* or deploys *safety behaviours* that abort the situation before the catastrophe can be shown not to happen. Because the feared outcome never gets a chance to be disconfirmed, the belief survives intact. CBT breaks this loop by getting the patient to stay in contact with the feared situation, or sensation, long enough to learn that the prediction was wrong.

GOOD TO REMEMBER

- **Cognitive behaviour therapy for anxiety:** the principle is that anxiety flows from a distorted *appraisal* (probability overestimation and catastrophic thinking) rather than the event itself, and is maintained by avoidance and safety behaviours that prevent the belief from being disconfirmed; the mechanism of change is disconfirmation of the catastrophic prediction through cognitive restructuring and exposure; it is first-line, of broadly similar efficacy to pharmacotherapy across the anxiety disorders.

9.2 The shape of a course: assessment, formulation, psychoeducation, homework

How a course of CBT is built. CBT begins with a structured assessment of the presenting complaint using validated measures (and disorder-relevant constructs such as worry-related metacognitions in GAD or anxiety sensitivity in panic), repeated over treatment to track outcome. The next step is psychoeducation: the patient is given a shared cognitive-behavioural formulation of their specific diagnosis and a treatment rationale, then therapist and patient collaboratively set targets, for example building the exposure hierarchy or eliciting the core fear (Kaplan and Sadock 2024). CBT is time-limited, structured and collaborative, and leans heavily on homework and self-monitoring between sessions so that skills generalise beyond the consulting room.

How long it takes. The course is short by psychotherapy standards. For panic disorder the optimal dose is **7 to 14 hours** of treatment, delivered weekly, typically over about four months (NICE). For GAD, a high-intensity individual CBT course is **12 to 15 weekly sessions** of one hour (NICE). This brevity is part of why guidelines can place CBT co-equal with drugs and why low-intensity and internet-delivered versions are pushed hard to widen access.

GOOD TO REMEMBER

- **Structure of CBT for anxiety:** assessment then shared cognitive-behavioural formulation and psychoeducation, collaborative goal-setting, and between-session homework and self-monitoring; it is brief and time-limited (panic 7 to 14 hours over about four months; GAD 12 to 15 weekly one-hour sessions per NICE), which is why it sits co-equal with pharmacotherapy as first-line.

9.3 Cognitive restructuring: Socratic dialogue, thought records, the downward arrow

What it is. Cognitive restructuring is the set of procedures for identifying and modifying the unhelpful appraisals. The three traditional techniques are (1) Socratic dialogue, a guided series of questions that helps the patient surface and challenge a fear-related belief and uncover disconfirming evidence; (2) the downward-arrow technique, repeatedly asking "and what would that mean?" to reach the deeper core belief; and (3) the thought record, in which the patient logs automatic thoughts, lists the evidence for and against, spots the cognitive error, and generates a more realistic, balanced alternative (Kaplan and Sadock 2024). The therapist does not simply reassure or argue; the patient is walked to the new conclusion so that they own it.

What it targets in anxiety. The restructuring is aimed squarely at the two anxiety appraisals, overestimating how likely the bad outcome is and catastrophising how bad it would be. In panic disorder that means challenging the catastrophic misinterpretation of a bodily sensation ("this pounding heart means I am having a heart attack"); in social anxiety it means challenging the prediction of humiliation and the distorted self-image seen "from the outside". Restructuring alone can reduce anxiety, but its power is greatest when it sets up a prediction that exposure can then test.

RULE **Restructure, then test.** Cognitive restructuring makes the catastrophic belief explicit and generates a specific prediction; exposure and behavioural experiments then supply the disconfirming experience, and it is the direct experience, not the argument, that shifts the belief.

GOOD TO REMEMBER

- **Cognitive restructuring:** identifying and modifying anxious appraisals (probability overestimation, catastrophising) via Socratic dialogue, thought records and the downward-arrow technique; the signature caution is that it is collaborative and guided, not reassurance or debate, and it works best when it produces a testable prediction that exposure can then disconfirm.

9.4 The behavioural experiment: testing a prediction against reality

The single most important technique. A behavioural experiment is the point where cognitive and behavioural methods fuse. Its goal is to test a belief about the nature and probability of a feared consequence under conditions that optimise exposure to, and encoding of, disconfirming

information (Kaplan and Sadock 2024). Before the experiment the patient makes a *detailed, specific prediction* of what they believe will happen, then carries out the relevant action and observes the actual result. Each time the catastrophe fails to occur, the patient is confronted with evidence against the belief. The worked panic example is canonical: a patient who fears they will "go crazy" if they feel dizzy is asked to spin in a chair, slowly then faster, and discovers that intense dizziness comes and goes without madness.

Why it beats reassurance. Homework assignments and behavioural experiments let the patient practise new behaviours and test the therapist's alternative explanations for themselves; even experiments that "fail" reveal more about the condition (Shorter Oxford Textbook). Because the learning is experiential and self-generated, it sticks in a way that being told "your heart is fine" never does, which is why the behavioural experiment is the engine of durable change in CBT for anxiety.

STEP	WHAT HAPPENS
Identify the belief	Elicit the specific catastrophic prediction (e.g. "if I feel dizzy I will collapse")
Make it testable	**Operationalise a concrete, falsifiable prediction with the patient**
Design the experiment	Choose an action that will expose the prediction to disconfirming evidence, drop safety behaviours
Run it	Carry out the action; the patient stays in contact and observes what actually happens
Review the evidence	**Compare prediction with outcome; update the belief from direct experience**

The anatomy of a behavioural experiment; the load-bearing steps are making the belief testable and then reviewing prediction against reality (Kaplan and Sadock 2024).

GOOD TO REMEMBER

- **Behavioural experiment:** a planned test in which the patient makes a specific prediction about a feared consequence, carries out an action (with safety behaviours dropped), and compares prediction with outcome; the principle is experiential disconfirmation of the catastrophic belief, and the signature caution is that the prediction must be concrete and falsifiable, and safety behaviours removed, or the experiment cannot disconfirm anything.

9.5 Exposure: the three classes, done without safety behaviours

What exposure is. Exposure therapy means intentionally confronting a feared but not actually dangerous object, situation, thought, memory or physical sensation, in order to reduce the fear and avoidance attached to it. Contemporary exposure divides into three classes: *in vivo*, *imaginal* and interoceptive, all conducted while encouraging the patient to *prevent safety behaviours*, the strategies that avert the feared outcome but, in doing so, block the new learning (Kaplan and Sadock 2024). Older systematic desensitisation paired graded imaginal or in vivo exposure with relaxation; that relaxation is now regarded as unnecessary and possibly counterproductive, and prolonged in vivo exposure has become the standard.

The three classes. *In vivo* exposure directly confronts feared objects, activities and situations, usually graded up a collaboratively agreed hierarchy (the snake photographed, then caged, then handled). *Imaginal* exposure has the patient vividly picture the feared scenario, thought or memory (its main use is confronting feared thoughts and traumatic memories, and it underpins imagery rescripting in PTSD). **Interoceptive exposure**, the most recent, deliberately induces the feared bodily sensations under control, hyperventilating for breathlessness and tingling, spinning for dizziness, straw-breathing for air-hunger, to teach that the sensations are not dangerous; it is the signature technique for panic disorder's "fear of fear".

CLASS	WHAT IS CONFRONTED	SIGNATURE USE
In vivo	Real feared objects, activities and situations, graded up a hierarchy	**Specific phobia, agoraphobic avoidance, social situations**
Imaginal	Feared thoughts, images and memories, vividly pictured	Traumatic memories (PTSD), feared consequences; imagery rescripting
Interoceptive	**Feared bodily sensations, induced on purpose (spin, hyperventilate, straw-breathe)**	**Panic disorder: the "fear of fear" / anxiety sensitivity**

The three classes of exposure; all are run while dropping safety behaviours, and interoceptive exposure is the panic-specific technique for anxiety sensitivity (Kaplan and Sadock 2024).

TRAP **Safety behaviours and reassurance sabotage exposure.** If the patient keeps a hidden crutch (clutching a water bottle, sitting near the exit, silent reassurance-seeking) or the exposure is too brief to let anxiety fall, the catastrophic belief is never disconfirmed, so the exposure looks like it "failed" when the design was at fault.

GOOD TO REMEMBER

- **Exposure (in vivo, imaginal, interoceptive):** graded confrontation of the feared stimulus without safety behaviours to allow new learning; in vivo for real situations and phobias, imaginal for feared thoughts and traumatic memories, interoceptive for the feared bodily sensations of panic; the signature caution is that safety behaviours, avoidance and reassurance-seeking must be dropped, and prolonged real (in vivo) exposure now replaces relaxation-paired systematic desensitisation.

9.6 Interoceptive exposure and the CBT model of panic

The panic cycle. The cognitive-behavioural model of panic (the Clark model) frames a panic attack as a vicious cycle: the person is hypervigilant for a bodily sensation, misinterprets it catastrophically ("this racing heart means a heart attack; this unreality means I am going mad"), which raises arousal and intensifies the sensation, spiralling into panic; agoraphobic avoidance then grows as an attempt to escape the situations where attacks might strike (Kaplan and Sadock 2024). The therapeutic implication is direct: break the catastrophic misinterpretation and the loop cannot close.

Where interoceptive exposure fits. CBT for panic has four components: psychoeducation about the panic cycle, cognitive restructuring of the catastrophic misinterpretation, **interoceptive**

exposure to the feared sensations to reduce the "fear of fear", and in vivo exposure to any avoided (agoraphobic) situations. Dismantling studies point to cognitive restructuring combined with in vivo or interoceptive exposure as the active ingredients, and adding interoceptive exposure is particularly helpful; in one meta-analysis the largest effect size was for cognitive therapy plus interoceptive exposure (**d = 0.88**), ahead of CBT without it and of medication alone. Between **41 and 87 per cent** of patients are panic-free after CBT, and CBT gains hold better than medication after treatment stops.

WORKED EXAMPLE

A 28-year-old with panic disorder is terrified that the dizziness and derealisation during an attack mean she is about to faint or lose her mind, so she sits down, grips a chair and sips water whenever they start (safety behaviours). Restructuring surfaces the prediction "if I let the dizziness build I will faint". The interoceptive exposure is to hyperventilate for a minute, then spin, deliberately bringing on the dizziness and unreality, without sitting, gripping or sipping. Over repeated trials she learns the sensations crest and pass without fainting or madness; the "fear of fear" falls, and in vivo exposure then returns her to the supermarket and the bus she had been avoiding.

GOOD TO REMEMBER

- **Interoceptive exposure in panic:** deliberate induction of feared bodily sensations (hyperventilation, spinning, straw-breathing) to break the catastrophic misinterpretation that drives the panic cycle and reduce the "fear of fear"; it is the panic-specific exposure class, one of the active ingredients of panic CBT, and the signature caution is that it fails if the patient keeps safety behaviours or the induced sensations are cut short.

9.7 Social anxiety CBT: dropping safety behaviours, shifting attention outward

The disorder-specific twist. In social anxiety disorder the Clark and Wells model adds two signature moves to the standard restructuring-plus-exposure package: a stronger emphasis on *identifying and eliminating safety behaviours* (over-rehearsing sentences, avoiding eye contact, gripping a glass to hide a tremor) and on *shifting attention outward* from the distorted, self-focused image the patient believes others can see (Kaplan and Sadock 2024). Exposures are integrated with cognitive challenge: the patient makes an explicit prediction, drops the safety behaviours, focuses attention on the other person rather than the self, and reviews the outcome afterwards, often with video feedback that contradicts the "I looked ridiculous" belief.

Why it works. Network meta-analysis puts individual CBT ahead of group CBT and of psychodynamic, supportive and mindfulness therapies for social anxiety, and the Clark and Wells version shows large effects against fluoxetine, exposure alone and group CBT. This is why NICE makes disorder-specific *individual* CBT the first-line treatment for social anxiety disorder, developed further in the Social anxiety disorder note.

PEARL

The two Clark-and-Wells refinements that lift social-anxiety CBT above generic exposure are *dropping safety behaviours* and *redirecting attention outward*. Self-focused attention manufactures the very "distorted self-image" the patient dreads others see; video feedback, showing the patient they did not visibly shake or blush as badly as they believed, is a behavioural experiment that disconfirms it directly.

GOOD TO REMEMBER

- **Social anxiety CBT (Clark and Wells):** cognitive restructuring of the fear of negative evaluation plus graded exposure, with two signature additions, systematically dropping safety behaviours and shifting attention outward from the self-focused image, tested with video-feedback experiments; individual CBT is first-line and outperforms group CBT for social anxiety disorder (NICE).

9.8 Evidence and place in the anxiety guidelines

What the guidelines say. The convergence is the exam point. NICE, BAP, CANMAT and the Indian Psychiatric Society all place **cbt for anxiety** as a first-line psychological treatment across generalised anxiety disorder, panic disorder and social anxiety disorder, of broadly similar efficacy to pharmacotherapy, with combination (CBT plus an SSRI or SNRI) reserved for partial or non-response. NICE makes CBT (or applied relaxation) one of two equivalent first-choice high-intensity options in GAD, first-line for panic (7 to 14 hours), and the first-line individual treatment for social anxiety disorder; BAP and CANMAT agree. For OCD the psychological arm is *exposure and response prevention*, taught in the OCD management notes; for PTSD it is trauma-focused CBT, taught in the PTSD notes.

The one durability advantage. A recurring finding is that CBT gains are more durable than medication gains once treatment stops (in panic, CBT alone held better than CBT plus imipramine after discontinuation), and cognitive therapy with exposure may reduce relapse better than drug treatment alone. That relapse-protection edge, plus lower dropout than medication, is why guidelines are keen to expand access through group, guided self-help and internet-delivered CBT.

DISORDER	CBT STATUS	DISORDER-SPECIFIC CBT INGREDIENT
Generalised anxiety disorder	**First-line (co-equal with drugs); 12 to 15 sessions**	Worry-focused restructuring; no standard in vivo target
Panic disorder	**First-line; 7 to 14 hours**	**Interoceptive exposure for the "fear of fear"**
Social anxiety disorder	First-line individual CBT (over group)	Drop safety behaviours, shift attention outward (Clark and Wells)
Specific phobia / agoraphobia	Exposure is treatment of choice	Graded in vivo exposure up a hierarchy
OCD	First-line psychotherapy (see OCD notes)	Exposure and response prevention

CBT across the anxiety block; the through-line is first-line status with a disorder-specific technique, and the durability edge over medication after stopping is the recurring evidence point.

INDIA

India has a wide anxiety, OCD and PTSD treatment gap, most sufferers never reach formal care, and where care is reached it too often means long-term benzodiazepine prescribing, alprazolam and clonazepam dispensed for "nervousness", which runs directly against the Indian Psychiatric Society CPGs. CBT is the evidence-based alternative that the gap most needs, yet trained CBT therapists are scarce outside metros. This is exactly where low-intensity and internet-delivered CBT, guided self-help and task-shifting to non-specialists matter: they are the realistic route to scaling a first-line psychological treatment in a low-resource setting, and they let the SSRI-plus-CBT model displace the benzodiazepine habit rather than reinforce it.

3	7 to 14 hours	0.88	10
CLASSES OF EXPOSURE (IN VIVO, IMAGINAL, INTEROCEPTIVE)	CBT DOSE FOR PANIC DISORDER (NICE)	EFFECT SIZE, COGNITIVE THERAPY PLUS INTEROCEPTIVE EXPOSURE IN PANIC	GAD-7 CLINICAL CUT-OFF (SCREEN THE DISORDER CBT TREATS)

HOLD THIS

CBT for anxiety works by disconfirming a catastrophic prediction through direct experience: cognitive restructuring makes the belief testable, the behavioural experiment and the three exposure classes (in vivo, imaginal, interoceptive, all with safety behaviours dropped) supply the disconfirming evidence, and it is first-line and co-equal with drugs across the anxiety disorders, with interoceptive exposure the signature technique for panic.

10 · Anxiety: differential diagnosis and medical mimics

Once the anxiety disorders have been learned one at a time, the examiner turns the question round: a patient walks in with palpitations, tremor, sweating and a racing sense of dread, and you must say *which* anxiety disorder this is, and first of all whether it is an anxiety disorder at all. This is the discrimination step. The **differential diagnosis of anxiety** has two limbs that must both be secured: separating the anxiety disorders from one another by the *focus of the fear*, and

separating a primary anxiety disorder from an organic cause, the **medical mimics**. The accompanying figure maps the anxiety disorders by the focus of the fear, and the figure alongside sorts the medical mimics by the feature that gives each away; this note is the text that unpacks both.

Why it matters, and the trap that fails candidates. The single discriminator that separates each anxiety disorder is a one-line fact the examiner expects you to produce instantly, and the classic error, the trap that turns a pass into a fail, is to reach for a psychiatric label while missing an organic mimic sitting in plain sight (**hyperthyroidism**, a **phaeochromocytoma**, an arrhythmia, hypoglycaemia, or a caffeine habit). The neurobiology of the fear circuit that these mimics hijack is developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the anxiolytic and withdrawal pharmacology that produces the substance-related pictures below lives in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes; what this note owns is the discrimination itself.

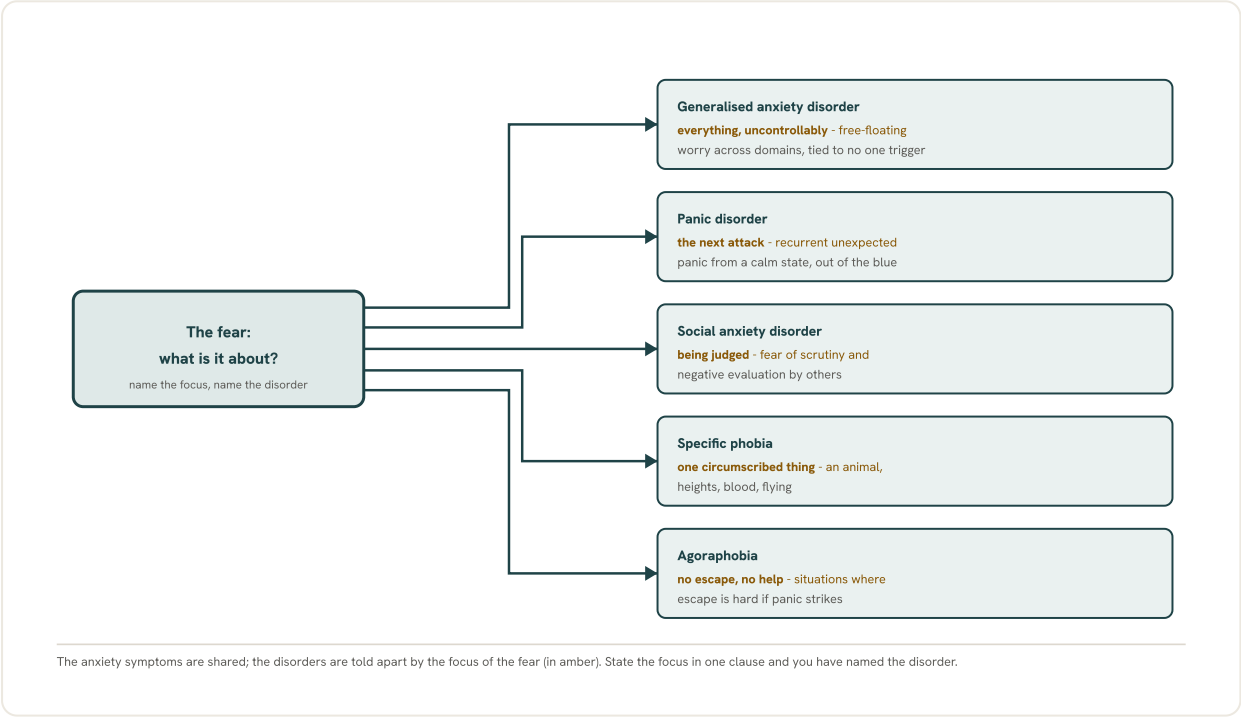


Fig 14.6 Discriminating the anxiety disorders by the focus of the fear. The somatic symptoms of anxiety are shared across all of these disorders, so they cannot separate them; what separates them is what the fear is about. Generalised anxiety fears everything and nothing in particular; panic fears the next attack; social anxiety fears being judged; specific phobia fears one circumscribed object or situation; agoraphobia fears being trapped where escape would be difficult or help unavailable. Name the focus and you have named the disorder.

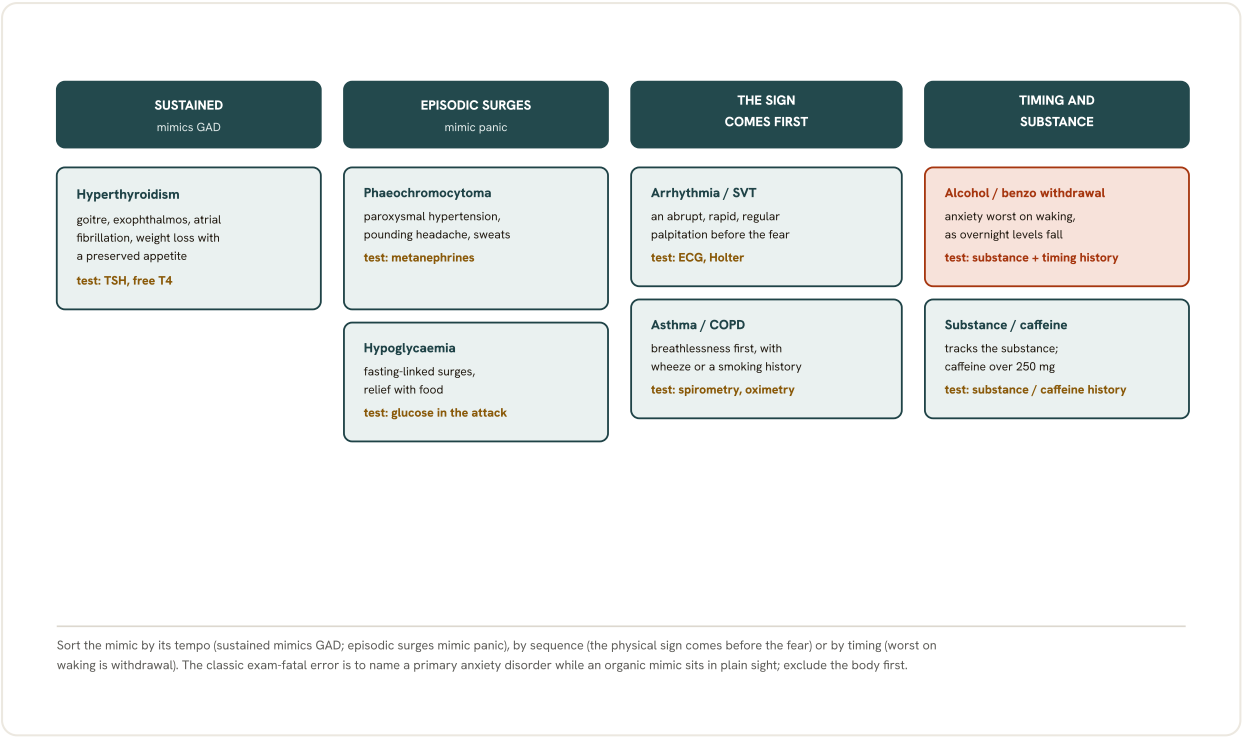


Fig 14.7 The medical mimics of anxiety, sorted by the feature that gives each away. Rather than a flat list, the mimics fall into four groups by their discriminating principle. A sustained driver (thyrotoxicosis) reproduces the steady picture of generalised anxiety; episodic paroxysmal surges (a phaeochromocytoma, hypoglycaemia) reproduce panic; where the physical sign comes first, an arrhythmia (a palpitation preceding the fear) or asthma and COPD (breathlessness first) is the answer; and anxiety that is worst on waking is alcohol or benzodiazepine withdrawal, while anxiety that tracks a substance or a heavy caffeine load is intoxication. Excluding the body, and choosing the test by the tempo, comes before any anxiety-disorder label.

10.1 The organising principle: one discriminator per disorder, the body ruled out first

Two questions, in order. Faced with an anxious patient, ask first "is this organic?" and only then "which anxiety disorder is it?". The order is deliberate: an SSRI started for what is actually thyrotoxicosis or a phaeochromocytoma is not merely useless but leaves a dangerous lesion untreated. The organic screen (thyroid function, a substance and caffeine history, attention to withdrawal timing, and where the story is episodic and physical, catecholamines and an ECG) comes before the psychiatric formulation, not after it.

Then the focus of the fear. Once the body is cleared, the anxiety disorders are told apart not by the *symptoms* of anxiety (which are shared) but by *what the fear is about*. GAD fears everything and nothing in particular; panic fears the next attack; social anxiety fears being judged; specific phobia fears one circumscribed thing; agoraphobia fears being trapped where escape is hard. Name the focus and you have named the disorder.

RULE **Exclude the body before you name the disorder.** Thyroid function, a caffeine and substance history, and (where symptoms are episodic and physical) an ECG and catecholamines precede any anxiety-disorder label; the focus of the fear then names the disorder.

10.2 Discriminating the anxiety disorders: the focus of the fear

The one-liner for each. The examiner wants the discriminating focus stated in a single clause. GAD is free-floating anxiety, chronic uncontrollable worry across many domains, not tied to any one trigger. Panic disorder is defined by *recurrent unexpected panic attacks* that come out of the

blue from a calm state, with the fear being of the attacks themselves (anticipatory anxiety about the next surge). Social anxiety disorder is a *fear of scrutiny and negative evaluation* in social or performance situations. Specific phobia is fear of a *circumscribed object or situation* (an animal, heights, blood, flying). Agoraphobia is fear of situations *where escape would be difficult or help unavailable* should a panic-like or incapacitating event strike, the fear is about escape and rescue, not the place itself.

DISORDER	THE ONE DISCRIMINATOR (FOCUS OF THE FEAR)	COURSE/CUE
Generalised anxiety disorder	**Free-floating, uncontrollable worry across many domains, not bound to any trigger**	Chronic, persistent
Panic disorder	**Fear of the attacks themselves; recurrent unexpected panic from a calm state**	Episodic, out of the blue
Social anxiety disorder	**Fear of scrutiny and negative evaluation by others**	Cued by social/performance settings
Specific phobia	Fear of one circumscribed object or situation	Cued by the single phobic stimulus
Agoraphobia	**Fear of situations where escape is difficult or help unavailable**	Cued by crowds, transport, open/enclosed spaces

The anxiety-disorders differentiation grid: each disorder is separated by the focus of the fear, not by the anxiety symptoms, which are shared (ICD-11 CDDR; DSM-5-TR 2022).

GOOD TO REMEMBER

- **Differential of the anxiety disorders:** the discriminator is the focus of the fear, GAD (everything, free-floating), panic (the next attack), social anxiety (negative evaluation), specific phobia (one circumscribed object), agoraphobia (being unable to escape or get help); state the focus in one clause and you have named the disorder.

10.3 Organic anxiety: the category and why episodic-versus-sustained matters

The concept. Organic anxiety disorder (organic anxiety disorder in ICD terms) is anxiety arising secondarily from a medical disorder, the fear-circuit output is real but the driver is bodily. The teaching pivot, drawn straight from the Shorter Oxford Textbook, is the *tempo* of the mimic. Sustained, low-grade organic drivers (thyrotoxicosis) reproduce the GAD picture; *episodic, paroxysmal* drivers (phaeochromocytoma, hypoglycaemia, paroxysmal arrhythmia) reproduce panic disorder or a phobic disorder, because they come in discrete surges (Shorter Oxford Textbook of Psychiatry). Matching the tempo of the mimic to the tempo of the psychiatric picture is how you decide which physical test to send.

The pointer to organicity. Features that should push you towards a physical cause rather than a primary anxiety disorder: a first presentation of anxiety in an older patient, prominent and disproportionate physical signs, anxiety without the cognitive content of worry or dread, a fluctuating episodic course with autonomic storms, and any hard sign on examination (goitre, exophthalmos, atrial fibrillation, sustained hypertension).

10.4 Hyperthyroidism: the sustained mimic of GAD

The picture. In hyperthyroidism (thyrotoxicosis) the patient is irritable and restless, with tremor and tachycardia, exactly the somatic tail of GAD, and it is the commonest and most examinable organic mimic (Shorter Oxford Textbook of Psychiatry). Because the thyroid drive is continuous, the resulting anxiety is *sustained*, so thyrotoxicosis is the classic mimic of generalised anxiety disorder rather than of panic.

The pointing feature, the test, the discriminator. The pointing features are the hard thyroid signs, an enlarged thyroid (goitre), atrial fibrillation, exophthalmos, heat intolerance and weight loss despite a good appetite. The screening test is thyroid function (a suppressed TSH with raised free T4). The discriminator from a primary anxiety disorder is that thyrotoxic patients lose weight while eating well and show the eye and gland signs, and their anxiety resolves when the thyroid is treated (Shorter Oxford Textbook of Psychiatry).

GOOD TO REMEMBER

- **Hyperthyroidism (thyrotoxicosis):** the sustained organic mimic of GAD (irritability, restlessness, tremor, tachycardia); pointing features are goitre, exophthalmos, atrial fibrillation and weight loss with preserved appetite; the screening test is thyroid function (suppressed TSH, raised free T4); the discriminator is the physical thyroid signs and resolution on treating the thyroid.

10.5 Phaeochromocytoma: the paroxysmal mimic of panic

The picture. A phaeochromocytoma is a catecholamine-secreting tumour that releases adrenaline and noradrenaline in bursts, producing paroxysmal episodes of palpitations, pounding headache, sweating and a surge of dread, indistinguishable at the bedside from a panic attack. Because the secretion is *episodic*, the phaeochromocytoma mimics panic disorder or a phobic disorder rather than GAD (Shorter Oxford Textbook of Psychiatry; New Oxford Textbook of Psychiatry).

The pointing feature, the test, the discriminator. The pointing feature is *paroxysmal hypertension*, blood pressure that spikes with each attack, together with the headache-palpitations-sweating triad. The screening tests are plasma or 24-hour urinary metanephrines and catecholamines. The discriminator from panic disorder is the objectively recorded hypertensive surge during an attack and the presence of the pounding headache, panic disorder does not raise the blood pressure to those levels or produce that headache. The classic exam pairing is that phaeochromocytoma and hypoglycaemia both cause *episodic* symptoms and therefore mimic panic or phobia (Shorter Oxford Textbook of Psychiatry).

GOOD TO REMEMBER

- **Phaeochromocytoma:** a catecholamine-secreting tumour producing paroxysmal palpitations, pounding headache and sweating that mimic panic; the pointing feature is paroxysmal hypertension; the screening test is plasma/urinary metanephrines and catecholamines; the discriminator is the recorded hypertensive surge and the headache during attacks.

10.6 Arrhythmia and supraventricular tachycardia, and hypoglycaemia

Cardiac: the palpitation that came first. A paroxysmal arrhythmia, above all a supraventricular tachycardia (SVT), produces sudden palpitations, breathlessness and a sense of doom that read as panic; paroxysmal tachycardia is on the standard organic-mimic list (New Oxford Textbook of Psychiatry). The pointing feature is a very rapid, regular, abruptly-starting-and-stopping palpitation that *precedes* the fear rather than following it, and, in panic disorder, mitral valve prolapse is a recognised association. The screening test is an ECG, and ideally a rhythm strip or ambulatory (Holter) monitor capturing an episode. The discriminator from panic is the temporal order and the rate: in SVT the tachycardia comes first and is faster and more regular than the sinus tachycardia of panic, which follows the psychological alarm.

Hypoglycaemia: the episodic autonomic surge. Recurrent hypoglycaemia produces episodic tremor, sweating, palpitations and anxiety and, like phaeochromocytoma, mimics panic or a phobic disorder because it is episodic (Shorter Oxford Textbook of Psychiatry; New Oxford Textbook of Psychiatry). The pointing feature is the relationship to fasting and the relief with food; the screening test is a paired capillary/venous glucose during an attack (Whipple's triad); the discriminator is the low glucose recorded during symptoms and their resolution with carbohydrate.

GOOD TO REMEMBER

- **SVT/arrhythmia:** abrupt rapid regular palpitations that come *before* the fear; test with ECG/Holter; discriminator is the tachycardia preceding the anxiety and being faster and more regular than panic's sinus tachycardia.
- **Hypoglycaemia:** episodic tremor, sweating and anxiety mimicking panic; test with glucose during symptoms; discriminator is the low glucose recorded in the attack and relief with food.

10.7 Asthma and COPD: the breathless mimic

The picture. Bronchospasm in asthma and hypoxia or hypercapnia in COPD produce breathlessness, chest tightness and a frightened, air-hungry arousal that is easily mislabelled panic, and the two genuinely co-occur and feed each other (breathlessness triggers panic, panic worsens breathlessness). The pointing feature is that the *breathlessness comes first* and is accompanied by wheeze, cough, a documented trigger (exertion, allergen, cold air) or a smoking history, rather than arising from a calm state. The screening test is peak expiratory flow or spirometry (and pulse oximetry in an acute episode). The discriminator from panic disorder is the demonstrable airflow obstruction and hypoxia, and the response to a bronchodilator, panic produces hyperventilation with a normal or low CO2, not true obstruction.

GOOD TO REMEMBER

- **Asthma/COPD:** breathlessness and chest tightness mimicking panic, with the dyspnoea coming first plus wheeze/cough/trigger or smoking history; test with peak flow/spirometry and oximetry; discriminator is demonstrable airflow obstruction and hypoxia responding to a bronchodilator, unlike the normocapnic hyperventilation of panic.

10.8 Substance and caffeine intoxication

Stimulant and substance-induced anxiety. Substance-induced anxiety is anxiety arising during intoxication with a stimulant, cocaine, amphetamine or other sympathomimetic, or from other agents, and it must be excluded before a primary diagnosis is made. The pointing feature is the temporal link to the substance and any intoxication signs (dilated pupils, tachycardia, hypertension, agitation); the screening test is a substance history and, where available, a urine drug screen; the discriminator is that the anxiety tracks the substance and clears as the drug is eliminated.

Caffeine, the ubiquitous and forgotten mimic. Caffeine anxiety (caffeinism, caffeine intoxication) is the mimic most often missed because it is legal and everyday. DSM defines caffeine intoxication as recent consumption usually in excess of **250 mg** of caffeine (about 2 to 3 cups of brewed coffee) with **five or more** of restlessness, nervousness, excitement, insomnia, flushed face, diuresis, gastrointestinal disturbance, muscle twitching, rambling thought, tachycardia, and psychomotor agitation (DSM-5-TR 2022). The pointing feature is a high daily caffeine load; the screening test is a careful dietary caffeine history (brewed coffee about 100 mg/cup, instant about 60 mg, tea about 45 mg, cola 25 to 50 mg per can); the discriminator is that the anxiety and insomnia settle on cutting caffeine down.

COMMON TRAP

The classic error is to diagnose a primary anxiety disorder and miss an organic mimic. Before labelling GAD or panic, exclude hyperthyroidism (goitre, exophthalmos, weight loss), a phaeochromocytoma and hypoglycaemia (episodic surges, paroxysmal hypertension in the phaeochromocytoma), an arrhythmia or SVT (palpitation preceding the fear), asthma or COPD (breathlessness first), and above all a caffeine habit or stimulant use, each reproduces the anxiety picture, and each is treated at its source, not with an SSRI.

GOOD TO REMEMBER

- **Substance-induced anxiety:** anxiety during stimulant/sympathomimetic intoxication; pointing feature is the temporal link plus intoxication signs; screen with substance history and urine drug screen; discriminator is clearance as the drug is eliminated.
- **Caffeine intoxication:** more than 250 mg caffeine plus 5 or more of restlessness, nervousness, insomnia, flushed face, diuresis, GI upset, twitching, tachycardia; screen with a caffeine dietary history; discriminator is resolution on reducing caffeine.

10.9 Alcohol and benzodiazepine withdrawal: the morning mimic

The picture. Withdrawal from alcohol or from a benzodiazepine reproduces GAD-like anxiety with tremor, sweating, tachycardia and insomnia, and it is a leading cause of "treatment-resistant anxiety" in a dependent patient who is really in daily micro-withdrawal (Shorter Oxford Textbook of Psychiatry). The pointing feature that Gelder emphasises is *timing*: anxiety that is worst on waking in the morning, when overnight alcohol and short-half-life benzodiazepine levels have fallen, points to withdrawal (and, separately, morning-worst anxiety also raises depressive disorder). The screening test is a detailed alcohol and sedative history with quantities

and timing; the discriminator from a primary anxiety disorder is the diurnal, dose-linked pattern of the anxiety and, on withdrawal from certain drug classes, hard signs such as pupillary changes.

GOOD TO REMEMBER

- **Alcohol/benzodiazepine withdrawal:** a GAD-like tremulous, sweaty, tachycardic anxiety that is worst on waking; the pointing feature is the morning timing as overnight levels fall; screen with a detailed substance-and-timing history; the discriminator is the diurnal, dose-linked pattern rather than the persistent free-floating worry of primary anxiety.

MIMIC	POINTING FEATURE	SCREENING TEST	DISCRIMINATOR FROM PRIMARY ANXIETY
Hyperthyroidism	**Goitre, exophthalmos, AF, weight loss with appetite**	Thyroid function (TSH, free T4)	Physical thyroid signs; sustained (mimics GAD); resolves on treating thyroid
Phaeochromocytoma	**Paroxysmal hypertension, pounding headache**	Plasma/urinary metanephrines, catecholamines	Recorded BP surge in attack; episodic (mimics panic)
Arrhythmia / SVT	Abrupt rapid regular palpitation before the fear	ECG, Holter/rhythm strip	Tachycardia precedes anxiety; faster, more regular than panic
Hypoglycaemia	Fasting-related surges, relief with food	Glucose during symptoms (Whipple's triad)	Low glucose recorded in attack; episodic (mimics panic)
Asthma / COPD	Breathlessness first, wheeze, smoking history	Peak flow/spirometry, oximetry	Airflow obstruction and hypoxia; responds to bronchodilator
Substance / caffeine intoxication	High stimulant or caffeine load, intoxication signs	Substance history, urine drug screen, caffeine history	Anxiety tracks the substance; clears on cessation
Alcohol / benzodiazepine withdrawal	**Anxiety worst on waking, dose-linked**	Detailed substance and timing history	Diurnal, dose-linked pattern; withdrawal signs

The anxiety-versus-medical-mimic grid: pointing feature, screening test and the discriminator from a primary anxiety disorder for each organic mimic (Shorter Oxford Textbook of Psychiatry; New Oxford Textbook of Psychiatry).

250 mg
CAFFEINE INTOXICATION THRESHOLD (PLUS 5 OR MORE SYMPTOMS)

5
DSM SYMPTOMS REQUIRED FOR CAFFEINE INTOXICATION

100 mg
CAFFEINE PER CUP OF BREWED COFFEE (INSTANT ABOUT 60)

TRAP **Missing an organic mimic is the exam-fatal error.** Episodic autonomic storms with paroxysmal hypertension are a phaeochromocytoma until proven otherwise; sustained tremor with weight loss is thyrotoxicosis; anxiety worst on waking is alcohol or benzodiazepine withdrawal, not "resistant GAD".

10.10 The India lens: the treatment gap and the benzodiazepine problem behind the differential

Two genuine Indian realities. First, the anxiety, OCD and PTSD treatment gap is wide, anxiety is under-recognised, heavily somatised (patients present with palpitations, tremor and "gas" rather than "worry"), and under-treated, so the organic mimics are precisely the physical complaints that get an anxious patient sent round the physicians for years without either an anxiety diagnosis or a thyroid test. Second, the entrenched over-prescription of benzodiazepines (typically alprazolam) means many "anxious" Indian patients are in chronic benzodiazepine dependence, so *benzodiazepine withdrawal* is itself a common, iatrogenic mimic of anxiety in Indian practice. The Indian Psychiatric Society CPGs exist to correct both, rule out the organic causes, treat the primary disorder with an SSRI or SNRI first-line, and reserve the benzodiazepine as a short, time-limited bridge rather than the standing prescription (the Indian Psychiatric Society 2020).

INDIA

The highest-yield Indian point on this discrimination topic is that the benzodiazepine over-prescription problem creates its own mimic: a large number of Indian patients labelled "anxiety" are actually in daily alprazolam micro-withdrawal, which reads as morning-worst anxiety. The correct Indian workup mirrors the global one, exclude hyperthyroidism (a cheap TSH), a phaeochromocytoma and hypoglycaemia where episodic, and a caffeine or substance load, then treat the primary disorder with an SSRI or SNRI (escitalopram Nexito or Rexipra, sertraline) rather than adding yet another benzodiazepine strip.

RULE **Tempo tells you which mimic.** Sustained anxiety with weight loss and tremor is thyrotoxicosis (mimics GAD); episodic autonomic surges are phaeochromocytoma or hypoglycaemia (mimic panic); a palpitation preceding the fear is an arrhythmia; morning-worst anxiety is withdrawal.

HOLD THIS

Before naming any anxiety disorder, exclude the organic mimics, thyrotoxicosis (sustained, mimics GAD), phaeochromocytoma and hypoglycaemia (episodic, mimic panic), arrhythmia/SVT (palpitation first), asthma/COPD (breathlessness first), caffeine and substance intoxication, and alcohol/benzodiazepine withdrawal (worst on waking); then separate the anxiety disorders by the focus of the fear, GAD (everything), panic (the next attack), social anxiety (negative evaluation), specific phobia (one object), agoraphobia (no escape).

Obsessive-compulsive and related disorders

11 · OCD: clinical features, dimensions and insight

Where anxiety disorders are about a feared object or a feared situation, **obsessive-compulsive disorder** is about a feared *thought* and the ritual built to undo it. **Obsessive-compulsive disorder** (**ocd**) is defined by **obsessions** (intrusive, unwanted, ego-dystonic thoughts, images or urges) and **compulsions** (repetitive behaviours or mental acts performed to neutralise the obsession or its dreaded consequence). It is the anchor diagnosis of the obsessive-compulsive and

related disorders grouping, which both DSM-5-TR and ICD-11 lifted out of the anxiety disorders into a spectrum of its own, and which the accompanying figure maps.

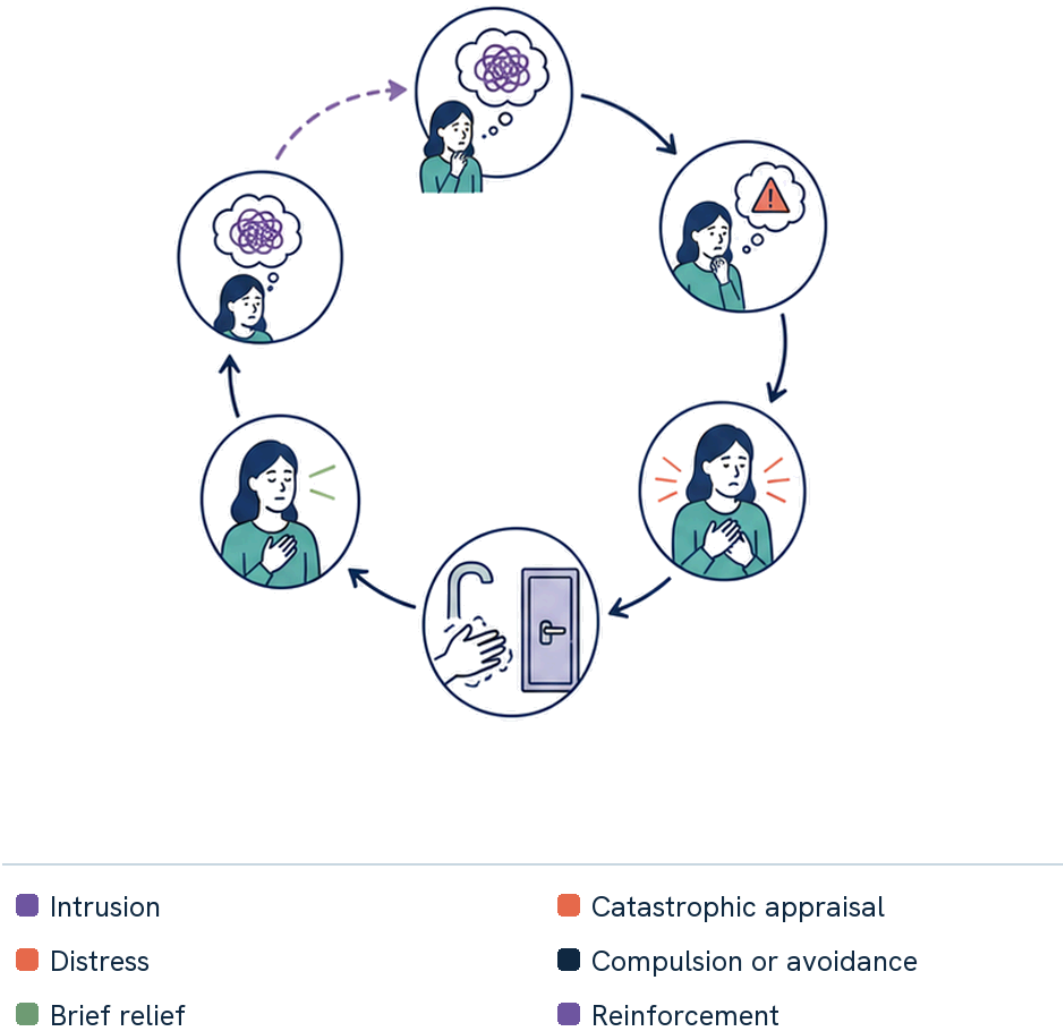


Fig 14.8 The OCD maintenance cycle: an intrusion is appraised as threatening, producing distress and a compulsion or avoidance response; brief relief negatively reinforces the response and strengthens the cycle.

Why it matters, and what this note owns. Examiners test three things on this topic and this note owns all three: the exact definitions of obsession and compulsion (the ego-dystonic, intrusive, resisted quality is the whole discriminator), the four **symptom dimensions** and how each obsession pairs to its compulsion, and the **insight specifier** that ranges from good insight to frankly delusional conviction, alongside the **tic-related ocd** specifier. The management story (a high-dose SSRI for a long trial, then clomipramine, then antipsychotic augmentation, with exposure and response prevention as the psychological spine) is developed in its own management note; the deep antidepressant pharmacology of the SSRIs and clomipramine lives in the Mood disorders: pharmacotherapy notes, and neurosurgery and deep brain stimulation for the refractory patient in the ECT and neurostimulation notes. What follows is the phenomenology, the dimensions, the insight and tic specifiers, and the epidemiology and course.

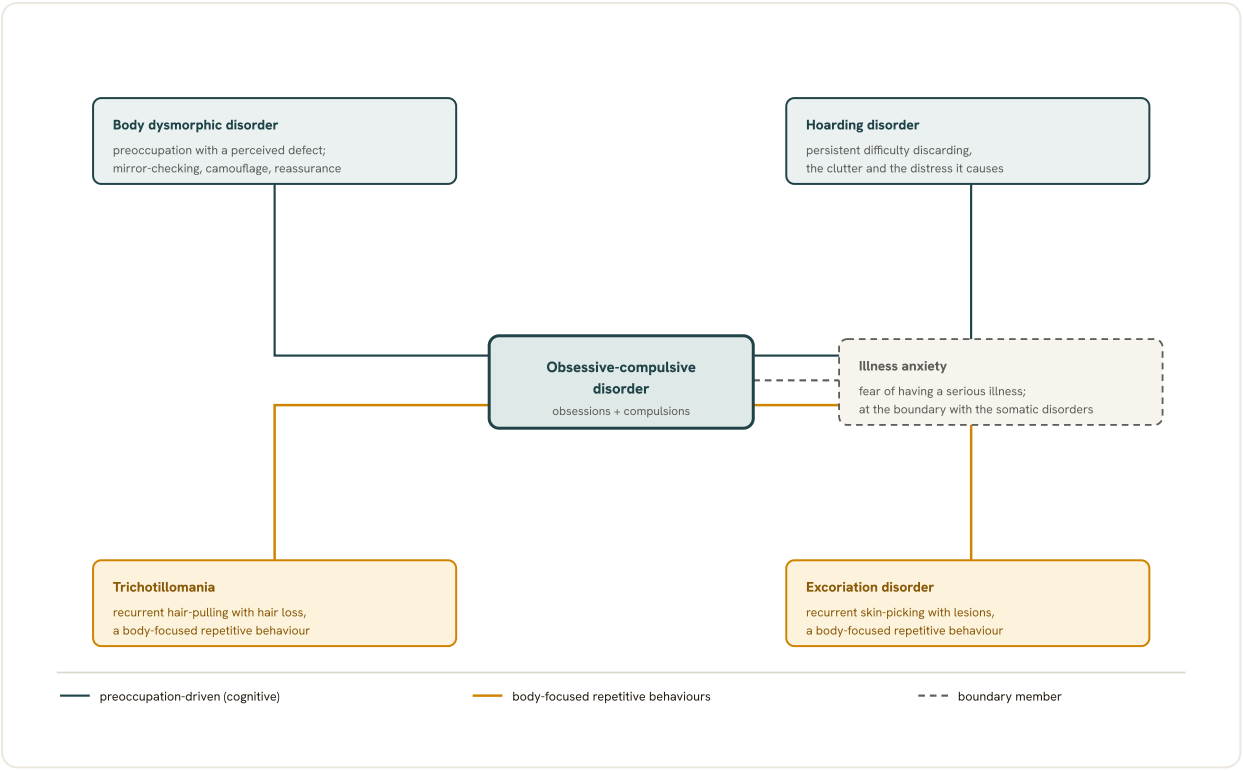


Fig 14.9 The obsessive-compulsive and related disorders spectrum. OCD sits at the centre; the related disorders share either a driving preoccupation or a repetitive behaviour. Body dysmorphic disorder (a preoccupation with a perceived defect), hoarding disorder (the difficulty discarding) and, at the boundary with the somatic-symptom disorders, illness anxiety are the preoccupation-driven members; trichotillomania (hair-pulling) and excoriation (skin-picking) are the body-focused repetitive behaviours. Grouping them as a spectrum is the pedagogic point: each is recognised by the shared thread of a repetitive act or a fixed preoccupation, and each responds, in part, to the serotonin reuptake inhibitors and to the behavioural therapies. The somatic-symptom boundary is taught in the Somatic-symptom, sexual, impulse-control disorders and suicide notes.

11.1 Obsessions: intrusive, unwanted, ego-dystonic mental events

The definition to state cold. Obsessions are recurrent and persistent thoughts (e.g. of contamination), images (e.g. of a violent or horrific scene) or urges/impulses (e.g. to stab someone) that are experienced as *intrusive and unwanted* and that, in most people, cause marked anxiety or distress (DSM-5-TR 2022; ICD-11 CDDR). Three qualities carry the diagnosis. They are **intrusive** (they force their way into awareness against the person's will), **unwanted** (not pleasurable, not experienced as voluntary), and **ego-dystonic** (felt as alien to the self and as senseless or repugnant, which is why the person tries to resist them). The individual attempts to ignore or suppress the obsession, or to neutralise it with another thought or action, that is, with a compulsion.

The ego-dystonic hinge. The ego-dystonic quality is the single most useful discriminator. A worry in generalised anxiety disorder is ego-syntonic (the person endorses it as a reasonable, if excessive, concern); a delusion is held as true; a ruminative depressive thought is congruent with low mood. An obsession, by contrast, is experienced as intrusive, senseless and one's own but unwanted, which is exactly why the patient fights it. That fight, and the distress it generates, is what makes it pathological rather than merely an odd thought.

GOOD TO REMEMBER

- **Obsession:** a recurrent, persistent thought, image or urge experienced as intrusive, unwanted and ego-dystonic, causing marked anxiety or distress; the person resists or tries to neutralise it (usually with a compulsion); the ego-dystonic, resisted quality is the defining discriminator from a GAD worry (ego-syntonic) and from a delusion (held as true).

11.2 Compulsions: repetitive acts that neutralise, not connected or clearly excessive

The definition to state cold. Compulsions are repetitive behaviours (e.g. hand washing, ordering, checking) or mental acts (e.g. praying, counting, repeating words silently) that the person feels *driven to perform* in response to an obsession or according to rules that must be applied rigidly (DSM-5-TR 2022). Their aim is to prevent or reduce anxiety or distress, or to prevent some dreaded event or situation, or to reach a sense of **completeness** or "just right" (ICD-11 CDDR). Two qualifiers are essential: the compulsion is either *not connected in a realistic way* to what it is meant to neutralise (arranging items symmetrically to stop harm coming to a relative), or is *clearly excessive* (showering for hours to prevent illness).

Mental compulsions are still compulsions. A high-yield trap is to equate compulsions with visible behaviours only. Mental acts, silent counting, praying to a formula, mentally reviewing a memory to be sure no harm was done, are compulsions too, and a patient with only intrusive thoughts and covert mental rituals ("pure O") can be mislabelled as having obsessions alone. Compulsions are not done for pleasure, though they may bring transient relief; that relief is what negatively reinforces and perpetuates the cycle.

WORKED EXAMPLE

A young man is plagued by intrusive images of harm coming to his mother whenever he leaves the house (obsession: intrusive, unwanted, ego-dystonic). To neutralise the image he touches the doorframe in sets of four and mentally recites a fixed phrase until it feels "just right" (compulsions: one overt, one mental, driven, rigidly ruled). The ritual is not realistically connected to his mother's safety and consumes over an hour a day. Obsession and compulsion are thematically paired (harm and checking/undoing), which is the typical structure.

GOOD TO REMEMBER

- **Compulsion:** a repetitive behaviour or mental act the person feels driven to perform in response to an obsession or by rigid rules, aimed at reducing distress or preventing a dreaded event or reaching a "just right" sense; it is either not realistically connected to what it neutralises or is clearly excessive; mental rituals (counting, praying, reviewing) count as compulsions.

11.3 Obsessions and compulsions are thematically paired

The pairing rule. Most people with OCD have both obsessions and compulsions, and the two are typically related in content or temporal sequence: contamination obsessions drive washing rituals, harm obsessions drive checking, symmetry obsessions drive ordering and repeating. Compulsions are usually performed *in response to* the obsession, but ICD-11 notes that early in the illness a compulsion may precede a clear obsession (a person checks the gas knob repeatedly

and only then concludes they must be afraid of fire). Understanding the obsession-compulsion link matters for treatment, because exposure and response prevention targets exactly that link.

Associated features that examiners like. Sensory phenomena, physical "just-right" sensations or a feeling of incompleteness that precede compulsions, are reported by up to **60%** of patients (DSM-5-TR 2022; Tasman). Avoidance of triggers is common, and the characteristic dysfunctional beliefs are an inflated sense of responsibility, overestimation of threat, perfectionism, intolerance of uncertainty and an overvaluation of the power of thoughts (believing that having a forbidden thought is as bad as acting on it). Family involvement in rituals, termed *accommodation*, maintains symptoms and is a treatment target, especially in children.

RULE **Obsession and compulsion are a matched pair.** The obsession is the intrusive, ego-dystonic thought; the compulsion is the driven, neutralising act; they are thematically linked (contamination and washing, harm and checking), and it is that link, not the behaviour alone, that defines and is treated in OCD.

11.4 The four symptom dimensions

The dimensional map. The content of obsessions and compulsions varies between individuals but clusters into recognised symptom dimensions that are consistent over time in adults, occur across cultures and may map onto partly different neural substrates (DSM-5-TR 2022; ICD-11 CDDR). DSM-5-TR names four: **contamination and washing** (contamination obsessions with cleaning/washing compulsions); **symmetry and ordering** (symmetry obsessions with repeating, ordering and counting compulsions, often with "just-right" sensory phenomena); **forbidden or taboo thoughts** (aggressive, sexual or religious/scrupulosity obsessions and related compulsions, often mental); and **harm and checking** (fears of harm to self or others with checking compulsions). ICD-11 CDDR groups the first three and treats **hoarding**-type accumulation arising from typical obsessions (e.g. fear of harming others) as a consequence rather than a dimension. Most patients have symptoms in more than one dimension.

The hoarding caveat. Accumulation driven by an obsession (keeping items for fear that discarding them will cause harm) sits within OCD, but it must be distinguished from primary *hoarding disorder*, now a separate diagnosis in the obsessive-compulsive and related grouping, in which the difficulty discarding is the primary problem and is driven by a perceived need to save and distress at discarding, not by a classic obsession. Naming that boundary is the examiner's expected nuance.

DIMENSION	TYPICAL OBSESSION	TYPICAL COMPULSION
Contamination and washing	**Fear of germs, dirt, illness, contamination**	Washing, cleaning, decontamination rituals, avoidance
Symmetry and ordering	Need for symmetry, exactness, "just right"	**Ordering, arranging, repeating, counting**
Forbidden or taboo thoughts	**Aggressive, sexual or religious (scrupulosity) intrusions**	Mental rituals, praying, confessing, reassurance-seeking
Harm and checking	Fear of harm to self or others	Checking locks, taps and gas; rechecking; reassurance-seeking

The four DSM-5-TR symptom dimensions of OCD; each obsession pairs to a characteristic compulsion, and most patients span more than one dimension (DSM-5-TR 2022; ICD-11 CDDR groups the first three).

GOOD TO REMEMBER

- **Symptom dimensions:** four DSM-5-TR clusters, contamination and washing; symmetry and ordering; forbidden or taboo thoughts (aggressive/sexual/religious); and harm with checking, ICD-11 grouping the first three; each obsession pairs to its compulsion, most patients span more than one dimension, and obsession-driven accumulation must be separated from primary hoarding disorder.

11.5 The insight specifier: good/fair, poor, absent/delusional

Insight is a spectrum, and it is specified. People with OCD vary in how far they recognise that their obsessive-compulsive beliefs are untrue or excessive, and DSM-5-TR captures this with a three-level insight specifier (DSM-5-TR 2022). *With good or fair insight*: the person recognises the OCD beliefs are definitely or probably not true, or may or may not be true. *With poor insight*: the person thinks the beliefs are probably true. *With absent insight/delusional beliefs*: the person is completely convinced the beliefs are true. Poorer insight is linked to worse long-term outcome, and insight can fluctuate within a person over the course of illness (and with the current anxiety level), which is why it should be judged over a period of a few days to a week rather than in a single anxious moment.

The ICD-11 two-level version. ICD-11 CDDR uses a two-level specifier, *with fair to good insight* and *with poor to absent insight*, collapsing the DSM's poor and absent categories; it applies the same insight logic across the cognitive obsessive-compulsive and related disorders (OCD, body dysmorphic disorder, olfactory reference disorder, hypochondriasis and hoarding disorder). The clinically vital point on both systems is that the delusional-conviction end of OCD is *not* reclassified as a psychotic disorder: an absent-insight/delusional OCD belief stays within OCD (with the specifier) and is treated as OCD, not as schizophrenia.

INSIGHT LEVEL (DSM-5-TR)	THE PERSON'S STANCE ON THE OCD BELIEF
Good or fair insight	Recognises beliefs are definitely/probably not true, or may or may not be true
Poor insight	**Thinks the beliefs are probably true**
Absent insight / delusional	**Completely convinced the beliefs are true (about 4% or fewer; still coded as OCD, not psychosis)**

The DSM-5-TR insight specifier; ICD-11 collapses the lower two into a single "poor to absent" level, and the delusional end stays within OCD rather than becoming a psychotic diagnosis (DSM-5-TR 2022; ICD-11 CDDR).

COMMON TRAP

Do not reclassify an absent-insight, delusionally-held OCD belief as a psychotic disorder. A small minority (around 4% or fewer) are completely convinced their obsessive belief is true; this is coded as OCD "with absent insight/delusional beliefs", not as schizophrenia or delusional disorder, and it is still treated with the OCD algorithm (SSRI, then augment), not primarily with an antipsychotic. Missing this leads to the wrong diagnosis and the wrong first-line drug.

GOOD TO REMEMBER

- **Insight specifier:** DSM-5-TR grades insight as good/fair, poor, or absent/delusional (about 4% or fewer are delusional); ICD-11 uses two levels (fair-to-good vs poor-to-absent); poorer insight predicts worse outcome; the delusional end stays coded as OCD, not a psychotic disorder, and keeps the OCD treatment algorithm.

11.6 The tic-related specifier

What it flags. DSM-5-TR adds a tic-related specifier: **tic-related ocd** is diagnosed when the individual has a current or past history of a tic disorder (DSM-5-TR 2022). It matters because up to **30%** of people with OCD have a lifetime tic disorder, most commonly males with childhood-onset OCD, and this subgroup differs in symptom themes (more symmetry, "just-right" and ordering), comorbidity (Tourette syndrome, ADHD), course and pattern of familial transmission. Tourette syndrome is cross-listed alongside OCD in ICD-11 precisely because of this high co-occurrence, the shared premonitory-urge phenomenology and the familial link.

The treatment relevance. The tic-related subtype is the one classic exception to the "antipsychotics do nothing on their own in OCD" rule: patients with comorbid tics tend to respond somewhat better to antipsychotic augmentation of an SSRI. So the specifier is not merely descriptive, it nudges the augmentation choice, which is why it is worth naming in an answer.

GOOD TO REMEMBER

- **Tic-related OCD:** the DSM-5-TR specifier for a current or past tic disorder; up to 30% of OCD patients have a lifetime tic disorder (mostly males, childhood onset); the subtype skews to symmetry/"just-right"/ordering symptoms with Tourette and ADHD comorbidity, and responds relatively better to antipsychotic augmentation of an SSRI.

11.7 Criteria in brief: the time-consuming threshold and the boundary with normality

The threshold. Beyond the presence of obsessions and/or compulsions, both systems require that they are *time-consuming* (a benchmark of more than **1 hour per day** is given) *or* cause clinically significant distress or functional impairment (DSM-5-TR 2022; ICD-11 CDDR). The symptoms must not be attributable to a substance or another medical condition, and must not be better explained by another mental disorder. ICD-11 lists a set of exclusions to work through, so a checking obsession is not GAD worry, a preoccupation with appearance is body dysmorphic disorder, difficulty discarding is hoarding disorder, hair-pulling is trichotillomania, and so on.

The boundary with normality. Intrusive thoughts and repetitive behaviours are common in the general population (a fleeting thought of harming a loved one, double-checking the front door). What converts them into OCD is the time-consuming, distressing, impairing quality; developmentally normative childhood rituals (avoiding pavement cracks) are transient, age-appropriate and not time-consuming, and should not be over-diagnosed. Sudden or unusually late onset should prompt a search for an organic cause, for example a basal ganglia lesion or, in children with abrupt onset, paediatric autoimmune neuropsychiatric disorders associated with streptococcal infection (PANDAS).

TRAP **Do not diagnose OCD from the content alone.** Intrusive thoughts and double-checking are near-universal; OCD needs the symptoms to be time-consuming (over an hour a day) or to cause significant distress or impairment, and a sudden or late-onset picture should trigger a hunt for an organic mimic (basal ganglia lesion, PANDAS) before the label is fixed.

11.8 The Yale-Brown Obsessive Compulsive Scale (Y-BOCS): the severity instrument

What it is. The Yale-Brown Obsessive Compulsive Scale (Y-BOCS) is the standard clinician-rated severity measure in OCD and the outcome instrument in virtually every drug trial (Kaplan and Sadock 2024). It has **10 items** rated from a semi-structured interview: the first five rate obsessions and the second five rate compulsions, across the same five parameters, time occupied, interference with functioning, distress caused, resistance, and degree of control. Each item scores **0 to 4**, so obsessions and compulsions each total 0 to 20 and the overall score runs **0 to 40**. It is preceded by a symptom checklist that captures the specific content across the dimensions, and it is reproduced on the accompanying scale plate rather than pasted here. The paediatric version is the CY-BOCS.

Reading the number. Higher scores mean greater severity, and typical scores for patients presenting with OCD fall in the **16 to 30** range; a threshold of **16** is the usual cut-off for entry into drug trials (Kaplan and Sadock 2024). The Y-BOCS is also how treatment "response" is defined in the literature, most often as a reduction of at least 25 to 35% from the baseline Y-BOCS score, which is why the scale, not just a clinical impression, anchors the decision on whether an adequate trial has failed.

GOOD TO REMEMBER

- **Y-BOCS:** clinician-rated, 10 items (5 obsessions + 5 compulsions across time, interference, distress, resistance, control), each 0 to 4, obsessions and compulsions each 0 to 20, total 0 to 40; typical OCD scores 16 to 30, with 16 the usual drug-trial entry threshold; it is the standard severity and outcome measure (response commonly defined as a 25 to 35% reduction). Paediatric form: CY-BOCS.

0 to 40	16	1 hour	30%
Y-BOCS TOTAL (10 ITEMS, EACH 0 TO 4)	Y-BOCS DRUG-TRIAL ENTRY THRESHOLD; TYPICAL OCD 16 TO 30	TIME-CONSUMING BENCHMARK (PER DAY) IN THE CRITERIA	LIFETIME TIC DISORDER IN OCD (TIC-RELATED SUBTYPE)

11.9 Epidemiology and course

The numbers. OCD has a lifetime prevalence of roughly **2 to 3%**, one of the more common serious psychiatric disorders; the classic Epidemiologic Catchment Area figures were about 2.9% in women and 2% in men, a modest female excess in adults (Tasman). The sex balance flips by age of onset: childhood-onset OCD, particularly before the age of 10, is commoner in males and carries greater genetic loading and poorer outcome, whereas adolescent-onset skews female. Around 30% of patients have a lifetime tic disorder, and only about 4% or fewer sit at the absent-insight/delusional end.

The course. Onset is typically in the late teens and early twenties, usually gradual; onset after 35 is uncommon and, like sudden onset, should prompt a search for an organic cause. Many adults (30 to 50%) report childhood onset. In adults OCD is generally a chronic condition with waxing and waning of symptoms; a minority run an episodic or a progressively worsening course. There is a more hopeful paediatric signal: of those with childhood or adolescent onset, roughly **40%** achieve full remission by early adulthood (ICD-11 CDDR). Depression is the commonest comorbidity, and untreated OCD is characteristically slow to reach care.

GOOD TO REMEMBER

- **OCD epidemiology and course:** lifetime prevalence about 2 to 3% (slight adult female excess; childhood onset before age 10 is male-predominant with worse prognosis); onset usually late teens to early twenties and gradual, with onset after 35 or sudden onset flagging an organic cause; adult course is chronic and waxing-waning, but around 40% of childhood-onset cases remit fully by early adulthood.

11.10 The India lens: a wide OCD treatment gap and a benzodiazepine reflex

Under-recognised and under-treated. OCD in India carries a wide treatment gap. Symptoms are hidden by shame (contamination, taboo sexual or religious/scrupulosity obsessions are rarely volunteered), long delays precede a first consultation, and the disorder is under-recognised in general practice. Culturally shaped content is genuine: scrupulosity and religious obsessions may be especially distressing where ritual exactitude matters, and contamination themes (concepts of ritual purity and pollution) are common; distinguishing a religious compulsion from devout normative practice sometimes needs a knowledgeable religious informant (ICD-11 CDDR). The

Indian Psychiatric Society CPGs frame the correct approach, an adequate high-dose SSRI trial with exposure and response prevention, developed in the management note.

The benzodiazepine problem. Into this gap flows the same reflex that dogs the anxiety disorders in Indian practice: a benzodiazepine (often alprazolam) prescribed as if it were treatment. It is not. Benzodiazepines do nothing for the core obsessions and compulsions, at best they blunt the accompanying anxiety, and long-term use brings tolerance and dependence. The first-line agents are cheap and familiar as Indian brands, escitalopram, sertraline, fluoxetine, fluvoxamine and paroxetine among the SSRIs, and clomipramine (Anafranil) as the tricyclic option, used at high dose for a long trial. Naming the ego-dystonic obsession and the neutralising compulsion, and reaching for an SSRI rather than an anxiolytic, is the practical correction.

INDIA

OCD is common (lifetime prevalence around 2 to 3%) but reaches Indian care late and often disguised, contamination and religious/scrupulosity themes are frequent and culturally shaped, and the treatment gap is wide. The recurring error is treating it with a benzodiazepine (typically alprazolam), which touches none of the obsessions or compulsions; the Indian Psychiatric Society line, and the correct answer, is a high-dose SSRI (escitalopram, sertraline, fluvoxamine, fluoxetine or paroxetine) or clomipramine (Anafranil) with exposure and response prevention, the benzodiazepine having no role in core OCD treatment.

MNEMONIC

CObRA-DIT

The features to reproduce. **CObRA** holds the definition and the four dimensions: **C**ontamination/washing, **O**rder/symmetry, **b**ad/forbidden taboo thoughts, **R**isk of harm with checking, all built from an **A**lien (ego-dystonic) obsession neutralised by a compulsion. **DIT** holds the specifiers and cut: **D**istress/time-consuming (over 1 hour a day), **I**nsight graded good-fair to absent/delusional, **T**ic-related subtype.

HOLD THIS

OCD is intrusive, unwanted, ego-dystonic obsessions neutralised by driven, rigidly-ruled compulsions (behavioural or mental) that are not realistically connected or clearly excessive and are time-consuming (over an hour a day) or impairing; it runs across four DSM-5-TR dimensions (contamination/washing, symmetry/ordering, forbidden thoughts, harm/checking), carries an insight specifier from good-or-fair through poor to absent/delusional (delusional OCD stays OCD, about 4% or fewer) and a tic-related specifier (up to 30% lifetime tics); severity is scored on the Y-BOCS (10 items, 0 to 40), lifetime prevalence is about 2 to 3%, and onset is usually the late teens to early twenties.

12 · The OCD management algorithm

OCD is one of the two topics that examiners use to test whether you actually understand psychiatric prescribing rather than reciting a first-line drug. The disorder responds to the same serotonergic agents as depression, but the *rules of engagement are different*: the dose runs higher,

the trial runs longer, and the response is judged on a scale rather than a gestalt. **ocd management** is therefore a small, tight algorithm with four rungs, and the whole thing turns on one idea you must be able to state in a single breath, a **high-dose ssri** given for a **long trial** alongside **erp**, then clomipramine, then antipsychotic augmentation, then the refractory options.

Why it matters, and what this note owns. This note owns the ladder and the numbers, the target doses, the trial durations, the Y-BOCS response and remission thresholds, and where each guideline sits. The deep pharmacology of the SSRIs and of clomipramine (kinetics, adverse effects, interactions) is developed in the Mood disorders: pharmacotherapy notes and is not re-derived here; the general CBT model and the wider exposure principle behind ERP live in the Psychotherapies, clinical assessment, MSE and nosology notes; and deep brain stimulation and ablative neurosurgery for the truly refractory patient are cross-referenced to the ECT and neurostimulation notes. The management algorithm itself is set out in the accompanying figure, and the Y-BOCS form on the accompanying scale plate.

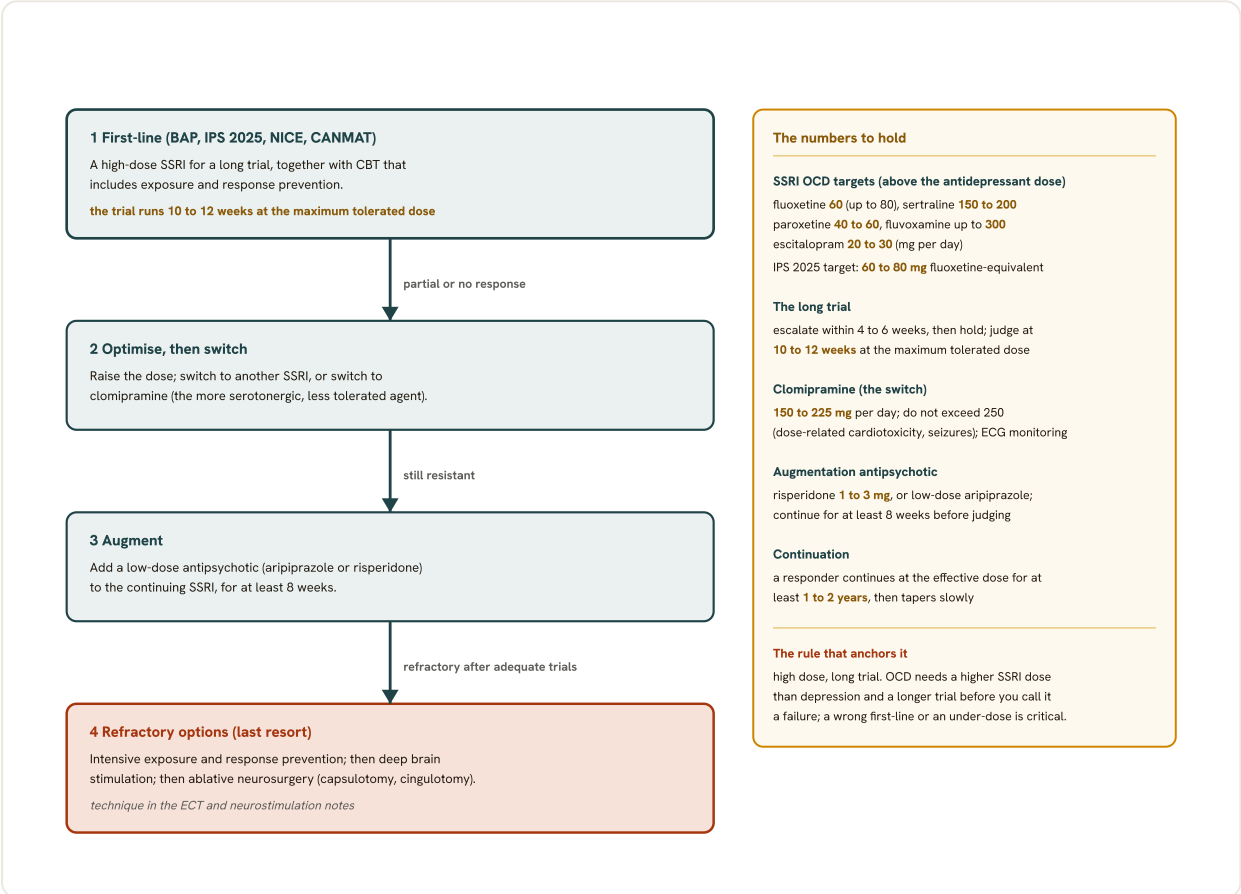


Fig 14.10 The OCD management algorithm. First-line, anchored on BAP, the IPS 2025 CPG, NICE and CANMAT, is a high-dose serotonin reuptake inhibitor given for a long trial of 10 to 12 weeks together with cognitive behaviour therapy that incorporates exposure and response prevention. On a partial or absent response the dose is optimised and the drug switched to another SSRI or to clomipramine (150 to 225 mg with ECG monitoring); a still-resistant illness is augmented with a low-dose antipsychotic (risperidone 1 to 3 mg or aripiprazole) for at least eight weeks; and the refractory case moves to intensive exposure and response prevention, then deep brain stimulation, then ablative neurosurgery. The anchoring rule is high dose, long trial: OCD needs a higher SSRI dose and a longer trial than depression, so under-dosing or stopping the trial early manufactures a false treatment failure. The deep antidepressant pharmacology is developed in the Mood disorders: pharmacotherapy notes, and the neurosurgical technique in the ECT and neurostimulation notes.

12.1 The shape of the ladder: four rungs and one governing principle

The four rungs. Every guideline collapses to the same staircase. *First-line* is a high-dose SSRI for a long trial *plus* CBT incorporating exposure and response prevention. *Partial or no response* means optimise the dose, then switch to another SSRI or to clomipramine. *Still resistant* means antipsychotic augmentation, low-dose aripiprazole or risperidone. *Refractory* means intensive ERP and, at a specialist centre, deep brain stimulation or ablative neurosurgery. Learn the staircase as a unit; the examiner wants the order, not a list.

The governing principle. The one line that runs through the whole ladder is that OCD is *under-treated by default*, because the doses are timid and the trials are cut short. Hold the principle first, then hang the drugs on it.

> **HOLD THIS**
> First-line OCD is a high-dose SSRI (target roughly fluoxetine 60 mg equivalent) for a long trial of about 10 to 12 weeks at the maximum tolerated dose, together with CBT incorporating exposure and response prevention; only then clomipramine, then aripiprazole or risperidone augmentation, then the refractory options.

12.2 First-line: a high-dose SSRI plus ERP, across every guideline

The BAP position. Lead with the British Association for Psychopharmacology: offer an SSRI as first-line pharmacological treatment for OCD, and consider higher daily SSRI doses, sometimes beyond standard formulary limits, because meta-analysis shows greater efficacy (though poorer tolerability) at higher dosages; offer exposure therapy or CBT as the evidence-based acute psychological treatment (BAP 2014). This is the verified **first-line ocd** anchor and must not be contradicted.

What the other guidelines say, and the IPS 2025 line to quote. The convergence is total. The Indian Psychiatric Society is explicit: offer an SSRI as the first-line pharmacological treatment and CBT with exposure and response prevention as first-line psychotherapy, treating OCD with *higher SSRI doses than those used for depression* and reducing to a low-to-medium dose only if the higher dose is not tolerated (the Indian Psychiatric Society 2025 / IPS 2025). NICE has adults choose an SSRI (fluoxetine, fluvoxamine, paroxetine, sertraline or citalopram) or more intensive CBT with ERP by degree of functional impairment, combining an SSRI with CBT for severe impairment (NICE 2005). CANMAT names an SSRI (escitalopram, fluoxetine, fluvoxamine, paroxetine or sertraline) and CBT with ERP as co-equal first-line, adding CBT to medication to enhance response and relapse prevention (CANMAT 2014). The WFSBP likewise puts an SSRI and CBT first-line across children, adolescents and adults (WFSBP 2023). Every source says the same thing: *SSRI plus ERP, and push the dose*.

GUIDELINE	FIRST-LINE PHARMACOLOGY	FIRST-LINE PSYCHOLOGY / KEY NOTE
BAP 2014	**SSRI, high dose (may exceed formulary limits)**	ERP / CBT; clomipramine equally efficacious but less tolerated
the Indian Psychiatric Society 2025	**SSRI, higher than depression doses**	CBT with ERP; monotherapy for mild-moderate, SSRI-combined for severe
NICE 2005	SSRI (fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram)	CBT with ERP matched to impairment; combined if severe
CANMAT 2014	SSRI (escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline)	CBT with ERP co-equal first-line

First-line OCD across the major guidelines; the shared message is a high-dose SSRI plus CBT incorporating exposure and response prevention, with the IPS 2025 CPG and BAP both stressing doses above the antidepressant range.

RULE **High dose, long trial, with ERP.** First-line OCD is an SSRI pushed to the maximum tolerated dose (above the depression range) for about 10 to 12 weeks, combined with CBT incorporating exposure and response prevention; this is unanimous across BAP, the Indian Psychiatric Society, NICE, CANMAT and WFSBP.

12.3 The high-dose rule: the SSRI target doses to quote

Higher than the antidepressant dose. The doses of SSRIs used in OCD run above those used in depression: fluoxetine to **60 mg** (sometimes 80), paroxetine **40 to 60 mg**, sertraline typically **150 to 200 mg** (the Maudsley notes sertraline has been pushed to 250 to 400 mg and even 650 mg without major safety problems), fluvoxamine to 300 mg, and escitalopram 20 to 30 mg (Maudsley Prescribing Guidelines; the Indian Psychiatric Society 2017/2025). The IPS 2025 target is pragmatic and worth quoting verbatim: aim for roughly the **60 to 80 mg** fluoxetine-equivalent, reducing to a tolerated dose only if the higher dose is not tolerated (IPS 2025). Escalate to the effective dose within about 4 to 6 weeks, then hold.

The one citalopram caution. The FDA cautions against citalopram above 40 mg/day because of dose-dependent QTc prolongation, so citalopram is the one SSRI whose OCD dose does *not* get pushed indefinitely (BAP 2014).

SSRI	INDIAN BRANDS (EXAMPLES)	OCD TARGET DOSE (MG/DAY)
Fluoxetine	Fludac, Prodep	**60 (up to 80)**
Sertraline	Daxid, Serta, Zosert	150 to 200 (higher tried)
Fluvoxamine	Fluvoxin	up to 300
Paroxetine	Paxidep, Xet	40 to 60
Escitalopram	Nexito, Stalopam	20 to 30

OCD SSRI target doses run above the antidepressant range; the exam anchor is fluoxetine 60 mg and the IPS 2025 target of 60 to 80 mg fluoxetine-equivalent (Maudsley; IPS 2025). Doses in cells are bare numbers; the unit is in the header.

GOOD TO REMEMBER

- **SSRI (first-line for OCD):** serotonin reuptake inhibitor; the OCD principle is a dose *higher* than the depression dose (fluoxetine 60 mg, target 60 to 80 mg fluoxetine-equivalent) held for a long trial; the signature caution is dose-dependent QTc prolongation limiting citalopram to 40 mg/day; the one first-line indication to state is high-dose SSRI plus ERP for all severities of OCD.

12.4 The long trial: judging response on the Y-BOCS at 10 to 12 weeks

Why the trial is long. Initial response in OCD emerges more slowly than in depression: it can take **10 to 12 weeks** at the maximum tolerated dose before you can call a trial failed (Maudsley; the Indian Psychiatric Society 2025). The IPS 2025 rule is precise: continue a maximally tolerated effective SSRI dose for at least **12 weeks** before judging efficacy, having escalated to the effective dose within 4 to 6 weeks (IPS 2025). The New Oxford Textbook frames the failure point the same way, under 25% reduction of the baseline Y-BOCS after 12 weeks of SRI treatment, of which at least 6 weeks should be at the maximal tolerated dose, counts as non-response.

The scale that governs the algorithm. The Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) is the clinician-rated, semi-structured instrument used at baseline and every 4 weeks to objectify response. It rates obsessions and compulsions separately on five aspects each (time, interference, distress, resistance, control), scored 0 to 4, for a total of **0 to 40**. The Goodman severity bands are worth memorising cold: 0 to 7 subclinical, 8 to 15 mild, 16 to 23 moderate, 24 to 31 severe, 32 to 40 extreme. A **25 to 35%** reduction is considered response; remission is a Y-BOCS of **12 or below** (the Indian Psychiatric Society 2017). In children the equivalent is the CY-BOCS (mild 16 to 19, moderate 20 to 29, severe 30 to 40) (the Indian Psychiatric Society 2019). The form itself is reproduced on the accompanying scale plate.

Y-BOCS TOTAL	SEVERITY BAND
0 to 7	Subclinical
8 to 15	Mild
16 to 23	**Moderate**
24 to 31	Severe
32 to 40	Extreme

Y-BOCS severity bands (Goodman et al 1989): 10 items each 0 to 4, total 0 to 40; response is a 25 to 35% reduction, remission a score of 12 or below.

GOOD TO REMEMBER

- **Y-BOCS:** clinician-rated 10-item scale, each 0 to 4, total 0 to 40; bands 0-7 subclinical, 8-15 mild, 16-23 moderate, 24-31 severe, 32-40 extreme; response = 25 to 35% reduction, remission = 12 or below; it is the instrument on which every rung of the OCD algorithm is judged, rated at baseline and every 4 weeks.

COMMON TRAP

The classic error is declaring an SSRI a failure too early or at too low a dose. An OCD trial is not adequate until the patient has had roughly 10 to 12 weeks at the maximum tolerated dose, with at least 6 of those weeks at the ceiling. Switching or augmenting before that, or judging on the depression-range dose, mislabels a slow-but-real responder as treatment-resistant and sends the ladder off prematurely.

12.5 CBT incorporating exposure and response prevention: the first-line psychotherapy

What it is. **cbt for ocd** (CBT tailored to obsessions and compulsions) is built around exposure and response prevention (erp): the patient is exposed, in a graded hierarchy, to the feared stimulus (the contaminated object, the intrusive thought) and then *prevented* from performing the neutralising ritual, so that anxiety habituates and the belief that the ritual averts catastrophe is disconfirmed. Foa's work established that exposure and ritual prevention must be delivered *together*, exposure alone or response prevention alone yields inferior outcomes. It is first-line psychotherapy in every guideline, monotherapy for mild-to-moderate illness and combined with an SSRI for severe illness (the Indian Psychiatric Society 2025; CANMAT 2014).

Where it sits on the ladder. ERP is not only a first-line treatment but also a first-line *augmentation* for partial or non-responders to an SSRI, where feasible (IPS 2025). Therapist-guided exposure is preferred to self-exposure (CANMAT 2014), and family accommodation should be assessed and reduced, since high accommodation predicts poor outcome (the Indian Psychiatric Society 2017).

GOOD TO REMEMBER

- **CBT with ERP (first-line psychotherapy for OCD):** graded exposure to the feared stimulus with prevention of the neutralising ritual, driving habituation and belief disconfirmation; the principle is that exposure and response prevention must be delivered together (either alone is inferior); the first-line indication is mild-to-moderate OCD as monotherapy and severe OCD combined with a high-dose SSRI.

12.6 Partial or no response: optimise, then switch SSRI or to clomipramine

Optimise first, then switch. When a first adequate SSRI trial fails, the sequence is optimise the dose (push to the maximum tolerated), then switch, either to a different SSRI or to clomipramine (BAP 2014; NICE 2005). Switching between treatments of proven efficacy helps some patients (BAP 2014). The IPS 2025 places clomipramine as a *second-line* agent, used when SSRIs are ineffective, given its poorer tolerability (IPS 2025).

The clomipramine-versus-SSRI point. This is the classic exam contrast. Clomipramine is the one tricyclic with genuine anti-obsessional efficacy (it is the most serotonergic TCA), and historically the first drug shown to work in OCD (1967). Its efficacy is at the margins of superiority over the SSRIs, but it is *less well tolerated* (anticholinergic burden, cardiac conduction effects, seizure risk in overdose), which is exactly why an SSRI is tried first and clomipramine held in reserve (BAP 2014). The OCD dose is **150 to 225 mg/day** (range 75 to 250), and ECG

monitoring is required (the Indian Psychiatric Society 2025 / 2017). Intravenous clomipramine is a specialist option after oral non-response.

TRAP **Clomipramine is not more effective enough to use first.** All SSRIs and clomipramine are efficacious in OCD; clomipramine sits at the margins of superiority but is less tolerated, so an adequate SSRI trial (high dose, long) comes first, with clomipramine as the switch on failure, under ECG monitoring.

GOOD TO REMEMBER

- **Clomipramine (Indian brand Anafranil):** the most serotonergic tricyclic and the original anti-obsessional drug; mechanism is potent serotonin (and noradrenaline) reuptake inhibition; second-line in OCD at 150 to 225 mg/day because it is less tolerated than an SSRI (anticholinergic, cardiac conduction, seizure in overdose), so it needs ECG monitoring and is used as the switch after an adequate SSRI trial fails.

12.7 Augmentation: low-dose aripiprazole or risperidone added to the SSRI

The third rung. For the patient who is a partial responder after an adequate SSRI or clomipramine trial, the next step is **augmentation** with a low-dose antipsychotic added to the continuing serotonergic drug. The IPS 2025 names low-dose aripiprazole or risperidone as the first-line pharmacological augmentation in treatment-resistant OCD, continued for at least 8 weeks; the doses are risperidone **1 to 3 mg/day** and aripiprazole in the low range (IPS 2025). BAP has the strongest augmentation evidence for risperidone, with aripiprazole also supported (BAP 2014), and CANMAT lists adjunctive aripiprazole or risperidone as the first-line adjuncts for treatment-resistant OCD (CANMAT 2014). The Maudsley agrees the usual second-line step is the addition of risperidone or aripiprazole.

The monotherapy caveat. Antipsychotics are for *augmentation only*: NICE is explicit that antipsychotics should not normally be used as monotherapy to treat OCD (NICE 2005). The augmentation target is often the patient with comorbid tic disorder or poorer insight.

GOOD TO REMEMBER

- **Antipsychotic augmentation (aripiprazole / risperidone):** low-dose dopamine blockade added to a continuing SSRI or clomipramine for treatment-resistant OCD (risperidone 1 to 3 mg/day, low-dose aripiprazole), for at least 8 weeks; strongest evidence is for risperidone; the signature caution is that antipsychotics are augmentation only and never monotherapy for OCD.

12.8 Refractory OCD: intensive ERP, then DBS and ablative neurosurgery

Define refractory first. **refractory ocd** means failure of at least two adequate SSRI trials, clomipramine, and CBT with ERP (with antipsychotic augmentation), each delivered at full dose and duration (the Indian Psychiatric Society 2017). Before escalating, the honest question is always whether the earlier trials were genuinely adequate, high dose, long enough, and with real ERP.

The refractory rung. For the genuinely refractory patient, intensify the psychological treatment (intensive, therapist-led ERP) and, at a specialist centre only, consider the somatic options:

intravenous clomipramine, then *deep brain stimulation*, and ablative neurosurgery (anterior capsulotomy or cingulotomy), reserved for treatment-refractory OCD after multidisciplinary review (BAP 2014; the Indian Psychiatric Society 2017; WFSBP 2023). In India this pathway runs through specialist centres such as NIMHANS. The neurostimulation and neurosurgical detail (DBS targets, capsulotomy) is developed in the ECT and neurostimulation notes. Neuromodulation such as rTMS or tDCS is an evolving, preliminary-evidence augmentation option (IPS 2025).

WORKED EXAMPLE

A 26-year-old man with contamination obsessions and washing rituals has a Y-BOCS of 28 (severe). He is started on fluoxetine, escalated to 60 mg over 5 weeks, and continued at 60 mg with weekly ERP. At 12 weeks his Y-BOCS is 25, under a 25% reduction, so this is non-response despite an adequate high-dose, long trial. The dose is optimised to 80 mg for a further period; still a partial responder, he is switched to a second SSRI, and on continued partial response low-dose risperidone (1 to 2 mg/day) is added for 8 weeks, with intensive ERP. Only after this whole sequence would clomipramine and, ultimately, specialist referral be considered.

12.9 Continuation and maintenance: at least 1 to 2 years at the effective dose

Do not stop early. OCD is chronic and relapsing, so a responder is continued on the effective SSRI (or clomipramine) at the *dose that produced improvement*. BAP and NICE say continue for at least 12 months; the IPS 2025 goes further, continue an effective SSRI or clomipramine for at least **1 to 2 years** after remission, at the dose that produced improvement (IPS 2025); CANMAT says at least 12 to 24 months (CANMAT 2014). The principle that motivates this: continuing an effective serotonin reuptake inhibitor markedly lowers the relapse rate compared with stopping after the initial response, so the effective dose is held rather than reduced. Taper slowly when eventually stopping, since anxiety-spectrum patients are sensitive to discontinuation.

60	10 to 12 weeks	32 to 40	1 to 2 years
FLUOXETINE OCD TARGET, MG (HIGHER THAN DEPRESSION)	ADEQUATE TRIAL AT MAXIMUM TOLERATED DOSE	Y-BOCS EXTREME BAND (RESPONSE = 25 TO 35% DROP)	IPS 2025 CONTINUATION AFTER REMISSION

INDIA

OCD sits inside India's wider anxiety-spectrum treatment gap: the disorder is common yet under-recognised, and the reflex of a benzodiazepine (still over-prescribed across Indian outpatient practice) does nothing for obsessions and risks dependence. The Indian Psychiatric Society CPGs, updated for OCD to 2025, anchor the same high-dose-SSRI-plus-ERP algorithm to Indian practice, and the tertiary pathway for refractory OCD (IV clomipramine, DBS, capsulotomy) runs through specialist centres such as NIMHANS. Indian brands are readily available, fluoxetine (Fludac, Prodep), sertraline (Daxid, Zosert), escitalopram (Nexito), fluvoxamine (Fluvoxin) and clomipramine (Anafranil), so the limiting factor is recognition and adequate dosing, not access.

MNEMONIC

SSRI → SWITCH → ADD → REFER

The four rungs in order: **SSRI** (high dose, long trial, with ERP) → **SWITCH** (optimise, then another SSRI or clomipramine) → **ADD** (aripiprazole or risperidone augmentation) → **REFER** (intensive ERP, then DBS / neurosurgery at a specialist centre).

PEARL

The single commonest reason "OCD does not respond to SSRIs" in the exam vignette is not true resistance but an inadequate trial, a depression-range dose stopped at 6 weeks. State the high-dose, long-trial rule and you have answered most OCD management questions before you reach the second rung.

13 · The Yale-Brown Obsessive Compulsive Scale

If a single instrument owns obsessive-compulsive disorder the way the HAM-D owns depression, it is this one. The **yale-brown obsessive compulsive scale** (**y-bocs**) is the standard clinician-rated severity measure for OCD and the outcome instrument in virtually every drug trial (Kaplan and Sadock 2024). Its design is deliberate and testable: it rates severity independently of symptom content, so a person whose only compulsion is silent counting and a person who washes for hours can be scored on the same scale and tracked over time. That content-blind design is exactly why examiners like it, and why it is the number that decides whether an adequate SSRI trial has actually failed.

Why it matters, and what this note owns. This is a scale note, so it teaches what the Y-BOCS is, how it is built, and, above all, its **severity bands**, the total-score ranges that convert a bare number into "mild", "moderate" or "extreme". The clinical phenomenology of obsessions and compulsions, the four symptom dimensions and the insight specifier live in the OCD clinical-features note; the high-dose SSRI, then clomipramine, then antipsychotic-augmentation algorithm lives in the OCD management note, and the deep antidepressant pharmacology in the Mood disorders: pharmacotherapy notes. What follows is the structure (a **ten-item** severity scale sitting on top of a symptom checklist), the scoring, the verified bands, and how the number is used to define response. The instrument is copyright Goodman and Rasmussen, so the accompanying scale plate typesets the structure and bands in our own words with a citation rather than reproducing the form; refer to that plate and do not expect the questionnaire pasted here.

Y-BOCS (TYPESET, NOT REPRODUCED)	VERIFIED STRUCTURE AND SEVERITY BANDS
Instrument	Yale-Brown Obsessive Compulsive Scale, clinician-rated, the reference severity measure for OCD (Goodman, Price, Rasmussen and colleagues, 1989)
Items	10 items: 5 rate the obsessions and 5 rate the compulsions, each across the same five parameters (time occupied, interference, distress, resistance and control); each item scored 0 to 4; total range 0 to 40
Companion	a symptom checklist precedes the severity scale, so the clinician first maps the symptom dimensions and then rates their severity
Severity bands	**0 to 7 subclinical, 8 to 15 mild, 16 to 23 moderate, 24 to 31 severe, 32 to 40 extreme**

Y-BOCS: typeset structure and verified bands only; the form is copyright Goodman and Rasmussen and its distribution is permission-required, so it is not reproduced (Goodman WK, Price LH, Rasmussen SA, et al. Arch Gen Psychiatry. 1989;46:1006-1011).

Fig 14.11 The Yale-Brown Obsessive Compulsive Scale (Y-BOCS). The reference severity measure for OCD: ten clinician-rated items, five for the obsessions and five for the compulsions, each rating time occupied, interference, distress, resistance and control on a 0 to 4 scale, for a total of 0 to 40, preceded by a symptom checklist. The severity bands run 0 to 7 subclinical, 8 to 15 mild, 16 to 23 moderate, 24 to 31 severe and 32 to 40 extreme. The form is copyright-restricted, so its structure and verified bands are given here in typeset form rather than reproduced.

13.1 What the Y-BOCS is, and who built it

The one-line definition. The Yale-Brown Obsessive Compulsive Scale is a semi-structured, clinician-administered interview that measures the *severity* of obsessive-compulsive symptoms, developed by Goodman, Rasmussen and colleagues in the late 1980s and published in 1989 (Kaplan and Sadock 2024; Goodman et al. 1989). It has become the standard instrument for assessing OCD severity and is used in virtually every drug trial, and it may also be used clinically to monitor treatment response. The paediatric adaptation is the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS), and a dimensional version (the DY-BOCS) also exists.

Severity, not diagnosis. The crucial framing point is that the Y-BOCS does not diagnose OCD; the diagnosis rests on the DSM-5-TR or ICD-11 criteria. The Y-BOCS presumes OCD is present and then quantifies how bad it is, which is why it is a severity and outcome measure rather than a screening or case-finding tool. It rates severity independently of the content or type of obsessions and compulsions, so the same score can be reached by very different symptom pictures.

GOOD TO REMEMBER

- **Y-BOCS:** a semi-structured, clinician-rated interview (Goodman, Rasmussen et al. 1989) that measures the *severity* of OCD, not the diagnosis; it is the standard OCD severity and outcome instrument used in virtually every drug trial; it rates severity independently of symptom content; paediatric version CY-BOCS.

13.2 Two parts: the symptom checklist, then the severity scale

The checklist comes first. The Y-BOCS is administered in two parts. Before the first use of the severity ratings, an associated symptom **checklist** is administered, a long menu (commonly cited as a 64-item checklist) covering the range of obsessions (aggressive, contamination, sexual, hoarding, religious/scrupulosity, symmetry, somatic) and compulsions (washing/cleaning, checking, repeating, counting, ordering/arranging, hoarding, mental rituals) organised by category (Kaplan and Sadock 2024; Foa et al.). Its job is to map *which* symptoms the patient has, which is invaluable for treatment planning and for anchoring the severity questions that follow.

The severity scale comes second. Once the clinician knows the range of symptoms the patient endorses, the **severity scale** proper is applied. This is the ten-item core that yields the 0 to 40 score, and its ratings are based on the range of symptoms the patient endorsed on the checklist. The distinction is a favourite exam point: the checklist tells you *what* the symptoms are; the severity scale tells you *how severe* they are and how they change with treatment. The severity scale is the more accurate tool for determining level of severity and tracking progress; the checklist is the better tool for understanding the range of a patient's symptoms.

RULE **Checklist maps content, severity scale measures severity.** Administer the symptom checklist first to establish *which* obsessions and compulsions are present; then apply the ten-item severity scale to those endorsed symptoms to produce the 0 to 40 severity score that is tracked over treatment.

13.3 The ten items: five obsessions, five compulsions, five parameters each

The architecture to state cold. The severity scale has **10 items**. The first five rate *obsessions* and the second five rate *compulsions*, and the two sets ask parallel questions across the same five parameters (Kaplan and Sadock 2024). The five parameters are: the **time** occupied by the symptoms, the **interference** they cause with functioning, the **distress** they cause, the patient's attempts to **resist** them, and the degree of **control** the patient has over them. Because the obsessions block and the compulsions block use the identical five parameters, learning the five parameters once gives you all ten items.

Why the parallel structure matters. The parallel obsessions-versus-compulsions design lets a clinician read an obsessions subtotal and a compulsions subtotal separately, which is useful when, for example, a "pure O" patient scores heavily on obsessions and lightly on compulsions. It also means treatment can be watched dimensionally: exposure and response prevention often moves the compulsions subscore first. The semi-structured interview and ratings can be completed in 15 minutes or less; a self-administered version takes about 10 to 15 minutes.

ITEM BLOCK	ITEMS	THE FIVE PARAMETERS RATED (EACH 0 TO 4)
Obsessions	**Items 1 to 5**	Time occupied; interference; distress; resistance; control
Compulsions	**Items 6 to 10**	Time occupied; interference; distress; resistance; control (parallel)

The ten-item severity scale: obsessions (items 1 to 5) and compulsions (items 6 to 10) rated across the identical five parameters, each item scored 0 to 4 (Kaplan and Sadock 2024).

COMMON TRAP

Do not confuse resistance with control, or read "high resistance" as a good sign. On the Y-BOCS a higher score is worse throughout, but the *resistance* item is scored counter-intuitively: making little or no effort to resist scores high (worse), while active resistance scores low. A patient who has "given up" fighting the compulsion scores worse on resistance, not better. Misreading the resistance item flips the interpretation of that item.

13.4 The scoring: 0 to 4 per item, subtotals 0 to 20, total 0 to 40

The arithmetic to memorise. Each of the ten items has item-specific anchors scored from **0 to 4** (Kaplan and Sadock 2024). The five obsessions items therefore sum to an obsessions subtotal of 0 to 20, the five compulsions items sum to a compulsions subtotal of 0 to 20, and the overall Y-BOCS total runs **0 to 40**. Higher scores mean greater severity. Typical scores for patients presenting with OCD fall in the **16 to 30** range, and a threshold of **16** is the value typically used for inclusion in drug trials, a number worth carrying because it recurs across the OCD trial literature.

The anchors, in words. Each 0 to 4 anchor is behaviourally defined, for example on the "time occupied by obsessions" item: 0 = none, 1 = mild (less than an hour a day), 2 = moderate (1 to 3 hours), 3 = severe (3 to 8 hours), 4 = extreme (more than 8 hours). That behavioural anchoring is what gives the scale its good inter-rater reliability. Reliability studies show good internal consistency, inter-rater reliability, and test-retest reliability over a one-week interval.

WORKED EXAMPLE

A patient rates 3 on obsession-time (3 to 8 hours of intrusive contamination thoughts), 3 on interference, 3 on distress, 2 on resistance and 2 on control: obsessions subtotal 13. On the compulsion side she rates 3, 3, 2, 2, 2 for washing rituals: compulsions subtotal 12. Y-BOCS total = 25, which places her in the *severe* band (24 to 31) and comfortably above the 16 trial-entry threshold. If a maximally tolerated, adequately long SSRI trial later brought her to 16, that is a 36% reduction, meeting the usual response definition.

13.5 The severity bands: subclinical, mild, moderate, severe, extreme

The five bands to know. The total score is conventionally read into five **severity bands** (Goodman et al. 1989; conventional Y-BOCS severity ranges). They are: **subclinical** 0 to 7, **mild** 8 to 15, **moderate** 16 to 23, **severe** 24 to 31, and **extreme** 32 to 40. The boundaries are worth over-learning because they are the exact numbers examiners ask for, and because they explain the trial-entry cut-off: a Y-BOCS of 16 is the floor of the *moderate* band, so trials enrolling at 16 and above are, by design, enrolling at least moderately ill patients. The bands are typeset (not reproduced) on the accompanying scale plate.

How the bands map to decisions. The bands are not merely descriptive. Mild-to-moderate OCD can reasonably be offered CBT with exposure and response prevention as monotherapy first-line; moderate-to-severe OCD warrants an SSRI, and severe illness warrants a combined SSRI plus

CBT/ERP from the outset (IPS 2025). At the extreme end, surgical candidates for neurosurgery or deep brain stimulation for refractory OCD typically carry Y-BOCS scores of a minimum of 26 to 30 of a possible 40 (Kaplan and Sadock 2024), which sits at the top of the severe band and into the extreme range.

BAND	Y-BOCS TOTAL (RANGE)	CLINICAL READING
Subclinical	0 to 7	Symptoms present but below clinical threshold
Mild	8 to 15	**Below the usual 16 trial-entry cut-off; CBT/ERP monotherapy reasonable**
Moderate	**16 to 23**	Floor is the 16 drug-trial threshold; SSRI indicated
Severe	24 to 31	Combined SSRI plus CBT/ERP from the outset
Extreme	32 to 40	**Top of scale; refractory-OCD neurosurgery/DBS candidates typically 26 to 30 minimum**

The five Y-BOCS severity bands and the total-score ranges that define them; note that 16, the usual drug-trial entry threshold, is the floor of the moderate band (Goodman et al. 1989; Kaplan and Sadock 2024).

GOOD TO REMEMBER

- **Severity bands:** subclinical 0 to 7; mild 8 to 15; moderate 16 to 23; severe 24 to 31; extreme 32 to 40. The 16 drug-trial cut-off is the floor of the moderate band; typical presenting OCD scores 16 to 30; neurosurgery/DBS candidates for refractory OCD usually score at least 26 to 30 out of a possible 40.

13.6 Using the number: defining response and an adequate trial

Response is a percentage fall on the Y-BOCS. The Y-BOCS is not only a snapshot; it is how "response" is operationalised in OCD. Across the trial literature, treatment response is most often defined as a reduction of at least **25 to 35%** from the baseline Y-BOCS total (New Oxford Textbook; Kaplan and Sadock 2024), and remission is often set at a low absolute score (for example a CY-BOCS below 11 in paediatric OCD). This is why the scale, rather than a clinical impression, is what tells you whether a trial has genuinely failed. A patient who "feels no better" but has moved from 28 to 19 has in fact responded (a 32% fall) and the SSRI should be continued, not abandoned.

The adequate-trial anchor. The single commonest error in OCD is calling a drug a failure too early. OCD needs a *high* SSRI dose held for a *long* trial: continue a maximally tolerated effective SSRI dose for at least **12 weeks** before judging efficacy, having escalated to the effective dose within the first 4 to 6 weeks (IPS 2025), and continue an effective agent for at least 1 to 2 years after remission. Only when the Y-BOCS has failed to fall by the response threshold after that full high-dose, long-duration trial is the patient a true non-responder who moves down the algorithm to clomipramine and then antipsychotic augmentation.

TRAP **Do not declare an SSRI failure before a full high-dose, long trial.** OCD demands a higher SSRI dose than depression, held for at least 12 weeks; judge failure by a less-than-25-to-35% fall on the Y-BOCS, not by the patient's subjective sense, before moving to clomipramine or augmentation.

INDIA

The highest-yield Indian point is that the Y-BOCS is the objective anchor the system most lacks. The OCD treatment gap in India is wide, OCD is frequently mislabelled (contamination fears dismissed as "habit", scrupulosity read as religiosity), and into that gap flows the same benzodiazepine over-prescription problem that dogs the anxiety disorders, with long-term alprazolam handed out where a high-dose SSRI and exposure and response prevention are indicated. A benzodiazepine has no place in OCD treatment (it does not treat obsessions or compulsions), and the Indian Psychiatric Society CPG (IPS 2025) is explicit: an SSRI at high dose first-line, escitalopram (Nexito, Rexipra), fluoxetine, sertraline or fluvoxamine, with CBT/ERP, then clomipramine (Anafranil) second-line, with the Y-BOCS tracked at baseline and through the trial so the "12 weeks at a high dose" rule is actually enforced rather than assumed.

0 to 40 Y-BOCS TOTAL, TEN-ITEM SCALE (EACH ITEM 0 TO 4)	**16** DRUG-TRIAL ENTRY CUT-OFF; FLOOR OF THE MODERATE BAND	**32 to 40** EXTREME SEVERITY BAND (TOP OF SCALE)	**12 weeks** MINIMUM HIGH-DOSE SSRI TRIAL BEFORE JUDGING FAILURE

MNEMONIC

TIDRC

The five parameters rated for both obsessions and compulsions: **T**ime occupied, **I**nterference with functioning, **D**istress, **R**esistance, and **C**ontrol. Rate these five for the obsessions (items 1 to 5) and the same five for the compulsions (items 6 to 10); each is 0 to 4, and the ten sum to the 0 to 40 total.

HOLD THIS

Ten items, each 0 to 4, total 0 to 40: subclinical 0 to 7, mild 8 to 15, moderate 16 to 23, severe 24 to 31, extreme 32 to 40, with 16 the drug-trial entry cut-off and the floor of the moderate band.

14 · The neurobiology of OCD: the CSTC circuit

Obsessive-compulsive disorder has the cleanest circuit story in psychiatry, and examiners love it precisely because it can be drawn as a loop. Where the anxiety disorders are diseases of an amygdala-centred fear circuit, OCD is a disease of a **cortico-striato-thalamic loop** that has lost its normal capacity to switch a thought or action off. The obsession is a message that will not stop repeating; the compulsion is the ritual the loop drives to try to discharge it. The anatomy to name is the **cortico-striato-thalamo-cortical** circuit, the **cstc** loop: from the **orbitofrontal** cortex and the anterior cingulate down to the striatum (the **caudate**), through the globus pallidus and substantia nigra, up to the **thalamus** and back to the cortex. Learn it as a loop with a brake, an

accelerator and a gate, and the imaging findings, the drug rationale and even the neurosurgical targets all fall into place.

Why it matters clinically. The imaging signature of OCD is a hyperactive orbitofronto-caudate-thalamic loop, and the two treatments that work, the high-dose serotonin reuptake inhibitor and exposure with response prevention, both turn that hyperactivity down; the neurobiology is therefore the rationale for the treatment, not decoration. Two ideas anchor the whole answer. First, the loop is normally self-limiting because the striatum gates and quietens cortical activity, so a healthy loop lets a thought arise, be checked, and be released. Second, OCD is modelled as an imbalance between a hyperactive *direct* (excitatory, "go") pathway and a relatively weak *indirect* (inhibitory, "stop") pathway through the **basal ganglia ocd**, so the loop reverberates and the thalamus over-drives the orbitofrontal cortex, and the patient cannot let the thought go. The direct and indirect pathway machinery and the receptor systems are developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; this topic applies that basal-ganglia anatomy to OCD and refers to the accompanying figure for the map.

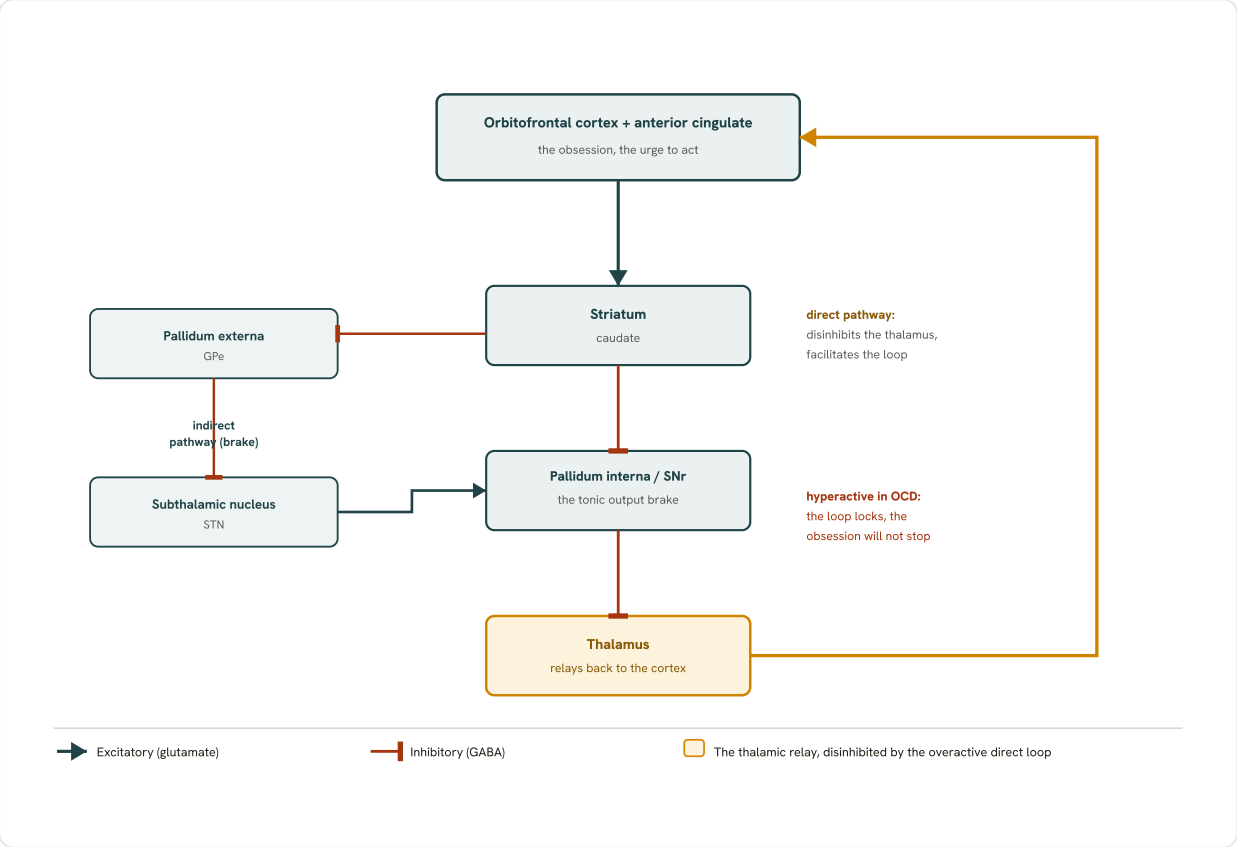


Fig 14.12 The cortico-striato-thalamo-cortical (CSTC) circuit in OCD. The orbitofrontal cortex and anterior cingulate drive the striatum (caudate); the direct pathway then runs striatum to pallidum interna and substantia nigra reticulata to thalamus, each step GABAergic and inhibitory, so the net effect is to lift the tonic brake on the thalamus and let the cortico-thalamic loop run; the indirect pathway, through the external pallidum and the subthalamic nucleus, is the opposing brake that normally damps it. In OCD the direct loop is overactive relative to the indirect brake, so the loop becomes hyperactive and self-sustaining, the neural correlate of an obsession and a compulsion that will not switch off, and the target that a serotonin reuptake inhibitor, exposure and response prevention, and in the last resort deep brain stimulation all act to quieten. The receptor systems and the wider pathway anatomy are taught in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

14.1 The loop in one sentence: cortex to striatum to pallidum to thalamus to cortex

The anatomy to draw first. The cortico-striato-thalamo-cortical circuit begins in the cortex, projects to the striatum (in OCD, chiefly the head of the caudate nucleus), which projects to the output nuclei of the basal ganglia (the globus pallidus interna and the substantia nigra pars reticulata), which project to the thalamus, which projects back up to the same region of cortex that started the loop (Kaplan & Sadock CTP 2024; Stahl's Essential Psychopharmacology). It is a closed re-entrant loop, and its job is to select and gate behaviour: to let a wanted action or thought proceed and to suppress the unwanted competitors.

Why the caudate is the pivot. The striatum is the entry gate of the loop and the caudate is the associative-territory striatum that receives the **orbitofrontal** and cingulate projections; it is the structure whose glutamatergic tone is raised in OCD and whose activity normalises when the patient responds to treatment (Kaplan & Sadock CTP 2024). Naming the caudate as the striatal node of the OCD loop is the single most examined anatomical fact of the topic.

14.2 The cortical origin: the orbitofrontal cortex and the anterior cingulate

The two cortical nodes to name. The OCD loop originates in two adjacent cortical regions. The **orbitofrontal** cortex (OFC) evaluates the affective and reward significance of stimuli and signals "something is wrong here, act on it"; the anterior cingulate cortex (ACC) is the error- and conflict-monitor that generates the nagging sense that an action is incomplete or a threat unaddressed (Kaplan & Sadock CTP 2024). In OCD both are over-active, so the loop is fed a continuous, false "error, not yet safe, do it again" signal, which is felt as the obsession and drives the checking or washing compulsion.

The clinical face of orbitofrontal over-activity. An over-active OFC is why the obsession carries a compelling sense of wrongness or danger that the patient cannot dismiss even when they know it is irrational; the ACC error-signal is why the compulsion never quite satisfies and must be repeated. The heightened error-monitoring is measurable as an exaggerated error-related negativity on EEG, a candidate endophenotype of OCD.

> **WORKED EXAMPLE**
>
> A patient leaves the house, then is gripped by the thought that the gas is on and the house will burn. The *orbitofrontal* cortex tags the situation as dangerous and salient; the anterior cingulate fires a persistent "this is not resolved" error-signal; the caudate fails to gate the signal, so it reverberates round the thalamus and back to the cortex. The patient returns and checks the stove. The check briefly quietens the loop, which negatively reinforces it, so the loop fires harder next time. That reverberating orbitofronto-caudate-thalamic circuit, not a real gas leak, is the disease.

14.3 The direct pathway: the excitatory "go" loop

How the accelerator works. Within the striatum two output pathways compete. The *direct pathway* runs from the striatum straight to the globus pallidus interna and substantia nigra pars reticulata (the basal-ganglia output nuclei); it is populated by excitatory D1 receptors and, by inhibiting those inhibitory output nuclei, it *releases* the thalamus, which then excites the cortex

(Stahl's Essential Psychopharmacology). The net effect is "go": the direct pathway is the accelerator that lets a cortical program, a thought or an action, proceed.

Why it is the villain in OCD. A relatively over-active direct pathway keeps the thalamus disinhibited, so it keeps driving the orbitofrontal cortex, and the loop cannot be switched off; the obsessional program runs on and on. The proposed core lesion of OCD is exactly this: an imbalance in which the excitatory direct loop dominates and the inhibitory indirect loop is too weak to counter it.

14.4 The indirect pathway: the inhibitory "stop" loop

How the brake works. The *indirect pathway* runs from the striatum to the globus pallidus *externa*, then to the subthalamic nucleus, then to the output nuclei; it is populated by inhibitory D2 receptors and its net effect is to *increase* inhibition of the thalamus, which reduces cortical excitation (Stahl's Essential Psychopharmacology). The indirect pathway is the brake that normally suppresses competing or unwanted programs, "stop".

The balance is the whole model. In the healthy loop the direct "go" and indirect "stop" pathways are balanced, so the striatum can select the wanted program and cancel the rest, a clean gate. In OCD the balance tips toward the direct pathway: too much "go", too little "stop", so unwanted intrusive programs are not cancelled and the thalamus is left over-driving the cortex. This direct-over-indirect imbalance is the mechanistic heart of the topic.

RULE **OCD is a hyperactive direct loop with a failing brake.** The imaging and modelling both point one way: an over-active excitatory direct pathway keeps the thalamus disinhibited and the orbitofronto-caudate-thalamic loop reverberating, while the inhibitory indirect pathway is too weak to gate the intrusive program, so the obsession cannot be switched off.

14.5 The output gate and the return to cortex: globus pallidus, substantia nigra and thalamus

The gate. The globus pallidus interna and the substantia nigra pars reticulata are the tonically active, inhibitory output gate of the basal ganglia; they normally clamp the thalamus down. The direct pathway *opens* the gate (disinhibits the thalamus) and the indirect pathway *closes* it (Stahl's Essential Psychopharmacology). Reduced globus pallidus volume is among the more replicated structural findings in OCD, consistent with a dysfunctional gate (Kaplan & Sadock CTP 2024).

The return limb. The **thalamus** is the relay that closes the loop, projecting back up to the orbitofrontal cortex and cingulate that started it. When the direct pathway holds the gate open, the thalamus over-excites the cortex, the cortex re-drives the striatum, and the circuit becomes a self-sustaining reverberation, which is the circuit-level description of an obsession that will not stop. Treatment-naive children with OCD show enlarged thalamic volumes, fitting an over-active return limb (Kaplan & Sadock CTP 2024).

MNEMONIC

CSTC = Cortex, Striatum (caudate), pallidum/nigra, Thalamus, back to Cortex

Trace the loop in order: **C**ortex (orbitofrontal + cingulate) to **S**triatum (the caudate gate) to the pallidum and substantia nigra (the output gate) to the **T**halamus (the relay) and back to **C**ortex. Then overlay the two pathways: *direct* = D1, "go", opens the gate; *indirect* = D2, "stop", closes the gate. OCD tips the balance toward "go".

14.6 The imaging signature: a hyperactive orbitofronto-caudate-thalamic loop

The finding to quote. Functional imaging in OCD shows increased resting glucose metabolism in the **orbitofrontal** cortex, the ventral striatum, the (right) **caudate** nucleus and the anterior cingulate, at rest and increasing further on symptom provocation (Kaplan & Sadock CTP 2024). Crucially, orbitofrontal and caudate metabolic rates are highly correlated, which is read as the interconnecting loops being "freed from their usual inhibitory influences and reverberating", the imaging translation of the failing brake.

The treatment proof. The same imaging validates the circuit as the target: both medication (a serotonin reuptake inhibitor) and behavioural therapy reduce orbitofrontal and caudate activity, and in children the raised caudate glutamate (Glx) falls to control levels after about **12 weeks** of an SSRI, tracking clinical response (Kaplan & Sadock CTP 2024). The circuit is not just correlated with OCD, it is where the treatments act, which is why the neurobiology carries the management rationale.

TRAP **Calling OCD an "amygdala" or "fear-circuit" disorder.** The anxiety disorders sit on the amygdala-centred fear circuit; OCD sits on the cortico-striato-thalamo-cortical loop through the *basal ganglia*, with the caudate, not the amygdala, as the pivot. Mixing the two circuits is the classic error, and it is why OCD is now classed apart from the anxiety disorders in DSM-5-TR and ICD-11.

14.7 The serotonin-glutamate chemistry that tunes the loop

Why serotonin, and why a high dose. The loop is tuned by serotonin: serotonergic projections from the raphe modulate the orbitofrontal-striatal circuit, and only the serotonergic antidepressants (the SSRIs and the serotonergic tricyclic clomipramine) work in OCD, which is the pharmacological argument for a serotonergic abnormality (Kaplan & Sadock CTP 2024). The clinical corollary is the OCD dosing rule: a *higher* SSRI dose than in depression, sustained for a *longer* trial of about **10 to 12 weeks** before judging response, because the circuit re-tunes slowly.

The glutamate layer. The excitatory transmitter of the cortico-striatal projection is glutamate, and raised caudate glutamate (Glx) in OCD is the neurochemical face of the over-active loop; it falls with successful SSRI treatment (Kaplan & Sadock CTP 2024). This glutamatergic model is why refractory OCD is a target for glutamate-modulating agents and, at the extreme, for neurosurgical or stimulation interruption of the loop. Deep brain stimulation and neurosurgery

for refractory OCD, which physically interrupt this circuit at the ventral capsule or cingulate, are developed in the ECT and neurostimulation notes.

GOOD TO REMEMBER

- **Serotonin reuptake inhibitor (mechanism and OCD rule):** only the serotonergic agents work in OCD (the SSRIs and clomipramine), the mechanism being a slow re-tuning of the hyperactive orbitofronto-caudate-thalamic loop; the signature principle is a *high* dose for a *long* trial of about **10 to 12 weeks** before declaring failure, and both drug and exposure therapy normalise the caudate hyperactivity on imaging.

14.8 Clomipramine, the serotonergic tricyclic that proved the loop

The historical anchor. Clomipramine (Anafranil), a non-selective serotonin reuptake-inhibiting tricyclic, was the first drug shown to work in OCD (used by Fernandez and Lopez-Ibor in the late 1960s) and remains the yardstick against which the SSRIs are compared. Its efficacy, tied to its serotonergic action, was the pharmacological evidence that fixed serotonin at the centre of the OCD circuit model.

Where it sits now. Clomipramine (75 to 300 mg/day) is at least as effective as the SSRIs and by some meta-analyses numerically more so, but its anticholinergic, cardiac and seizure burden means the better-tolerated SSRI is first-line and clomipramine is held for SSRI non-response; the response is better when depression coexists. The detailed antidepressant pharmacology, the SSRIs, SNRIs and clomipramine, their doses, adverse effects and interactions, is developed in the Mood disorders: pharmacotherapy notes.

GOOD TO REMEMBER

- **Clomipramine (mechanism and role):** a non-selective serotonin reuptake-inhibiting tricyclic, the *first* effective OCD drug and the proof that OCD is a serotonergic circuit disorder; the signature caution is its anticholinergic, cardiotoxic and seizure-lowering load, so despite efficacy equal to or better than the SSRIs it is second-line, reserved for SSRI non-response (typical range 75 to 300 mg/day).

14.9 Measuring the loop clinically: the Y-BOCS

What the scale is. The Y-BOCS (Yale-Brown Obsessive-Compulsive Scale), developed by Goodman and Charney in 1989, is the clinician-administered gold-standard severity measure for OCD; it rates obsessions and compulsions across five dimensions each (time, interference, distress, resistance and control), on a 0 to 4 anchor, for a total of **0 to 40** (Clinical Methods in Psychiatry, AIIMS; Tasman Psychiatry). It is the instrument used to define response (conventionally a 25 to 35 percent fall) and remission (a score of about **10 or less**) in the OCD trials. The instrument form itself is reproduced on the accompanying scale plate.

The severity bands to hold. The Goodman severity anchors are: 0 to 7 subclinical, 8 to 15 mild, 16 to 23 moderate, 24 to 31 severe, and 32 to 40 extreme; a total of 16 and above is the usual threshold for a clinical trial and for committing to pharmacotherapy. Anchoring "moderate OCD" to a Y-BOCS of 16 to 23 is the number examiners most often want.

0 to 40	16 to 23	10 to 12	75 to 300
Y-BOCS TOTAL RANGE (10 ITEMS)	Y-BOCS MODERATE BAND	WEEKS: ADEQUATE SSRI TRIAL IN OCD	CLOMIPRAMINE (MG/DAY)

INDIA

OCD in India carries a large treatment gap: the disorder is common, chronically under-recognised and, when it does present, often mislabelled and mistreated. A recurring Indian pattern is the reflex prescription of a *benzodiazepine* for the anxiety and distress of OCD, which sedates the patient but does nothing to the serotonergic loop and courts dependence; the benzodiazepine is not a treatment for OCD. The Indian Psychiatric Society Clinical Practice Guidelines for OCD frame the correct sequence, a high-dose serotonin reuptake inhibitor for an adequate trial, then clomipramine, then antipsychotic augmentation, with exposure and response prevention throughout, and the SSRIs and clomipramine (Anafranil) are all widely available as inexpensive Indian generics. The gap is not a drug-availability problem, it is a recognition-and-rational-prescribing problem.

HOLD THIS

OCD is a hyperactive cortico-striato-thalamo-cortical loop: an over-active orbitofrontal cortex and anterior cingulate drive a caudate that cannot gate them, so an excess of the excitatory direct ("go") pathway over the inhibitory indirect ("stop") pathway leaves the thalamus disinhibited and the loop reverberating, and the high-dose serotonin reuptake inhibitor and exposure therapy both work by turning that orbitofronto-caudate hyperactivity back down.

15 · Clomipramine versus SSRIs in OCD

This is the single most reliably examined drug comparison in the whole anxiety-spectrum syllabus, because it hides a trap in plain sight. The naive candidate reasons that if clomipramine is *marginally more efficacious* on meta-analysis it ought to be first-line; the examiner is testing whether you understand that a first-line recommendation is a decision about the *whole* risk-benefit balance, not about the point estimate of efficacy alone. The **clomipramine versus ssri** question turns on one sentence you should be able to deliver cold: the two are comparably effective (clomipramine perhaps a whisker ahead), but clomipramine is far less tolerable and more dangerous, so the SSRIs win first-line on tolerability and safety.

Why it matters, and what this note owns. This note owns the head-to-head: the serotonergic-specificity argument that explains why clomipramine (alone among tricyclics) works in OCD at all, the meta-analytic evidence on relative **efficacy in ocd**, the **tolerability ocd** reasons clomipramine loses first-line, and exactly where it sits on the ladder. The wider four-rung OCD algorithm (high-dose SSRI, long trial, then augmentation, then refractory options) is set out in the OCD management algorithm note and only referenced here; the deep antidepressant pharmacology of the SSRIs and clomipramine, their kinetics, adverse effects and interactions, is developed in the Mood disorders: pharmacotherapy notes. The comparison itself is laid out in the accompanying figure.

15.1 The serotonergic-specificity argument: why clomipramine works when other TCAs do not

The founding observation. Clomipramine was the *first* drug shown to work in OCD, in studies from the late 1960s onward, and this is not incidental trivia: it is the pharmacological clue that shaped the whole serotonin hypothesis of OCD. Clomipramine is the one tricyclic that is a *potent serotonin reuptake inhibitor*; the Companion notes it was the first drug to inhibit serotonergic uptake without primarily inhibiting noradrenergic reuptake (its active metabolite desmethylclomipramine is the noradrenergic one). Conventional tricyclics, with the exception of clomipramine, are *not* effective in OCD (Shorter Oxford). That single dissociation is the argument.

The desipramine experiment that clinches it. The clean demonstration is the head-to-head against a noradrenergic TCA: clomipramine (serotonergic) beats desipramine (noradrenergic) in OCD, and the same pattern of serotonergic-reuptake inhibitors outperforming non-serotonergic agents recurs across the obsessive-compulsive spectrum (New Oxford Textbook). The take-home is a mechanism rule, only drugs that potently block the serotonin transporter, whether the SSRIs or clomipramine, are anti-obsessional. The amygdala and cortico-striatal fear-circuit substrate behind this is in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

RULE **Serotonergic potency, not the tricyclic class, is what treats OCD.** Clomipramine works because it potently blocks the serotonin transporter; noradrenergic tricyclics such as desipramine do not, which is why clomipramine and the SSRIs are the only anti-obsessional agents.

15.2 The efficacy evidence: clomipramine marginally ahead, but not significantly

What the meta-analyses actually show. On placebo-referenced **meta-analysis ocd** data, both clomipramine and all SSRIs are efficacious; the SSRIs are roughly twice as likely as placebo to produce a clinical response (the Soomro meta-analysis, 17 adult studies, 3097 participants; New Oxford Textbook). The nuance the examiner wants is the *relative* comparison. The Companion states it plainly: in meta-analyses clomipramine is *marginally more efficacious* than the SSRIs, but the SSRIs are somewhat better tolerated. BAP frames the same finding as clomipramine sitting *at the margins of superiority* over SSRIs while being less well tolerated (BAP 2014).

The statistical caveat, and the confound. The apparent clomipramine edge is fragile. The Skapinakis network meta-analysis, combining direct and indirect evidence, found clomipramine had a larger effect size against placebo than the SSRIs, but *this difference was not statistically significant*, and individual SSRIs produced similar effect sizes with no single compound superior (New Oxford Textbook). The classic explanation for the apparent gap is a confound of era: the older clomipramine trials enrolled more severe, more treatment-naive samples and used indirect (cross-study) rather than head-to-head comparison, inflating its relative effect. When the evidence is pooled properly the two are, for practical purposes, equally effective.

DIMENSION	CLOMIPRAMINE	SSRIS (CLASS)
Serotonergic mechanism	Potent SERT block (most serotonergic TCA)	Selective, potent SERT block
Placebo-referenced efficacy	**Marginally higher effect size, not statistically significant**	Robustly efficacious, no single SSRI superior
Tolerability	**Poorer (anticholinergic, sedation, weight)**	Better tolerated
Safety in overdose	Cardiotoxic, seizure risk, dangerous	Relatively safe
Line of treatment	Second-line / switch after SSRI	**First-line**

The clomipramine-versus-SSRI head-to-head: comparable efficacy (clomipramine perhaps marginally ahead but not significantly), decisively worse tolerability and overdose safety, hence SSRIs first-line and clomipramine reserved (Companion; New Oxford; BAP 2014).

15.3 The tolerability and safety cost: why the marginal edge does not buy first-line

The three dangers. Clomipramine carries the full tricyclic liability that the SSRIs largely shed. First, the *anticholinergic* burden, dry mouth, constipation, urinary retention, blurred vision, sedation and weight gain, which drives dropout. Second, *cardiac* effects, QTc prolongation and slowed intracardiac conduction, so an ECG is checked before and during treatment and it is avoided after recent myocardial infarction or with uncorrected hypokalaemia (Stahl; NICE 2005). Third, the *seizure* risk, which is dose-dependent and the reason the ceiling is fixed: at 300 mg/day the seizure incidence approaches **7 per 1000**, a generally unacceptable risk, so the maximum is held at **250 mg/day** (Stahl; New Oxford Textbook). Clomipramine is also markedly more dangerous in overdose than any SSRI.

Why this decides the line. When two drugs are near-identical in efficacy, the tie is broken by tolerability and safety, and here the gap is not marginal at all. That is the entire logic of first-line: the SSRIs deliver essentially the same benefit at a fraction of the harm, so they are tried first and clomipramine is held in reserve for when an SSRI has failed or cannot be tolerated (BAP 2014; NICE 2005).

TRAP **"More efficacious, therefore first-line" is the wrong inference.** Clomipramine's meta-analytic efficacy edge is marginal and non-significant, and it is bought at a heavy tolerability and overdose-safety price, so an SSRI is first-line and clomipramine is the switch, never the opening move.

15.4 Where clomipramine sits on the ladder: the switch after an adequate SSRI trial

The BAP position, first. Lead with the British Association for Psychopharmacology: offer an SSRI as first-line pharmacological treatment for OCD, since all SSRIs and clomipramine have efficacy but SSRIs are generally better tolerated; clomipramine is an evidence-based acute treatment whose efficacy is at the margins of superiority over SSRIs but which is less well tolerated (BAP 2014). Clomipramine is therefore the drug you switch to, not the drug you start with, and the switch is made after an adequate first SSRI trial fails or is not tolerated.

What the other guidelines recommend, at guideline level. The convergence is total. The Indian Psychiatric Society places clomipramine explicitly as a *second-line* agent, used at 150 to 225 mg/day when SSRIs are ineffective, given its poorer tolerability (the Indian Psychiatric Society 2025). NICE recommends offering clomipramine after an adequate SSRI trial has been ineffective or poorly tolerated, or if the patient prefers it or previously responded, checking an ECG and blood pressure first where there is significant cardiovascular risk (NICE 2005, the CG31 OCD guideline). CANMAT lists clomipramine (with citalopram, mirtazapine or venlafaxine XR) as *second-line* pharmacotherapy for OCD (CANMAT 2014). The WFSBP likewise keeps an SSRI first-line and reserves clomipramine as second-line when first-line treatment is inadequate (WFSBP 2022). Every source says the same thing, SSRI first, clomipramine as the reserve.

GUIDELINE	CLOMIPRAMINE'S PLACE	DOSE (MG/DAY) / NOTE
BAP 2014	**Evidence-based, but second-line (less tolerated)**	marginal efficacy edge, offered as switch
the Indian Psychiatric Society 2025	**Second-line when SSRIs ineffective**	150 to 225
NICE 2005 (CG31)	After adequate SSRI ineffective / not tolerated	ECG + BP first if cardiovascular risk
CANMAT 2014	Second-line pharmacotherapy	with citalopram, mirtazapine, venlafaxine XR

Clomipramine is uniformly second-line for OCD across BAP, the Indian Psychiatric Society, NICE, CANMAT and WFSBP, reached as the switch after an adequate first-line SSRI trial fails; the OCD dose is 150 to 225 mg/day with ECG monitoring.

15.5 The dose and monitoring: 150 to 225 mg/day, ECG, and the 250 mg ceiling

The numbers to quote. The OCD dose of clomipramine is **150 to 225 mg/day** (starting from 75 mg and titrating), and the maximum recommended dose of **250 mg/day** should not usually be exceeded because of dose-related cardiotoxicity and seizures (the Indian Psychiatric Society 2025; New Oxford Textbook). Patients treated for OCD often need the high end of the wider dosing range, 200 to 250 mg/day, still under the 250 mg ceiling (Stahl). ECG monitoring is required before and during treatment, and blood pressure is checked (the Indian Psychiatric Society 2017; NICE 2005).

The interaction that catches people out. An SSRI switch to clomipramine is not always clean, because fluvoxamine (a CYP1A2 inhibitor) and fluoxetine/paroxetine (CYP2D6 inhibitors) raise clomipramine levels, so an unwary cross-taper can push a "standard" clomipramine dose into toxic, pro-convulsant, cardiotoxic territory (Stahl; the Indian Psychiatric Society 2019). Combining an SSRI with clomipramine also risks serotonin syndrome. The full interaction map is in the Mood disorders: pharmacotherapy notes.

150 to 225	250	7 per 1000
CLOMIPRAMINE OCD DOSE (MG PER DAY)	MAXIMUM DOSE CEILING, MG PER DAY (SEIZURE / CARDIAC RISK)	SEIZURE INCIDENCE AT 300 MG PER DAY (UNACCEPTABLE)

WORKED EXAMPLE

A 34-year-old woman with checking compulsions has failed an adequate trial of sertraline pushed to 200 mg/day for 12 weeks and a second adequate trial of fluoxetine 80 mg/day, both with real ERP, without response. Rather than reach for clomipramine first (its efficacy edge is marginal and non-significant), the switch is now justified precisely because two first-line SSRI trials have genuinely failed. She is started on clomipramine 75 mg, titrated toward 150 to 225 mg/day, with a baseline ECG and blood pressure and repeat ECG on dose increases. Because her prior fluoxetine is a CYP2D6 inhibitor with a long half-life, the clomipramine is introduced cautiously to avoid a levels spike into cardiotoxic or pro-convulsant range.

15.6 The whole comparison in one line, and the India lens

The one-line answer. If asked to compare in a sentence: clomipramine and the SSRIs are comparably effective anti-obsessional agents (clomipramine perhaps marginally more efficacious on meta-analysis, but not significantly so), and because clomipramine is less well tolerated and more dangerous in overdose, the SSRIs are first-line on the tolerability-and-safety balance, with clomipramine reserved as second-line for the patient in whom an adequate SSRI trial has failed. Everything above is scaffolding for that sentence.

INDIA

The comparison is not academic in India, where the anxiety and OCD treatment gap is wide, recognition is patchy, and the reflex prescription is too often a benzodiazepine, which does nothing for obsessions and risks dependence (the benzodiazepine over-prescription problem in Indian outpatient practice is discussed in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes). Both drug classes are cheap and available: the SSRIs as fluoxetine (Indian brands Fludac, Prodep), sertraline (Daxid, Zosert) and escitalopram (Nexito), and clomipramine as Anafranil. The Indian Psychiatric Society CPGs, updated for OCD to 2025, anchor exactly the SSRI-first, clomipramine-second-line logic to Indian practice, so the practical barrier is under-recognition and timid dosing, not access.

HOLD THIS

Clomipramine (most serotonergic TCA) and the SSRIs are comparably effective in OCD, with clomipramine only marginally and non-significantly ahead on meta-analysis; because clomipramine is less tolerable (anticholinergic, cardiac, seizure-risk) and dangerous in overdose, the SSRIs are first-line and clomipramine is the second-line switch after an adequate SSRI trial fails, dosed 150 to 225 mg/day with ECG monitoring.

MNEMONIC

SAME PUNCH, WORSE SIDES

Clomipramine and the SSRIs land the **same anti-obsessional punch** (equal-ish efficacy, clomipramine a marginal, non-significant nudge ahead), but clomipramine has the **worse side effects and worse overdose safety**, so tolerability, not efficacy, decides the line and the SSRIs go first.

GOOD TO REMEMBER

- **Clomipramine (Indian brand Anafranil):** the most serotonergic tricyclic and the original anti-obsessional drug (its serotonergic potency, not its tricyclic class, is why it works); mechanism is potent serotonin reuptake inhibition; marginally, non-significantly more efficacious than SSRIs on meta-analysis yet second-line in OCD at 150 to 225 mg/day because it is less tolerable (anticholinergic, cardiac conduction, seizure above 250 mg/day) and dangerous in overdose, so it is the switch after an adequate SSRI trial fails, under ECG monitoring.
- **SSRIs (first-line for OCD):** selective potent serotonin reuptake inhibitors; robustly efficacious with no single SSRI superior; the signature reason they beat clomipramine to first-line is superior tolerability and overdose safety at comparable efficacy; the one first-line principle is a high-dose SSRI plus ERP before any switch to clomipramine.

PEARL

The whole topic is a worked example of a general prescribing principle: when two drugs are equally effective, the first-line choice is decided by tolerability and safety, not by a marginal, non-significant efficacy point estimate. State that principle and the clomipramine-versus-SSRI answer writes itself.

16 · Exposure and response prevention

Exposure and response prevention (**erp**) is the specific behavioural treatment for obsessive-compulsive disorder, and it is one of the highest-yield psychotherapy answers in the whole anxiety block. Where the wider exposure principle and the general CBT model belong to the Psychotherapies, clinical assessment, MSE and nosology notes, this note owns the disorder-specific machinery: how the graded **exposure hierarchy** is built, what the **response prevention** component actually forbids, why anxiety falls on repeated exposure without the ritual, and the evidence base and delivery. Every major guideline, BAP 2014, NICE 2005 and the Indian Psychiatric Society CPG updated to 2025, names CBT incorporating ERP as first-line psychotherapy for OCD, co-equal with a high-dose SSRI and superior at holding gains.

Why it matters, and how to answer it. ERP is not "exposure with some talking"; it is a precise procedure with two named halves and a named mechanism. The candidate who scores states the mechanism (**habituation** of anxiety on prolonged, repeated exposure to a feared cue while the neutralising ritual is blocked), names both components (graded exposure plus **ritual prevention**), and knows the line placement (first-line, roughly as effective as an SSRI acutely and better at preventing relapse). Hold one sentence above all others: ERP works because staying with the anxiety, and refusing the compulsion that would abort it, lets the patient learn by direct experience that the feared catastrophe does not occur and that the anxiety subsides on its own.

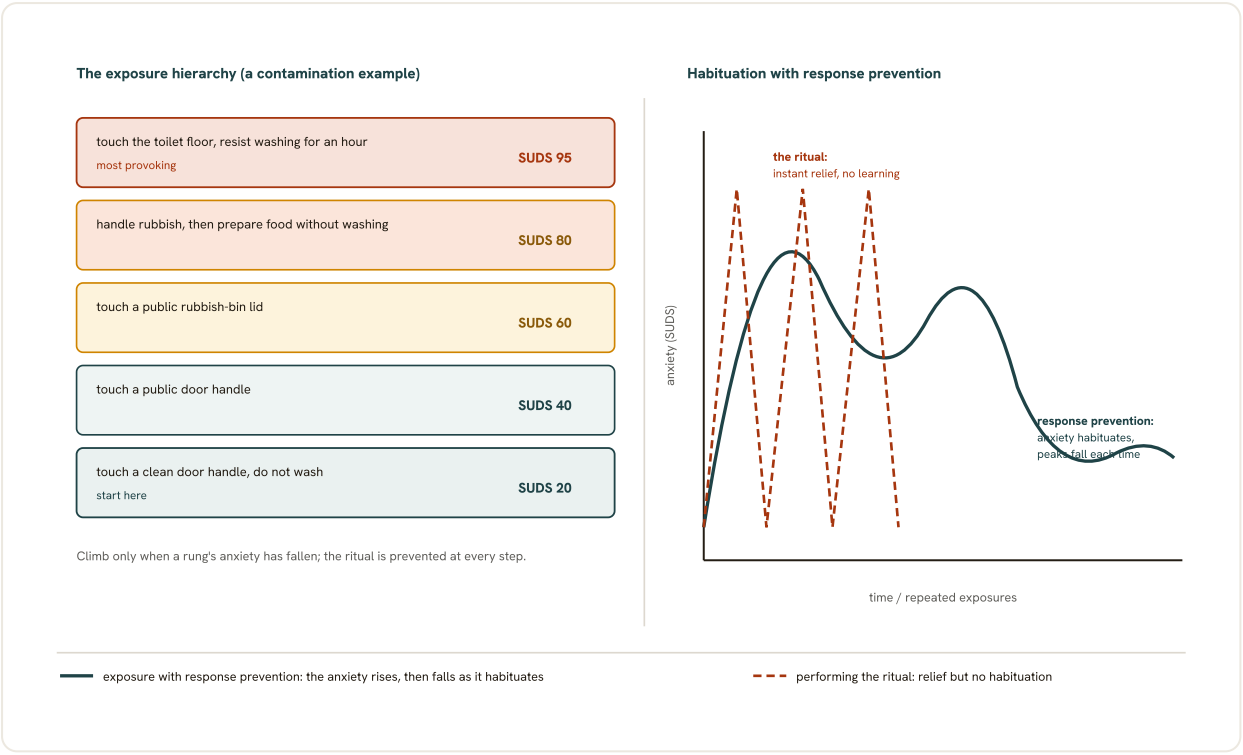


Fig 14.13 Exposure and response prevention (ERP). The patient and therapist build a hierarchy of feared situations, each rated for anxiety on a 0 to 100 subjective-units-of-distress scale, and work up it from the least to the most provoking. At each rung the patient stays in the situation and the compulsion is prevented; the anxiety rises, plateaus and then falls of its own accord as the body habituates, and the peak is lower on each repetition. Performing the ritual instead gives instant relief but teaches nothing, so the fear re-spikes to the same height every time. Preventing the response is therefore the active ingredient, and the wider exposure technique is taught in the Psychotherapies, clinical assessment, MSE and nosology notes.

16.1 What ERP is: two components with one mechanism

The definition. Exposure and response prevention is a manualised cognitive-behavioural treatment in which the patient is deliberately and repeatedly brought into contact with the situations, objects, thoughts or images that trigger obsessional distress (*exposure*), while refraining from the compulsion or avoidance that would normally relieve that distress (*response prevention*, also called ritual prevention) (Kaplan and Sadock 2024; Foa, Yadin and Lichner). Foa's canonical protocol, marketed as EX/RP, has five working parts: in-vivo exposure, imaginal exposure, ritual prevention, processing of the experience, and home practice. The exposure and the response prevention are not optional extras of each other; exposure without ritual prevention lets the patient neutralise and learn nothing, and ritual prevention without exposure gives the anxiety nothing to habituate to.

Exposure

Deliberate, planned contact with a feared cue (a situation, object, thought or image) sufficient to raise obsessional anxiety.

Response prevention

Blocking the compulsive ritual and the covert neutralising or avoidance that would otherwise discharge the anxiety.

Habituation

The automatic decline of an emotional response on repeated, prolonged exposure to the same stimulus once the ritual no longer aborts it.

16.2 The mechanism: habituation of anxiety when the ritual is blocked

The vicious cycle ERP breaks. In OCD an obsession provokes anxiety, the compulsion (or avoidance) discharges that anxiety, and the relief negatively reinforces the ritual, so the loop tightens with every repetition. Because the ritual is performed *before* the anxiety could fall by itself, the patient never learns that it would have fallen anyway, and never learns that the dreaded outcome would not have happened. Habituation is the principle that irrational fear and its behaviours fade on repeated and prolonged exposure to the source of the fear (Reddy, NIMHANS patient guide). ERP engineers exactly this: by exposing the patient to the trigger and forbidding the ritual, the anxiety is allowed to rise and then, if the patient stays with it, to subside on its own; with repetition the trigger progressively loses its power to provoke distress.

What the patient must not do. The habituation curve is fragile. Substituting one compulsion for another, using a distraction or relaxation trick to blunt the anxiety, or escaping the situation early all abort the exposure before habituation can occur, so the belief survives intact (Reddy). The instruction is to stay with the anxiety until it comes down substantially. Rituals and compulsions typically settle first; the obsessions themselves take longer to "wear out".

RULE **Block the ritual, or nothing changes.** Exposure only works if the neutralising response is prevented, because habituation and the disconfirmation of the feared outcome both require the patient to stay in the anxiety without the compulsion aborting it.

16.3 The exposure hierarchy: least to most anxiety-provoking

How it is built. Treatment begins by listing every situation, object, thought and image that triggers the patient's obsessions and rituals, plus everything the patient avoids to keep rituals at bay, and then arranging them in a graded hierarchy from the least to the most anxiety-provoking (Reddy; Kaplan and Sadock 2024). Each item is rated by the patient for the distress it provokes, conventionally on a subjective-units-of-distress scale, so the ladder is calibrated to that individual. The accompanying figure sets out this exposure-hierarchy ladder: low-distress rungs at the bottom, the most feared cue at the top, with the patient climbing only when the current rung has habituated. Exposure proceeds up the ladder, starting where anxiety is tolerable and moving to a harder item only once the easier one has stopped provoking much distress.

Graded, not flooding. The "graded" quality is deliberate and is what makes ERP tolerable enough to complete. Both in-vivo exposure (real contact, for example touching a "contaminated" surface and not washing) and imaginal exposure (vividly confronting the feared consequence, for example that harm will befall a loved one) are worked up the same hierarchy. This is the sense in which ERP is disorder-specific exposure: the ladder is composed of the patient's own obsessional cues and the response-prevention rule is attached to every rung.

16.4 Response (ritual) prevention: the discipline that makes exposure count

What is prevented. Ritual prevention bans the overt compulsion (the washing, checking, counting, reassurance-seeking) and, just as importantly, the covert neutralising and the mental rituals that patients substitute when the overt act is blocked. It also targets the avoidance that keeps triggers out of reach in the first place, for instance avoiding public toilets so as never to

have to wash extensively (Reddy). Where obsessions and compulsions occur only at home, treatment must become home-based, with the family briefed so they neither perform the ritual for the patient nor supply reassurance.

Family accommodation. A family that carries out rituals for the patient or endlessly reassures is accommodating the OCD and directly undermining response prevention; high family accommodation predicts poorer outcome, and reducing it through structured psychoeducation is part of the work (IPS 2025). A willing family member can be trained as a co-therapist to support graded exposure and ritual prevention at home.

TRAP **The hidden ritual.** A patient who stops washing but silently counts, prays or seeks reassurance instead has substituted a covert ritual for an overt one; habituation will not occur, and the therapist who misses it wrongly concludes ERP has failed.

16.5 Evidence base and effectiveness

How well it works. ERP is the most effective and most widely used behaviour therapy for OCD, effective in roughly **60 to 70%** of patients who engage with it (Reddy, NIMHANS). Guideline-level evidence places CBT with ERP as first-line psychotherapy, of broadly similar acute efficacy to an SSRI for mild-to-moderate OCD and superior in maintaining gains over time (BAP 2014; IPS 2025). A rigorous adult trial found that ERP augmentation of an ongoing SSRI outperformed risperidone augmentation, which is a favourite exam point: when an SSRI response is partial, adding ERP is a first-line augmentation strategy, ahead of an antipsychotic (Kaplan and Sadock 2024; IPS 2025). Combined ERP plus a high-dose SSRI is the recommended package for moderate-to-severe OCD, while ERP monotherapy suffices for milder illness.

Its limits. ERP demands motivation and the willingness to tolerate deliberate distress, and there can be significant resistance to undertaking it; a skilled therapist is needed where self-help does not suffice (Kaplan and Sadock 2024). Poor insight, entrenched family accommodation and comorbid depression all blunt response. Adequate "dose and duration" of exposure matter exactly as they do for a drug: too little exposure, like too low an SSRI dose, is a common reason for apparent failure.

60 to 70	10 to 12	1 to 2
PERCENT RESPOND TO ERP (NIMHANS)	HOURS OF ERP FOR MOST TO RESPOND	HOURS A SINGLE PROLONGED EXPOSURE MAY NEED

16.6 Delivery: dose, duration and format

How much is enough. Habituation takes time within a session and across the course. A single exposure may need to run long enough for anxiety to fall, sometimes only **30 minutes** but often a prolonged **1 to 2 hours** in more resistant fears; most patients show response between **10 to 12 hours** of exposure and response prevention overall (Reddy). Foa's protocol delivers this across roughly 17 to 20 sessions combining therapist-supervised and self-directed home practice. Daily home practice is the engine of change: ERP done only in the clinic, without between-session exposure, tends to stall.

Formats and access. ERP can be delivered face-to-face, in low-intensity or guided-self-help form for milder OCD (up to about 10 therapist hours per NICE 2005), by group or telephone CBT, and increasingly through internet-delivered programmes, though therapist-led ERP outperforms computerised CBT. Response is objectified by tracking OCD symptom severity on the Yale-Brown Obsessive-Compulsive Scale, whose severity bands and trial-entry threshold are taught, and the instrument reproduced, on the accompanying scale plate in the Y-BOCS note.

WORKED EXAMPLE

A young man with contamination obsessions washes for hours and avoids all public surfaces. Therapist and patient list his triggers and rank them from least to most distressing: touching his own front door (low), a shared office keyboard (mid), a hospital door handle (high), a public-toilet flush (top). Starting at the bottom, he touches the door and, under response prevention, does not wash; his anxiety climbs, then falls over the next hour as he stays with it. After several repetitions the door provokes almost nothing, and he climbs to the next rung. The covert urge to "wash later" is named early and blocked, so habituation, not a delayed ritual, is doing the work.

COMMON TRAP

Calling ERP off too soon. Like an under-dosed SSRI trial, an ERP course that is too short, too shallow up the hierarchy, or done only in sessions without daily home practice will look like non-response. Before concluding ERP has failed, confirm the exposures were adequate in intensity and duration, that no covert ritual or reassurance was smuggled in, and that family accommodation was addressed.

INDIA

Some of the most usable ERP material for Indian patients is Indian: the NIMHANS OCD patient guide (Reddy) lays out the hierarchy, the habituation rationale and the 60-to-70% figure in plain language, and the IPS CPG (updated for OCD to 2025) anchors CBT-with-ERP as first-line psychotherapy for Indian practice. This matters because OCD sits inside India's wide anxiety-spectrum treatment gap, and the reflex prescription of a benzodiazepine, still over-prescribed across Indian outpatient care, does nothing for obsessions: it neither provides exposure nor allows habituation, and it can blunt the very anxiety ERP needs the patient to feel. Where medication is combined with ERP the Indian-brand SSRIs are freely available, fluoxetine (Fludac, Prodep), sertraline (Daxid, Zosert), fluvoxamine (Fluvoxin) and escitalopram (Nexito), so the limiting factor is trained delivery of ERP, not drug access.

MNEMONIC

EXPOSE → PREVENT → STAY → HABITUATE

EXPOSE to the feared cue, up a graded hierarchy → **PREVENT** the ritual and the covert neutralising → **STAY** with the anxiety instead of escaping → **HABITUATE**, as the anxiety falls on its own and the trigger loses its power.

HOLD THIS

ERP works by blocking the ritual so the patient stays in the anxiety long enough to habituate and to learn the feared catastrophe never comes: two components (graded exposure plus response prevention), one mechanism (habituation), first-line for OCD.

GOOD TO REMEMBER

- **Exposure and response prevention:** the disorder-specific behaviour therapy for OCD, combining graded exposure up a patient-built hierarchy (in-vivo and imaginal) with response (ritual) prevention that blocks both overt and covert neutralising; the mechanism is habituation of anxiety once the ritual can no longer abort it, with disconfirmation of the feared outcome; first-line psychotherapy, roughly as effective as a high-dose SSRI acutely and better at maintaining gains, effective in about 60 to 70% of engaged patients, and the preferred first-line augmentation (ahead of an antipsychotic) for a partial SSRI response; the signature caution is that a hidden covert ritual, too-short exposure, or family accommodation will abort habituation and mimic non-response.

17 · Treatment-resistant OCD

Roughly a third to a half of OCD patients fail to respond adequately to a first serotonergic drug, and the examiner uses this fact to test one thing: can you tell a genuinely refractory patient from an *under-treated* one. The commonest cause of apparent non-response is not biology but an inadequate first trial, a depression-range dose stopped too soon and delivered without exposure and response prevention. **treatment-resistant ocd** is therefore a diagnosis of exclusion that you earn only after confirming an adequate trial, and its ladder then runs through **antipsychotic augmentation**, combined ERP, and finally the somatic options of neuromodulation and **neurosurgery ocd**.

Why it matters, and what this note owns. This note owns the resistance ladder above first-line: what counts as an adequate trial, how augmentation is sequenced, and where the neuromodulation and ablative options sit. The full first-line algorithm (the high-dose SSRI, the long trial, the Y-BOCS thresholds, clomipramine as the switch) is developed in the OCD management notes and is not re-derived here; the SSRI and clomipramine pharmacology lives in the Mood disorders: pharmacotherapy notes; the general exposure principle behind ERP lives in the Psychotherapies, clinical assessment, MSE and nosology notes; and the technical detail of **deep brain stimulation** and ablative neurosurgery (electrode targets, capsulotomy, cingulotomy technique) is cross-referenced to the ECT and neurostimulation notes. The refractory ladder is set out in the accompanying figure.

17.1 Confirm an adequate trial before you call it resistant

Adequate means high dose, long duration, real adherence. Before anything is added or switched, confirm the failed trial was genuinely adequate on three axes. A *high dose*, pushed to the maximum tolerated (SSRI target roughly **60 to 80 mg** fluoxetine-equivalent, above the depression range). A *long duration*, at least **10 to 12 weeks** at that ceiling before the trial is judged failed, with escalation to the effective dose within about 4 to 6 weeks (IPS 2025). And *adherence*, that the patient actually took the drug and, critically, received exposure and response prevention rather than a drug alone. The New Oxford Textbook frames the failure point as under

a 25% reduction of baseline Y-BOCS after 12 weeks of SRI treatment, of which at least 6 weeks are at the maximal tolerated dose.

The formal definition. True resistance is failure of at least two adequate SSRI trials, an adequate clomipramine trial, and CBT with ERP, each at full dose and duration (the Indian Psychiatric Society 2017). The honest first question at every rung is whether the earlier steps were real.

HOLD THIS

Do not call OCD treatment-resistant until you have confirmed an adequate trial on all three axes: a high dose (60 to 80 mg fluoxetine-equivalent), a long duration (10 to 12 weeks at the maximum tolerated dose), and genuine adherence including ERP; most apparent non-response is an under-treated first trial, not true resistance.

RULE **Adequate trial first, ladder second.** The first move in a "non-responder" is to re-audit the failed trial for dose, duration and adherence, not to reach for the next drug.

17.2 Optimise and switch: the steps that precede augmentation

Optimise, then switch. Once the trial is confirmed adequate but the response is partial or absent, the sequence before augmentation is to optimise the dose to the maximum tolerated, then switch, either to a different SSRI or to clomipramine (BAP 2014; NICE 2005). Switching between treatments of proven efficacy helps some patients (BAP 2014). Clomipramine is the second-line agent, at **150 to 225 mg/day** under ECG monitoring, used because it is the most serotonergic tricyclic but less well tolerated than an SSRI (the Indian Psychiatric Society 2025). The clomipramine-versus-SSRI contrast is developed in the clomipramine notes; here it is simply the switch on the way up the ladder.

COMMON TRAP

Jumping to augmentation or neurosurgery while the earlier rungs were sub-therapeutic. A patient who "failed" fluoxetine 20 mg for 6 weeks without ERP has not failed OCD treatment at all; augmenting that with an antipsychotic exposes them to metabolic risk for no reason and mislabels a slow-but-real responder as refractory.

17.3 Antipsychotic augmentation: the best-evidenced next rung

What it is and the doses. For the confirmed partial responder to an adequate SSRI or clomipramine trial, **antipsychotic augmentation** means adding a low-dose antipsychotic to the continuing serotonergic drug. BAP has the strongest augmentation evidence for risperidone, with aripiprazole also supported (BAP 2014). The Indian Psychiatric Society names low-dose aripiprazole or risperidone as the first-line pharmacological augmentation in treatment-resistant OCD, continued for at least **8 weeks**, at risperidone **1 to 3 mg/day** and aripiprazole in the low range (the Indian Psychiatric Society 2025). CANMAT lists adjunctive aripiprazole or risperidone as the first-line adjuncts, reserved for inadequate SSRI response given tolerability concerns (CANMAT 2014). WFSBP likewise puts antipsychotic augmentation first among the pharmacological options for resistant OCD (WFSBP 2023).

The monotherapy caveat and the serotonergic alternatives. Antipsychotics are for augmentation only: NICE is explicit that they should not normally be used as monotherapy for OCD, and reserves augmentation for after failed SSRI, combined SSRI-plus-CBT and clomipramine trials, under multidisciplinary review (NICE 2005). Beyond dopamine blockade, the guidelines note serotonergic augmentation with the 5-HT3 antagonists ondansetron or granisetron, and glutamatergic options (topiramate, lamotrigine, riluzole, memantine) that BAP regards as weaker or unproven (BAP 2014). The augmentation target is often the patient with comorbid tics or poorer insight.

AUGMENTATION OPTION	GUIDELINE STANDING	DOSE / NOTE
Risperidone (Sizodon, Risdone)	**First-line augmentation; strongest evidence (BAP, IPS, CANMAT)**	1 to 3 mg/day, at least 8 weeks
Aripiprazole (Arpizol, Asprito)	First-line augmentation, co-equal with risperidone	low range, at least 8 weeks
Ondansetron / granisetron	Serotonergic (5-HT3) augmentation option	added to fluoxetine or fluvoxamine
Topiramate / lamotrigine	Weaker glutamatergic augmentation	SSRI add-on, limited evidence

Augmentation in treatment-resistant OCD; low-dose risperidone or aripiprazole added to a continuing SSRI or clomipramine is the best-evidenced next rung, never monotherapy (BAP 2014; IPS 2025; CANMAT 2014). Doses are bare numbers in the cells; the unit is in the header line.

GOOD TO REMEMBER

- **Antipsychotic augmentation (risperidone / aripiprazole):** low-dose dopamine blockade *added* to a continuing SSRI or clomipramine for the confirmed partial responder in treatment-resistant OCD (risperidone 1 to 3 mg/day, low-dose aripiprazole) for at least 8 weeks; strongest evidence is for risperidone; the signature caution is that antipsychotics are augmentation only and never monotherapy for OCD.

17.4 Combining and intensifying ERP

ERP is a first-line augmentation, not just a first-line treatment. Where the failed pharmacological trial did not include structured exposure, adding or intensifying exposure and response prevention is itself a first-line augmentation strategy for the partial or non-responder to an SSRI, wherever feasible (the Indian Psychiatric Society 2025). BAP frames combining an SSRI or clomipramine with ERP as the step when efficacy needs to be maximised (BAP 2014), and for the refractory patient the psychological arm is intensified to therapist-led, high-frequency ERP. Family accommodation should be assessed and reduced, since high accommodation predicts poor outcome (the Indian Psychiatric Society 2017). The general exposure principle sits in the Psychotherapies, clinical assessment, MSE and nosology notes.

GOOD TO REMEMBER

- **Combining and intensifying ERP:** graded exposure with prevention of the neutralising ritual, added to pharmacotherapy as a first-line augmentation for partial responders; the principle is that a drug trial without ERP is an incomplete trial, so intensifying therapist-led exposure is a legitimate rung before escalating to somatic options; the first-line indication is the SSRI partial responder in whom real exposure has not yet been delivered.

17.5 Neuromodulation and the neurosurgical threshold

Non-invasive neuromodulation. Before the invasive options, rTMS and tDCS augmenting an SSRI are an evolving, preliminary-evidence option in partial or treatment-resistant OCD (the Indian Psychiatric Society 2025), and WFSBP lists rTMS among the non-pharmacological choices for resistant illness (WFSBP 2023). These sit below the ablative and stimulation options in invasiveness and are detailed in the ECT and neurostimulation notes.

Who crosses the neurosurgical threshold. The invasive options are reserved for severe, incapacitating OCD that has exhausted conventional drug and behavioural therapy. The practical selection criteria worth carrying: a chronic, severe, disabling illness (typically over 5 years), a surgical-candidate Y-BOCS of at least **26 to 30** out of a possible 40, and documented failure of an exhaustive array of adequate trials (each medication trial no less than 2 months), all confirmed by a multidisciplinary committee with formal informed consent (Kaplan and Sadock 2024). Fewer than 1% of treatment-seeking OCD patients meet current surgical criteria. In India this pathway runs through specialist tertiary centres such as NIMHANS; intravenous clomipramine is a further specialist option before device or lesion procedures (the Indian Psychiatric Society 2017).

TRAP **Neurosurgery is for the exhausted ladder, not the difficult patient.** The bar is a Y-BOCS of 26 to 40, years of failed adequate trials, and multidisciplinary consent; a distressing but incompletely treated case does not qualify.

17.6 Deep brain stimulation: reversible modulation of the CSTC circuit

What DBS is. **dbs** (deep brain stimulation) delivers high-frequency electrical stimulation through bilateral electrodes implanted stereotactically, connected to a subcutaneous pulse generator in the chest wall. Unlike a lesion it is *reversible and adjustable*: it can be switched off or reprogrammed if it causes adverse effects or is ineffective, though it commits the patient to indefinite specialist follow-up (Kaplan and Sadock 2024). It received FDA humanitarian device exemption for intractable OCD in 2009 and is an approved treatment in the European Union; other psychiatric uses remain investigational.

The targets and the numbers. The most frequent DBS target for OCD is the ventral capsule/ventral striatum (VC/VS), evolved from the anterior limb of the internal capsule and now extending posteriorly to include the ventral internal capsule, caudate and nucleus accumbens; other reported OCD targets are the nucleus accumbens directly, the subthalamic nucleus, the inferior thalamic peduncle and the medial forebrain bundle (New Oxford Textbook). A cohort of 34 patients at the VC/VS target on high-frequency stimulation for 36 months showed a **62%**

response rate, response being at least a **35%** Y-BOCS reduction; full effects typically take about 3 months to evolve. The rationale is modulation of the hyperactive cortico-striato-thalamo-cortical (CSTC) circuit; the fear-circuit anatomy sits in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes. Transient stimulation-related hypomania affects a substantial minority and resolves with parameter changes.

GOOD TO REMEMBER

- **Deep brain stimulation (DBS) for OCD:** reversible, adjustable high-frequency stimulation via bilateral implanted electrodes; the mechanism is modulation of the hyperactive CSTC circuit; the commonest target is the ventral capsule/ventral striatum (VC/VS), with roughly a 62% response rate (at least 35% Y-BOCS reduction) at 36 months; the signature point is FDA humanitarian device exemption for intractable OCD (2009), reserved for the fully exhausted ladder with a surgical Y-BOCS of 26 to 40.

17.7 Ablative neurosurgery: capsulotomy and cingulotomy

The two lesion procedures in use. Where DBS modulates, ablative **neurosurgery ocd** makes a permanent stereotactic lesion. Four bilateral lesion procedures were historically used; two remain current, anterior capsulotomy and anterior cingulotomy (Kaplan and Sadock 2024). *Anterior capsulotomy* (Leksell, Sweden) lesions the ventral part of the anterior limb of the internal capsule, impinging on the adjacent ventral striatum (the modern "ventral capsulotomy"), interrupting fibres between ventral prefrontal cortex and subcortical nuclei; a large review found about **64%** of cases substantially benefited. *Anterior cingulotomy* (Ballantine, Massachusetts General Hospital) places small thermocoagulation lesions in the anterior cingulate cortex (Brodmann areas 24 and 32) at the margin of the cingulum bundle; recent reviews show about 38 to 47% of OCD patients are full responders, with non-responders sometimes responding to a repeat procedure.

The trade-off with DBS. Ablation is a permanent, non-adjustable lesion and its outcome cannot be fairly judged for up to 2 years, but once done it needs no device team; DBS is reversible and acts within months but commits the patient to indefinite specialist programming. Both are last-rung options at specialist centres after the whole ladder has genuinely failed. The technical detail lives in the ECT and neurostimulation notes.

WORKED EXAMPLE

A 34-year-old woman has had incapacitating contamination OCD for 9 years, Y-BOCS 34 (extreme). Records confirm two adequate high-dose SSRI trials (fluoxetine 80 mg and sertraline 250 mg, each over 12 weeks with therapist-led ERP), an adequate clomipramine trial at 225 mg/day, and 8-week augmentation trials of risperidone then aripiprazole, all failed. After multidisciplinary review and formal consent at a tertiary centre, she is offered a reversible option first: VC/VS deep brain stimulation, with intensive ERP resumed within the first month post-implant. Only if that fails would an ablative capsulotomy be weighed. The point the examiner wants is that the whole ladder was audited as adequate before the somatic threshold was crossed.

10 to 12 weeks	1 to 3	26 to 30	62
ADEQUATE SSRI TRIAL AT MAXIMUM TOLERATED DOSE	RISPERIDONE AUGMENTATION, MG/DAY, AT LEAST 8 WEEKS	MINIMUM SURGICAL-CANDIDATE Y-BOCS (0 TO 40 SCALE)	VC/VS DBS RESPONSE RATE, PER CENT, AT 36 MONTHS

INDIA

Treatment-resistant OCD sits inside India's wider anxiety-spectrum treatment gap: the disorder is common yet under-recognised, and much "resistance" in Indian outpatient practice is really under-dosing plus the reflex of a benzodiazepine, still over-prescribed, that does nothing for obsessions and risks dependence. The Indian Psychiatric Society CPGs, updated for OCD to 2025, anchor the same audit-the-trial-then-augment ladder, and reserve the tertiary pathway (intravenous clomipramine, DBS, capsulotomy) for the genuinely refractory patient managed through specialist centres such as NIMHANS. Indian brands for the augmentation and switch drugs are readily available, risperidone (Sizodon, Risdone), aripiprazole (Arpizol, Asprito) and clomipramine (Anafranil), so the true limiting factor is confirming an adequate trial, not access.

MNEMONIC

AUDIT → SWITCH → AUGMENT → MODULATE → LESION

The resistance ladder in order: **AUDIT** the failed trial (high dose, long duration, adherence, ERP) → **SWITCH** (optimise, then another SSRI or clomipramine) → **AUGMENT** (low-dose risperidone or aripiprazole, plus intensified ERP) → **MODULATE** (rTMS/tDCS, then reversible DBS at the VC/VS) → **LESION** (ablative capsulotomy or cingulotomy at a specialist centre).

PEARL

In the resistant-OCD vignette the marks are almost never in the neurosurgery; they are in proving the earlier ladder was adequate. Name the three axes of an adequate trial (high dose, 10 to 12 weeks, adherence with ERP) and place DBS and capsulotomy only after two SSRIs, clomipramine, augmentation and ERP have genuinely failed, and you have answered the question before you reach the operating theatre.

18 · Body dysmorphic disorder

The exam sells body dysmorphic disorder (**bdd**) as the "ugliness" disorder, but that framing hides the point: the defect is not there, or is so slight that no one else can see it, and the whole clinical picture is built out of an intrusive preoccupation plus repetitive behaviours done to check or fix it. That architecture, a distressing appearance-related thought that will not leave and a compulsive ritual done in response, is why the DSM-5-TR and ICD-11 moved **bdd** out of the somatoform group and into the **obsessive-compulsive and related disorders**, sitting alongside OCD, hoarding and the body-focused repetitive behaviours (Kaplan and Sadock 2024; ICD-11 CDDR). Read it as OCD wearing a mirror: the same obsession-then-compulsion loop, but the content is fixed on how the person looks.

Why it matters, and what this note owns. Two things make BDD disproportionately examinable and clinically dangerous. First, it is *under-recognised*, patients present to dermatology and

cosmetic surgery, not psychiatry, and hide the concern from shame, so the diagnosis is missed unless you ask. Second, it carries one of the highest suicide burdens in psychiatry, higher rates of suicidal ideation and attempts than most disorders it is confused with. This note teaches the diagnosis and its discriminations (the **imagined defect**, the repetitive behaviours, the muscle-dysmorphia variant, the poor-insight and delusional forms), then the guideline-anchored treatment: a serotonin reuptake inhibitor at high dose and BDD-tailored CBT, first-line for every insight level including the delusional one. The general OCD algorithm and deep antidepressant dosing live elsewhere and are cross-referenced.

18.1 The core: preoccupation with an imagined or slight defect

The defining criterion. BDD is a **preoccupation** with one or more perceived defects or flaws in physical appearance that are *not observable or appear only slight to others* (DSM-5-TR 2022; ICD-11 CDDR). That last clause is the whole diagnosis: the concern is out of all proportion to any objective finding. The preoccupation is time-consuming (typically occupying at least an hour a day and often far more), intrusive, distressing and hard to resist, exactly the phenomenology of an obsession. Concerns most often focus on the skin, hair and nose but can involve any body area, and most patients are preoccupied with several areas over the course of the illness.

Not a normal appearance concern. Everyone dislikes something about how they look; BDD is separated from that by the distress, the time consumed, the functional wreckage and the repetitive behaviours. Insight is characteristically poor, the belief that one is disfigured feels true, which is why simple reassurance and even a mirror showing an ordinary face do not shift it.

GOOD TO REMEMBER

- **Body dysmorphic disorder (defining criterion):** preoccupation with one or more perceived defects in appearance that are *not observable or appear only slight to others*, plus repetitive behaviours or mental acts performed in response, causing clinically significant distress or impairment; classified with the obsessive-compulsive and related disorders (DSM-5-TR 2022; ICD-11 CDDR).

18.2 The second pillar: repetitive behaviours and mental acts

The compulsive half is required. A DSM-5-TR diagnosis needs the person, at some point, to have performed *repetitive behaviours or mental acts* in response to the appearance concern (DSM-5-TR 2022). These are the BDD compulsions: mirror checking (repeated checking of mirrors and other reflective surfaces such as windows), excessive grooming (hair styling, make-up), camouflaging (a hat over "balding", sunglasses over "asymmetrical" eyes, heavy make-up), reassurance seeking, skin picking to "fix" the skin, and repeatedly comparing one's appearance with other people's (New Oxford Textbook; Kaplan and Sadock 2024). They average a striking **3 to 8 hours a day**, are distressing and hard to resist, and, like OCD compulsions, do not relieve the distress and often worsen it.

Medical risks live here. Some behaviours are physically dangerous: compulsive skin picking (done by roughly 27 to 45% of BDD patients) can cause serious skin damage occasionally needing emergency surgery, and compulsive tanning raises cancer risk. Camouflaging doubles as a *safety*

behaviour, motivated by avoiding a feared outcome, which is why it is a target in CBT rather than something to accommodate.

RULE **Obsession plus compulsion, aimed at appearance.** BDD is diagnosed only when the appearance preoccupation is accompanied by repetitive behaviours or mental acts (mirror checking, grooming, camouflaging, reassurance seeking, comparing) done in response to it, the OCD loop with appearance as its content.

18.3 Muscle dysmorphia: the specifier that runs the other way

Too small, not too flawed. Muscle dysmorphia is a DSM-5-TR specifier of BDD in which the person is preoccupied with the idea that their body build is *too small or insufficiently muscular* (DSM-5-TR 2022). It occurs nearly always in men, who describe themselves as "puny", "tiny" or "too small" while in reality looking normal or unusually muscular from excessive weightlifting or steroid use (Kaplan and Sadock 2024; ICD-11 CDDR). The specifier applies even if the person is also preoccupied with other body areas.

Why it is the severe variant. Muscle dysmorphia carries *poorer* quality of life and *higher* rates of suicidality and substance use than other forms of BDD, in particular anabolic-androgenic steroid abuse, with the attendant medical harms (New Oxford Textbook; Kaplan and Sadock 2024). Practical trap: it is easily missed because gym culture normalises the behaviour, and it must be separated from an eating disorder, if the preoccupation is with body fat or weight in someone meeting eating-disorder criteria, that diagnosis takes precedence and BDD is not coded.

GOOD TO REMEMBER

- **Muscle dysmorphia:** a DSM-5-TR specifier of BDD, preoccupation that one's body build is too small or insufficiently muscular; nearly always in men; associated with anabolic-androgenic steroid abuse and higher suicidality; excluded when the focus is body fat/weight in an eating disorder (DSM-5-TR 2022; Kaplan and Sadock 2024).

18.4 Insight, referential thinking and the delusional variant

Insight is a specifier, not a separate disorder. Both DSM-5-TR and ICD-11 grade insight rather than splitting off a "delusional" diagnosis. DSM-5-TR specifies *with good or fair insight*, *with poor insight*, and *with absent insight / delusional beliefs*; ICD-11 collapses these to **fair to good insight** versus **poor to absent insight** (DSM-5-TR 2022; ICD-11 CDDR). Insight is characteristically poor, most patients hold their belief with over-valued-idea or delusional conviction.

The delusional form is still BDD. The old label "delusional dysmorphophobia" is gone: when the appearance belief reaches delusional intensity it is coded as BDD with absent insight, *not* as a delusional disorder, provided the belief stays within the appearance theme (ICD-11 CDDR; Companion to Psychiatric Studies). This matters for treatment (18.6): delusional BDD responds to the SRI, not to an antipsychotic alone. Add to this a strong streak of *referential thinking*, most patients believe others take special notice of the "defect", stare or mock, and an interpretive bias that reads neutral faces as contemptuous, which fuels social withdrawal.

TRAP **Do not rediagnose delusional BDD as a psychotic disorder.** A delusional-intensity appearance belief confined to the appearance theme is BDD with absent insight; treat it with a serotonin reuptake inhibitor, because dopamine-antagonist monotherapy is usually ineffective for delusional BDD.

18.5 The discriminations that get tested

Four boundaries own the marks. BDD sits at the crossroads of several disorders, and the exam lives on the seams. Hold the discriminators as a table rather than prose.

CONFUSED WITH	SHARED SURFACE	THE DISCRIMINATOR
Social anxiety disorder	Fear of being looked at, social avoidance	**In BDD the fear is specifically about others judging a *perceived appearance defect*; in social anxiety the fear spans behaviour and evaluation across social contexts, not one defect (ICD-11 CDDR)**
Eating disorder (anorexia/bulimia)	Distorted body image, appearance preoccupation	**If the preoccupation is with body fat or weight in someone meeting eating-disorder criteria, diagnose the eating disorder; BDD covers non-weight defects (DSM-5-TR 2022)**
Obsessive-compulsive disorder	Obsessions plus compulsions, poor-insight spectrum	**Content: BDD obsessions/compulsions are confined to *appearance*; if wider obsessional themes are present code OCD too (Kaplan and Sadock 2024)**
Normal appearance concern	Disliking a feature	**BDD adds an hour-plus daily preoccupation, repetitive behaviours, marked distress and functional impairment (DSM-5-TR 2022)**
Delusional disorder (somatic)	Fixed false belief about the body	**If the belief stays within the appearance theme it is BDD with absent insight, not delusional disorder (ICD-11 CDDR)**

The five boundary calls for body dysmorphic disorder; in each, the discriminator is the *content and breadth* of the concern, not its intensity (DSM-5-TR 2022; ICD-11 CDDR).

GOOD TO REMEMBER

- **BDD discriminators:** vs social anxiety, the fear is about a *specific perceived defect*; vs eating disorders, the focus is *not* body fat/weight; vs OCD, the obsessions/compulsions are confined to *appearance*; a delusional-intensity appearance belief is still BDD (absent insight), not delusional disorder (DSM-5-TR 2022; ICD-11 CDDR).

18.6 The high suicide risk, and the cosmetic-surgery trap

This is the number that matters most. BDD carries one of the highest suicide burdens in psychiatry. In clinical samples, lifetime rates of suicidal ideation run **78 to 81%** and suicide attempts **24 to 28%** (New Oxford Textbook). Population studies show appearance-specific suicidal ideation and attempts many-fold higher than in non-BDD groups, and the completed-suicide rate, though preliminary, appears markedly elevated. Mental-health quality-of-life scores in BDD are *poorer* than in depression, OCD, schizophrenia or bipolar disorder, and hospitalisation and unemployment rates are high. Muscle dysmorphia and adolescent BDD carry even higher suicidality.

Cosmetic treatment does not work and can harm. A majority of BDD patients seek and receive costly cosmetic, dermatologic or dental treatment; it is essentially *ineffective* for BDD and can worsen the picture, with some patients performing dangerous self-surgery (New Oxford Textbook). The first clinical move on suspecting BDD is therefore to *redirect away* from the surgeon and toward psychiatric treatment, screening suicide risk from the outset.

> **PEARL**
>
> The patient in front of the dermatologist or cosmetic surgeon who returns again and again dissatisfied, or who fixates on a barely visible "flaw", is the classic undetected BDD. Because they hide the concern from shame and rarely volunteer it, you must ask directly, and once you suspect it, screen suicide risk before anything else. Cosmetic intervention rarely satisfies and can precipitate crisis.

18.7 First-line treatment: a high-dose SRI

SRIs are first-line for every insight level. Serotonin reuptake inhibitors (SSRIs, and clomipramine as the SRI-class TCA) are, with BDD-tailored CBT, the recommended first-line pharmacotherapy, endorsed by the NICE OCD/BDD guideline (New Oxford Textbook; NICE 2005). The evidence base includes a placebo-controlled fluoxetine trial and a blinded crossover showing the SRI clomipramine (Anafranil) beating the non-SRI desipramine, the direct parallel to the clomipramine-versus-SSRI point in OCD: it is the *serotonergic* action that matters, not the tricyclic structure. Crucially, delusional (absent-insight) patients respond to the SRI alone; antipsychotic monotherapy is usually ineffective for delusional BDD, so the SRI is given regardless of insight.

Dose high, choose escitalopram or fluoxetine. BDD, like OCD, needs *higher SRI doses than depression* (New Oxford Textbook). Escitalopram (Nexito, Rexipra) and fluoxetine are the best-studied and usual first choices, escitalopram having few drug interactions; a relapse-prevention trial used escitalopram at a mean of about **26 mg/day**. Citalopram is least preferred because its dosing ceiling sits below the dose usually needed. The brand names to lead with in India are the escitalopram, fluoxetine, sertraline and fluvoxamine antidepressant brands; clomipramine is Anafranil.

AGENT	ROLE IN BDD	ANCHOR / DOSE NOTE (MG/DAY WHERE GIVEN)
Escitalopram (Nexito, Rexipra)	**Preferred first-line SRI**	Best-studied with fluoxetine; few interactions; relapse-prevention trial mean about 26
Fluoxetine	First-line SRI	Placebo-controlled trial positive; dose higher than for depression
Sertraline / fluvoxamine	Alternative first-line SRIs	Open-label support; high-dose principle applies
Clomipramine (Anafranil)	**Reserved: SRI-class TCA after SSRI non-response**	Beat desipramine in a crossover; TCA cautions; kept behind SSRIs on tolerability
Antipsychotic alone	Not for delusional BDD as monotherapy	Dopamine-antagonist monotherapy usually ineffective; give the SRI

Pharmacotherapy of BDD: a high-dose SRI first-line for every insight level, with clomipramine reserved for SSRI non-response (New Oxford Textbook; NICE 2005). Doses in the header; bare figures in the cells.

WORKED EXAMPLE

A man is fixated that his nose is grossly deformed; it looks normal, he checks mirrors and windows for hours, cancels social plans and has begun asking about rhinoplasty. Screen suicide risk (elevated in BDD), redirect from the surgeon, and start escitalopram, titrating toward a *high* dose and holding it for a full 12 to 16 weeks, at the highest tolerated dose for at least 3 to 4 of those weeks, before judging response. Add BDD-tailored CBT. Even if his conviction is delusional, the SRI, not an antipsychotic alone, is the treatment.

GOOD TO REMEMBER

- **SRI in BDD:** first-line pharmacotherapy at *high dose* (higher than for depression), escitalopram or fluoxetine preferred, clomipramine reserved for SSRI non-response; given for *all* insight levels because delusional BDD responds to the SRI while antipsychotic monotherapy usually does not; adequate trial 12 to 16 weeks at maximal tolerated dose (New Oxford Textbook; NICE 2005).

18.8 First-line treatment: BDD-tailored CBT

Generic CBT is not enough. The recommended psychotherapy is *cognitive behavioural therapy specifically tailored to BDD*, not off-the-shelf CBT (New Oxford Textbook; NICE 2005). It targets the appearance-related core beliefs ("I am defective", "I am unlovable"), uses **exposure and response prevention** against the rituals and safety/camouflaging behaviours, perceptual and mirror-retraining to break the zoomed-in scrutiny, and cognitive restructuring of the referential and threat-interpretation biases. The wider CBT model and the exposure principle are developed in the Psychotherapies, clinical assessment, MSE and nosology notes.

How the two combine. A high-dose SRI and BDD-tailored CBT are the two first-line pillars; combining them is standard for more severe or treatment-resistant cases, and psychiatric treatment (not cosmetic intervention) is what actually improves BDD symptoms and functioning.

GOOD TO REMEMBER

- **BDD-tailored CBT:** first-line psychotherapy; core = exposure and response prevention against checking/camouflaging plus cognitive restructuring of appearance beliefs and mirror-retraining; must be BDD-specific, not generic CBT; combined with a high-dose SRI in severe or resistant cases (New Oxford Textbook; NICE 2005).

18.9 Definitions to hold cold

Imagined defect

The appearance flaw central to BDD is not observable, or appears only slight, to others; the concern is disproportionate to any objective finding.

Mirror checking

The signature BDD compulsion: repeated checking of mirrors and reflective surfaces (also windows) to inspect the perceived defect; averages hours a day and does not relieve distress.

Camouflaging

Hiding the disliked area (hats, sunglasses, make-up, posture); both a compulsion and a safety behaviour, a CBT target.

Muscle dysmorphia

BDD specifier: preoccupation that the body is too small/insufficiently muscular; nearly always male; linked to anabolic steroid use and higher suicidality.

Absent insight / delusional

Highest-conviction insight specifier; the appearance belief is held with delusional certainty yet remains BDD, responsive to the SRI.

INDIA

BDD is a textbook casualty of the Indian treatment gap for the anxiety, OCD and related disorders: it presents to dermatology, cosmetic and "fairness"-focused services, not psychiatry, and is rarely named, so a high-suicide-risk disorder goes untreated while the cosmetic industry profits from an intervention that does not work. The same benzodiazepine over-prescription reflex that plagues Indian anxiety practice is misplaced here too, an alprazolam script does nothing for the appearance preoccupation and delays the treatment that helps. The Indian Psychiatric Society CPGs anchor the obsessive-compulsive-spectrum standard: a high-dose SSRI first-line, escitalopram (Nexito, Rexipra) or fluoxetine, then clomipramine (Anafranil), with BDD-tailored CBT, and no place for a benzodiazepine as treatment. The genuinely high-yield Indian move is recognition and suicide screening: ask about hidden appearance preoccupation, and refer away from the surgeon.

78 to 81%	24 to 28%	3 to 8	12 to 16
LIFETIME SUICIDAL IDEATION IN CLINICAL BDD SAMPLES	LIFETIME SUICIDE ATTEMPTS IN CLINICAL BDD SAMPLES	HOURS A DAY OCCUPIED BY BDD COMPULSIVE BEHAVIOURS	WEEKS: ADEQUATE HIGH-DOSE SRI TRIAL BEFORE JUDGING RESPONSE

MNEMONIC

MIRROR

Muscle-dysmorphia specifier (too small, male, steroids); **I**magined or slight defect, not observable to others; **R**epetitive behaviours required (mirror checking, camouflaging, comparing); **R**eferential thinking and poor insight (delusional variant is still BDD); **O**CD-spectrum classification; **R**isk of suicide very high, and cosmetic surgery does not help. Treatment: high-dose SRI plus BDD-tailored CBT for every insight level.

HOLD THIS

BDD = preoccupation with a perceived defect that is unobservable or slight to others, *plus* repetitive behaviours (mirror checking, camouflaging, comparing), in the OCD spectrum; very high suicide risk; treat with a *high-dose* SRI (escitalopram or fluoxetine, clomipramine reserved) and BDD-tailored CBT for all insight levels, because delusional BDD responds to the SRI and cosmetic surgery does not.

19 · Hoarding, trichotillomania and excoriation

The exam packs three disorders into one short block, and the reason to learn them together is that all three are new arrivals in the **obsessive-compulsive and related disorders** chapter, sitting beside OCD and body dysmorphic disorder in both DSM-5-TR and ICD-11 (DSM-5-TR 2022; ICD-11 CDDR). Hoarding disorder was a subtype of OCD and is now a separable syndrome; trichotillomania moved out of the old impulse-control chapter; and excoriation disorder is brand new. Trichotillomania and excoriation are the two **body-focused repetitive** behaviour disorders, and the phrase you must be able to say is exactly that: recurrent, self-directed grooming behaviours (hair-pulling, skin-picking) that produce a physical lesion and that the person keeps trying, and failing, to stop.

Why it matters, and what this note owns. This is a low-yield block by volume but a high-yield one for keywords: each entity is a one-line viva answer built around a single defining criterion. The traps are all discriminations, hoarding versus normal collecting, trichotillomania versus alopecia, skin-picking versus an OCD compulsion, so the note teaches the criterion first and the discriminator second. On treatment, one behavioural technique carries the whole block: habit reversal training. The deep antidepressant dosing that these SSRIs share with OCD lives in the Mood disorders: pharmacotherapy notes and is cross-referenced, not repeated.

19.1 Hoarding disorder: the defining criterion is difficulty discarding

Persistent difficulty discarding, not the clutter. The essential feature of hoarding disorder is a *persistent* **difficulty discarding** or parting with possessions, regardless of their actual value (DSM-5-TR Criterion A). The examinable point is that the diagnosis is anchored on the *discarding difficulty*, not on the mess: the clutter is a downstream consequence. The difficulty is driven by a perceived need to save the items and by distress at the thought of discarding them (Criterion B), which is what makes the saving *purposeful* and separates it from passive accumulation.

Clutter, distress and the third-party clause. The retained possessions congest and clutter *active living areas* so their intended use is compromised, the person cannot cook in the kitchen or sleep in the bed (Criterion C), and this causes clinically significant distress or impairment, including an unsafe home (Criterion D). A neat examiner's hook sits in Criterion C: if the living areas are uncluttered *only because a third party* (family, cleaners, authorities) cleared them, the person still has the disorder. The *with excessive acquisition* specifier applies to the 80 to 90% who also over-buy or over-collect, and insight is graded good/fair, poor, or absent/delusional.

GOOD TO REMEMBER

- **Hoarding disorder (defining criterion):** persistent *difficulty discarding* possessions regardless of value, driven by a perceived need to save and distress at discarding (Criteria A to B), producing clutter that compromises active living areas (C) and significant distress/impairment (D); coded with the obsessive-compulsive and related disorders; specify *with excessive acquisition* (DSM-5-TR 2022; ICD-11 6B24).

19.2 Hoarding versus normal collecting, and versus the OCD it left

Collecting is organised; hoarding is not. The first discrimination is against **normative collecting**, which is organised, selective and a source of pleasure, and does *not* produce the clutter, distress or functional impairment of the disorder (DSM-5-TR 2022). Even when the sheer quantity is similar, the collector's items are curated and the living space stays usable; the hoarder's are piled in disorganised heaps in spaces meant for other purposes.

Why it is no longer an OCD subtype. In OCD, accumulation would be driven by an *obsession* (for example not discarding papers because they might contain harm-preventing information) and the saving feels ego-dystonic and unwanted. In hoarding disorder the saving is *not* triggered by an intrusive obsession; the person genuinely wants to keep the items and feels distress only when made to discard (New Oxford Textbook; DSM-5-TR 2022). Criterion F also forces you to exclude the medical and other-disorder mimics, brain injury and cerebrovascular disease, the low energy of depression, psychotic delusions, and the accumulation seen in major neurocognitive disorder, which is why new-onset hoarding in an older adult demands a cognitive and neurological work-up first.

TRAP **New-onset hoarding in an older adult is a red flag, not a diagnosis.** Before coding hoarding disorder, exclude brain injury, cerebrovascular disease and a major neurocognitive disorder (Criterion F); late-onset accumulation is disproportionately organic.

19.3 Hoarding: what actually helps

Disorder-specific CBT is the mainstay; drugs are weak. Hoarding disorder responds *poorly* to the SSRI-plus-ERP algorithm that works for OCD, part of the evidence that it is a distinct condition (New Oxford Textbook). The best-supported treatment is a *hoarding-specific* cognitive behavioural therapy that targets the discarding difficulty directly, sorting-and-discarding practice, cognitive work on saving beliefs and decision-making, motivational enhancement for the characteristically limited insight, and skills training for the organising and planning deficits. It is

delivered over many months and gains are partial; there is no quick pharmacological fix, so the framing to hold is behavioural-first.

GOOD TO REMEMBER

- **Hoarding-specific CBT:** the first-line treatment for hoarding disorder; targets the difficulty discarding, saving beliefs, decision-making, motivation and organising skills; the disorder responds *poorly* to the standard OCD SSRI regimen, so behaviour therapy, not a drug, leads (New Oxford Textbook).

19.4 Trichotillomania: recurrent hair-pulling with hair loss

The five-part criterion. Trichotillomania (hair-pulling disorder) is recurrent pulling out of one's own **hair-pulling** resulting in *hair loss* (Criterion A), with repeated attempts to decrease or stop (B), clinically significant distress or impairment (C), not attributable to another medical/dermatological condition (D), and not better explained by another mental disorder such as body dysmorphic disorder (E) (DSM-5-TR 2022). The commonest sites are scalp, eyebrows and eyelashes; pulling may be a focused ritual (with mounting tension then relief) or automatic (outside full awareness), and the person may examine, manipulate or swallow the pulled hair.

Two clinical hooks worth marks. It is a **body-focused repetitive** behaviour: crucially, it is *not* triggered by an obsession, which is exactly how it separates from OCD. And *trichophagia* (swallowing hair) can build a trichobezoar, a gastric hairball causing obstruction, anaemia or perforation, the classic surgical complication and a favourite viva twist. Onset typically coincides with puberty and the course is chronic with waxing and waning.

GOOD TO REMEMBER

- **Trichotillomania (defining criterion):** recurrent *hair-pulling resulting in hair loss* with repeated attempts to stop (Criteria A to B), distress/impairment (C), not due to a dermatological condition (D) and not explained by BDD (E); a body-focused repetitive behaviour *not* driven by an obsession; watch for trichophagia and trichobezoar (DSM-5-TR 2022).

19.5 Excoriation (skin-picking) disorder: the parallel entity

The same architecture, on skin. Excoriation (skin-picking) disorder is recurrent **skin-picking** resulting in *skin lesions* (Criterion A), with repeated attempts to decrease or stop (B), significant distress or impairment (C), not attributable to a substance (for example cocaine) or another medical condition such as scabies (D), and not better explained by another mental disorder (E) (DSM-5-TR 2022). Read it as the dermatological twin of trichotillomania: the second **body-focused repetitive** behaviour disorder, most often targeting the face, arms and hands, and, like hair-pulling, running from focused to automatic and not obsession-driven.

The exclusions carry the traps. Criterion D is the examiner's ground: skin-picking in amphetamine or cocaine intoxication ("meth mites", the delusion of infestation) is coded as a substance-induced obsessive-compulsive and related disorder, not excoriation disorder; and picking to correct a perceived appearance flaw is *body dysmorphic disorder*, not excoriation. Onset is often around puberty and the female preponderance is marked in clinical samples.

GOOD TO REMEMBER

- **Excoriation (skin-picking) disorder (defining criterion):** recurrent *skin-picking resulting in skin lesions* with repeated attempts to stop (Criteria A to B), distress/impairment (C), not due to a substance (cocaine) or medical condition (scabies) (D) and not explained by another disorder such as BDD (E); the second body-focused repetitive behaviour disorder (DSM-5-TR 2022).

RULE **Body-focused repetitive behaviours are not compulsions.** Hair-pulling and skin-picking produce a lesion and are *not* triggered by an obsession; that missing obsession is what separates trichotillomania and excoriation from OCD.

19.6 The four entities at a glance

One table fixes the criterion and the discriminator. The block is easiest to hold as a grid of "defining act" against "the thing it is *not*".

DISORDER (ICD-11)	DEFINING CRITERION	KEY DISCRIMINATOR
Hoarding disorder (6B24)	Persistent difficulty discarding possessions, driven by need to save + distress	**Not normal collecting (that is organised, no distress); not obsession-driven as in OCD; exclude organic/neurocognitive causes**
Trichotillomania (6B25.0)	Recurrent hair-pulling with hair loss, repeated attempts to stop	**A body-focused repetitive behaviour, *no* obsession; not dermatological alopecia; not BDD hair removal; beware trichobezoar**
Excoriation / skin-picking (6B25.1)	Recurrent skin-picking with skin lesions, repeated attempts to stop	**Body-focused repetitive behaviour, *no* obsession; not stimulant-induced picking; not BDD skin-picking to fix a flaw**
OCD (6B20, for contrast)	Obsessions and/or compulsions; compulsions relieve obsession-driven distress	**The presence of an *obsession* driving the behaviour is what the three OCRDs above lack**

The compact OCRD block: each entity is anchored on its defining act, and every discrimination turns on whether an *obsession* drives the behaviour (DSM-5-TR 2022; ICD-11 CDDR).

2.5	1 to 2	10:1	1200 to 2400
HOARDING DISORDER POINT PREVALENCE, %	TRICHOTILLOMANIA 12-MONTH PREVALENCE, %	FEMALE-TO-MALE RATIO, TRICHOTILLOMANIA CLINICAL SAMPLES	N-ACETYLCYSTEINE (MG/DAY) TRIALLED IN TRICHOTILLOMANIA

19.7 Habit reversal training: the shared first-line psychotherapy

The one behavioural technique for the block. Habit reversal training (HRT), developed by Azrin, is the first-line treatment for the body-focused repetitive behaviours (Kaplan and Sadock 2024). Its three core elements are the answer to any viva: *awareness training* (self-monitoring, to catch the urge and the moments that precede pulling or picking); *stimulus control* (changing the environment so the behaviour is less likely to start, for example gloves, plasters or a barrier); and *competing response training*, the core, engaging at the first sign of the urge in a motor behaviour

physically *incompatible* with the habit (classically clenching a fist for a minute) until the urge passes. Relaxation and social/contingency reinforcement support the package.

Where drugs sit. Pharmacotherapy is adjunctive and the evidence is thin. SSRIs are the usual first-line drug for the body-focused repetitive behaviours on tolerability grounds, and clomipramine (Anafranil) has the best trichotillomania trial data among the antidepressants; the glutamate modulator N-acetylcysteine reduced hair-pulling in a placebo-controlled trial and reads as comparable to behaviour therapy (Kaplan and Sadock 2024). Combining HRT with medication may beat either alone.

GOOD TO REMEMBER

- **Habit reversal training (principle and structure):** Azrin's first-line behavioural treatment for trichotillomania and excoriation; three elements, *awareness training*, *stimulus control*, and *competing response training* (a motor act incompatible with the habit); drugs (SSRIs, clomipramine, N-acetylcysteine) are adjunctive with a thin evidence base (Kaplan and Sadock 2024).

INDIA

This block magnifies the Indian treatment gap for the anxiety, OCD and related disorders, because these are the disorders patients hide hardest. Trichotillomania and excoriation present to dermatology and cosmetic services as "alopecia" or "acne", and hoarding is dismissed as untidiness or eccentricity, so the psychiatric diagnosis is rarely named. The reflex prescription of a benzodiazepine, still over-prescribed across Indian outpatient practice, does nothing for a body-focused repetitive behaviour and delays the behaviour therapy that helps. The Indian Psychiatric Society CPGs anchor the obsessive-compulsive-spectrum standard for the SSRI half, and Indian brands are readily available, fluoxetine (Fludac, Prodep), sertraline (Daxid, Zosert), escitalopram (Nexito), fluvoxamine (Fluvoxin) and clomipramine (Anafranil), so the limiting factor is recognition, not access. The genuinely high-yield Indian move is to ask directly about hair-pulling, skin-picking and discarding difficulty, and to refer to habit reversal training rather than reach for an anxiolytic.

PEARL

All four OCRDs in this block separate on one axis. OCD has an *obsession* driving a compulsion that relieves it. Hoarding, trichotillomania and excoriation have no obsession: the person *wants* to keep the objects, or the pulling/picking simply discharges tension. If you can find the obsession, you are in OCD; if you cannot, you are in one of the three new neighbours.

HOLD THIS

Hoarding is anchored on *difficulty discarding*; trichotillomania and excoriation are the two *body-focused repetitive* behaviours (hair-pulling with hair loss, skin-picking with skin lesions), none of them obsession-driven, and habit reversal training is the shared first-line treatment for the two body-focused ones.

20 · Illness anxiety and the OCRD spectrum

This is the short topic that fixes a favourite exam trap: where does illness anxiety actually live, and what is the **ocrd spectrum** that keeps trying to claim it? The clinical picture is old, the patient preoccupied with the fear of having a serious disease, checking the body and seeking or avoiding doctors, on a scale out of all proportion to any finding. The classical name was hypochondriasis; the stigma attached to that word is why DSM-5 renamed it (Kaplan and Sadock 2024). The examinable point is that the two manuals split it in opposite directions, and understanding why turns on the **obsessive-compulsive spectrum** idea.

Why it matters, and what this note owns. The whole disorder is built from an intrusive preoccupation plus repetitive behaviours (checking, reassurance-seeking) done in response, the same obsession-then-compulsion architecture as OCD, which is exactly why ICD-11 files **health anxiety** disorder inside the obsessive-compulsive and related disorders while DSM-5-TR files illness anxiety among the somatic-symptom disorders. This note teaches that placement, the criterion-anchored diagnosis of illness anxiety, the concept of the OCRD spectrum that binds OCD, BDD, hoarding, the body-focused behaviours and health anxiety by their shared repetitive-behaviour feature, and the first-line treatment. The illness-anxiety-versus-somatic-symptom-disorder boundary (how much bodily symptom is present) is worked out in the Somatic-symptom, sexual, impulse-control disorders and suicide notes; here we own the OCRD-facing side.

20.1 Illness anxiety disorder: the criterion and the two subtypes

The defining criterion. Illness anxiety disorder is a **preoccupation** with having or acquiring a serious illness, in which somatic symptoms are absent or, if present, only mild, and the preoccupation persists despite appropriate medical evaluation and reassurance (DSM-5-TR 2022; Kaplan and Sadock 2024). It is not held with delusional intensity and is not restricted to a concern about appearance (that would be body dysmorphic disorder). The person has a high level of health anxiety and performs excessive health-related behaviours, or shows maladaptive avoidance, and the duration must be at least **6 months** (though the specific feared illness may change over that time).

Two subtypes, opposite behaviours. DSM-5-TR specifies a *care-seeking type*, in which medical care including physician visits, tests and procedures is used frequently, and a *care-avoidant type*, in which medical care is rarely used (DSM-5-TR 2022). The care-avoidant patient is easy to miss precisely because they stay away from clinics; the fear is so intense that they avoid the very reassurance they crave. Core phenomenology, in the older language, is disease conviction, disease fear and bodily preoccupation.

GOOD TO REMEMBER

- **Illness anxiety disorder (defining criterion):** preoccupation with having or acquiring a serious illness with somatic symptoms absent or only mild, persisting *despite* appropriate evaluation and reassurance, for at least **6 months**; not delusional, not confined to appearance; specify *care-seeking* vs *care-avoidant* type (DSM-5-TR 2022).

20.2 The DSM-versus-ICD split: same patient, two chapters

DSM-5-TR: renamed and split across the somatic group. DSM-5 removed the term hypochondriasis for its pejorative connotation. About two-thirds to three-quarters of former hypochondriasis cases, those with prominent somatic symptoms, are recoded as *somatic symptom disorder*; the remaining minority (around **20%**), whose symptoms are minor and whose focus is the fear of illness itself, become *illness anxiety disorder* (Kaplan and Sadock 2024; DSM-5-TR 2022). Both sit in the somatic-symptom-and-related-disorders chapter. The dividing line is the amount of somatic symptom present.

ICD-11: kept the name, moved it into the OCRD grouping. ICD-11 retained the label *hypochondriasis (health anxiety disorder)* and placed it, as code 6B23, inside the **obsessive-compulsive or related disorders** grouping, not the somatic block (ICD-11 CDDR). Its stated rationale is shared phenomenology, repetitive intrusive thoughts about having an illness and repetitive or excessive health-related behaviours driven by that preoccupation, plus a similar treatment response. In ICD-11 the presence of somatic symptoms is explicitly *not* an essential feature, so the label turns on the anxious preoccupation and the checking, not on bodily complaints.

FEATURE	DSM-5-TR	ICD-11 CDDR
Name	Illness anxiety disorder	**Hypochondriasis (health anxiety disorder)**
Chapter	Somatic symptom and related disorders	**Obsessive-compulsive and related disorders (6B23)**
Somatic symptoms	Absent or mild; if prominent, code somatic symptom disorder instead	**Not an essential feature**
Rationale for placement	Health-focused somatic preoccupation	**Repetitive intrusive thoughts + checking, like OCD; shared treatment response**
Insight	Not of delusional intensity	**Insight specifier applies (fair-to-good vs poor-to-absent)**

The single most tested fact on this topic: the same clinical picture is an OCRD in ICD-11 but a somatic-symptom disorder in DSM-5-TR (ICD-11 CDDR; DSM-5-TR 2022).

RULE **Two manuals, opposite files.** Hypochondriasis / illness anxiety is an *obsessive-compulsive related disorder* in ICD-11 (6B23) but a *somatic-symptom disorder* in DSM-5-TR, split off by how much bodily symptom is present.

20.2b The OCRD spectrum: what binds the group

The unifying feature. The **ocrd spectrum** (the obsessive-compulsive related, or obsessive-compulsive spectrum, disorders) is the family of conditions linked by a shared core: an intrusive, repetitive *preoccupation* and the repetitive *behaviours* performed in response to it (New Oxford Textbook; ICD-11 CDDR). In ICD-11 the grouping contains obsessive-compulsive disorder (6B20), body dysmorphic disorder (6B21), olfactory reference disorder (6B22), hypochondriasis /

health anxiety disorder (6B23), hoarding disorder (6B24) and the body-focused repetitive behaviour disorders (6B25, trichotillomania and excoriation/skin-picking); Tourette syndrome is cross-listed for its analogous premonitory-urge-and-repetitive-behaviour phenomenology. The historical idea, proposed by Hollander, arranged these on a compulsivity-to-impulsivity dimension, harm-avoidant checking at one pole, reward-driven grooming behaviours at the other.

What earns a place, and what does not. Membership is defined by the repetitive-behaviour-or-preoccupation feature and by serotonergic treatment response, which is why illness anxiety, whose sufferers check the body and seek reassurance, fits so naturally that ICD-11 moved it in. The spectrum is a *conceptual* bridge: it explains why these disorders cluster, co-occur and respond to serotonin reuptake inhibitors, but it does not collapse them into one diagnosis. The insight specifier (fair-to-good vs poor-to-absent) applies across OCD, BDD, olfactory reference disorder, hypochondriasis and hoarding, another shared thread (ICD-11 CDDR).

Obsessive-compulsive spectrum
disorders linked by intrusive repetitive preoccupation, repetitive behaviours in response, and serotonergic treatment response

OCD (6B20)
obsessions and compulsions across varied content

Body dysmorphic disorder (6B21)
the loop fixed on a perceived appearance defect

Hoarding disorder (6B24)
difficulty discarding, driven by perceived need to save

Body-focused repetitive behaviours (6B25)
trichotillomania (hair-pulling), excoriation (skin-picking)

Hypochondriasis / health anxiety (6B23)
the loop fixed on the fear of serious illness

GOOD TO REMEMBER

- **OCRD spectrum (unifying feature):** conditions bound by an intrusive repetitive *preoccupation* plus repetitive *behaviours* done in response, and by serotonergic treatment response; ICD-11 grouping = OCD, BDD, olfactory reference disorder, hypochondriasis, hoarding, body-focused repetitive behaviours, with Tourette cross-listed (ICD-11 CDDR).

20.3 The discriminations: what illness anxiety is not

Four boundaries carry the marks. Illness anxiety sits between the somatic, anxious, obsessional and psychotic groups, and each seam is testable. Hold them as a table.

CONFUSED WITH	SHARED SURFACE	THE DISCRIMINATOR
Somatic symptom disorder	Health preoccupation, doctor-shopping	**In SSD there are prominent, distressing *somatic symptoms*; in illness anxiety somatic symptoms are absent or mild and the focus is the *fear of illness* (DSM-5-TR 2022)**
Generalised anxiety disorder	Worry about health	**GAD worry spans many domains (finances, family, work); illness anxiety worry is *specifically and persistently* about having a serious disease (New Oxford Textbook)**
Obsessive-compulsive disorder	Intrusive illness thoughts, checking	**OCD illness thoughts are usually experienced as intrusive and senseless with wider obsessional content; illness anxiety fear is a sustained, ego-syntonic disease conviction (Kaplan and Sadock 2024)**
Delusional disorder, somatic type	Fixed belief about having a disease	**Illness anxiety belief is *not* of delusional intensity and yields, at least briefly, to evidence; a truly unshakeable somatic delusion is delusional disorder (Kaplan and Sadock 2024)**

The four boundary calls for illness anxiety; the discriminator is the *somatic load, the breadth of worry, and the fixity of belief*, not the health theme itself (DSM-5-TR 2022; Kaplan and Sadock 2024).

TRAP **Do not upgrade illness anxiety to a somatic delusion.** The illness-anxiety belief is over-valued, not delusional; it softens with evidence even if it returns. A fixed, evidence-proof conviction of disease is delusional disorder (somatic type), a different diagnosis and a different treatment.

20.4 First-line treatment: the SSRI and CBT

An SSRI, at an adequate trial. The serotonin reuptake inhibitors are the first-line pharmacotherapy for health anxiety, consistent with its OCRD placement and serotonergic response (Kaplan and Sadock 2024). The pivotal evidence is Fallon and colleagues' placebo-controlled trial of fluoxetine (Fludac, Prodep) at **20 to 80 mg/day**: responders separated from placebo by around 8 weeks and the gain held to 24 weeks, so the trial must run long enough (about **12 weeks**) before it is judged a failure. As across the OCRD group, doses tend to the higher end, and any of the SSRIs, escitalopram (Nexito, Rexipra), sertraline (Daxid, Zosert), fluvoxamine (Fluvoxin) or fluoxetine, is reasonable; deep dosing lives in the Mood disorders: pharmacotherapy notes. Reassurance, though part of every intervention, is not a treatment on its own and, given repeatedly, feeds the checking loop.

CBT is the prototype psychotherapy. Cognitive behavioural therapy is the first-line, best-evidenced psychological treatment for health anxiety; controlled trials, including Barsky and

Ahern's brief six-session individual CBT, show durable falls in hypochondriacal beliefs and health anxiety at one-year follow-up (Kaplan and Sadock 2024). CBT targets the misinterpretation of benign bodily sensations, the catastrophic disease beliefs, and the safety behaviours (body-checking, reassurance-seeking, symptom-Googling) that maintain the fear, exactly the exposure-and-response-prevention logic of the wider OCRD group; the general CBT model lives in the Psychotherapies, clinical assessment, MSE and nosology notes.

GOOD TO REMEMBER

- **SSRI (in health anxiety):** first-line drug, serotonergic response mirroring the OCRD group; Fallon's RCT used fluoxetine at **20 to 80 mg/day** with response by ~8 weeks, so give an adequate (~**12-week**) trial before calling it a failure (Kaplan and Sadock 2024).
- **CBT (in health anxiety):** first-line, best-evidenced psychotherapy; targets misinterpretation of bodily sensations and the reassurance-seeking / checking safety behaviours, with durable one-year gains (Barsky and Ahern; Kaplan and Sadock 2024).

6 months	20 to 80	~20%	6B23
MINIMUM DURATION FOR ILLNESS ANXIETY DISORDER	FLUOXETINE TRIAL DOSE IN HEALTH ANXIETY (MG/DAY)	OF FORMER HYPOCHONDRIASIS BECOMES ILLNESS ANXIETY (REST = SSD)	ICD-11 CODE, INSIDE THE OCRD GROUPING

INDIA

Health anxiety is common in Indian general practice yet reaches psychiatry late, part of the wider anxiety and OCD treatment gap, and it is a prime setting for the country's benzodiazepine over-prescription problem: a worried, somatising patient is handed alprazolam or clonazepam for the anxiety rather than started on the SSRI and CBT that actually treat the disorder. The Indian Psychiatric Society clinical practice guidelines keep an SSRI (with CBT) as first-line for the anxiety and obsessive-compulsive disorders and reserve benzodiazepines for short-term crisis use only; the anxiolytic dependence story is in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes. The SSRIs are widely and cheaply available under Indian brands, escitalopram as Nexito or Rexipra, fluoxetine as Fludac or Prodep, sertraline as Daxid or Zosert, so cost is rarely the barrier; recognition is.

PEARL

Read illness anxiety as OCD wearing a stethoscope: the intrusive thought is *"I have a serious disease"*, the compulsions are body-checking, symptom-Googling and reassurance-seeking, and the relief is momentary before the doubt returns. That framing tells you why ICD-11 put it in the OCRD grouping and why the treatment is the OCRD treatment, an SSRI at an adequate dose plus CBT with response prevention, not endless investigation and not a benzodiazepine.

HOLD THIS

Illness anxiety (hypochondriasis) is a somatic-symptom disorder in DSM-5-TR but an obsessive-compulsive related disorder (6B23) in ICD-11; first-line treatment is an SSRI plus CBT, never a benzodiazepine.

Trauma and stressor-related disorders

21 · PTSD: clinical features and criteria

Post-traumatic stress disorder is the disorder in which a terrifying event does not become a memory. In health, a horrific experience is filed away as something that happened *there* and *then*; in **ptsd** it is relived *here* and *now*, forcing itself back into the present through intrusive images, flashbacks and nightmares, so that the person is driven to avoid every reminder and lives permanently braced for the next catastrophe. Examiners test this on a tight lattice of exact points, the definition of the qualifying trauma, the symptom clusters (four in DSM-5, three in ICD-11), the greater-than-one-month duration, the delayed-onset and dissociative subtypes, the epidemiology, and the **pcl-5** with its provisional cut-off, and the classic trap is to accept a personality-disorder label, or a benzodiazepine, where the answer is trauma.

Why it matters clinically. Trauma exposure is near-universal but **ptsd** follows in only a minority, which makes the diagnosis about a *specific* post-exposure syndrome rather than distress alone. Two facts anchor every answer. First, the phenomenological signature is re-experiencing *in the present* plus a persistent sense of current threat, which separates true **post-traumatic stress disorder** from ordinary painful recollection. Second, the two classifications no longer align neatly, so a full answer must hold both the DSM-5 four-cluster and the **icd-11 ptsd** three-cluster architecture side by side, and know that a patient can meet one and miss the other. The amygdala and fear-circuit anatomy on which the alarm is built is developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes, and the treatment (trauma-focused psychotherapy first, then the SSRIs/SNRI, prazosin for nightmares, no benzodiazepine) sits in a separate management note; it is not re-derived here.

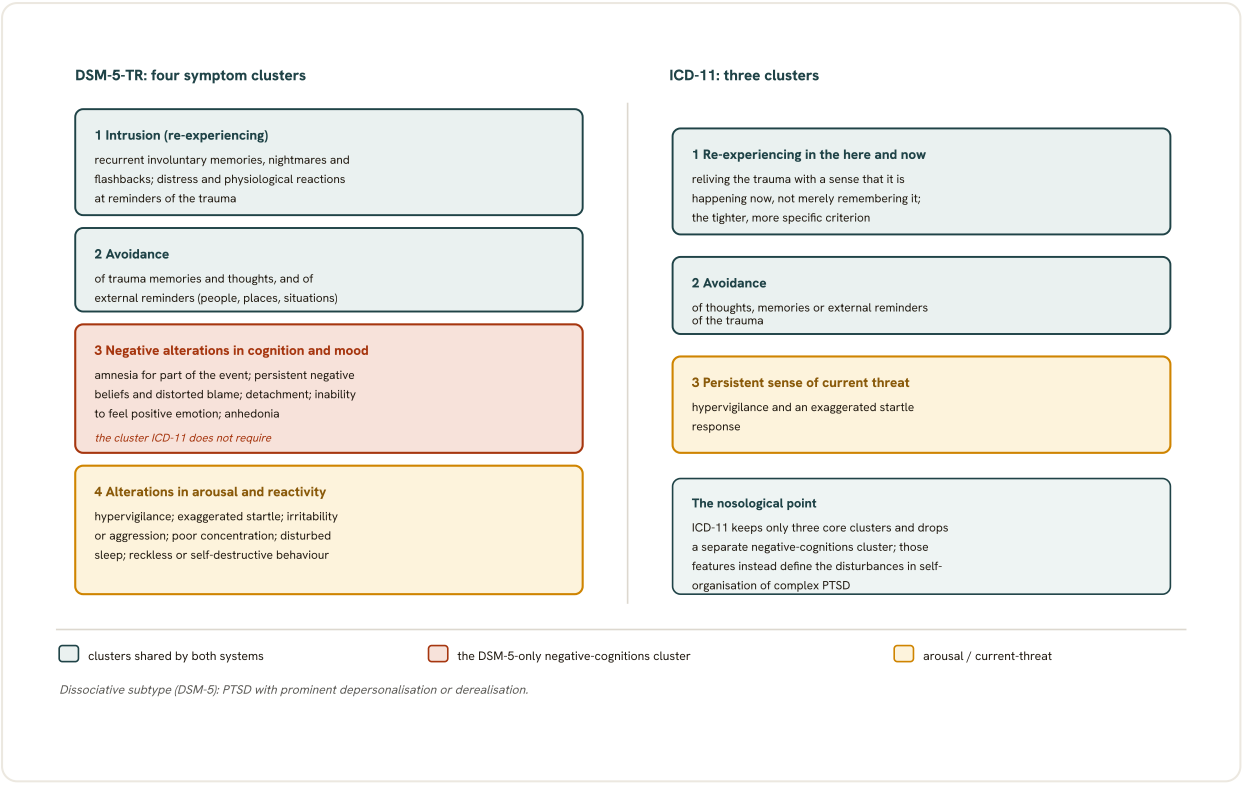


Fig 14.14 The PTSD symptom clusters, DSM-5-TR against ICD-11. DSM-5-TR requires all four clusters: intrusion, avoidance, negative alterations in cognition and mood, and alterations in arousal and reactivity. ICD-11 keeps a tighter three: re-experiencing in the here and now (a sense that the trauma is happening now, not just being remembered), avoidance, and a persistent sense of current threat; it deliberately drops the separate negative-cognitions cluster, whose features instead define the disturbances in self-organisation of complex PTSD. DSM-5 also recognises a dissociative subtype with prominent depersonalisation or derealisation.

PCL-5

Instructions: Below is a list of problems that people sometimes have in response to a very stressful experience. Keeping your worst event in mind, please read each problem carefully and then select one of the numbers to the right to indicate how much you have been bothered by that problem in the past month.

Your worst event: _____

In the past month, how much were you bothered by:	Not at all	A little bit	Moderately	Quite a bit	Extremely
1. Repeated, disturbing, and unwanted memories of the stressful experience?	0 ○	1 ○	2 ○	3 ○	4 ○
2. Repeated, disturbing dreams of the stressful experience?	0 ○	1 ○	2 ○	3 ○	4 ○
3. Suddenly feeling or acting as if the stressful experience were actually happening again (as if you were actually back there reliving it)?	0 ○	1 ○	2 ○	3 ○	4 ○
4. Feeling very upset when something reminded you of the stressful experience?	0 ○	1 ○	2 ○	3 ○	4 ○
5. Having strong physical reactions when something reminded you of the stressful experience (for example, heart pounding, trouble breathing, sweating)?	0 ○	1 ○	2 ○	3 ○	4 ○
6. Avoiding memories, thoughts, or feelings related to the stressful experience?	0 ○	1 ○	2 ○	3 ○	4 ○
7. Avoiding external reminders of the stressful experience (for example, people, places, conversations, activities, objects, or situations)?	0 ○	1 ○	2 ○	3 ○	4 ○
8. Trouble remembering important parts of the stressful experience?	0 ○	1 ○	2 ○	3 ○	4 ○
9. Having strong negative beliefs about yourself, other people, or the world (for example, having thoughts such as: I am bad, there is something seriously wrong with me, no one can be trusted, the world is completely dangerous)?	0 ○	1 ○	2 ○	3 ○	4 ○
10. Blaming yourself or someone else for the stressful experience or what happened after it?	0 ○	1 ○	2 ○	3 ○	4 ○
11. Having strong negative feelings such as fear, horror, anger, guilt, or shame?	0 ○	1 ○	2 ○	3 ○	4 ○
12. Loss of interest in activities that you used to enjoy?	0 ○	1 ○	2 ○	3 ○	4 ○
13. Feeling distant or cut off from other people?	0 ○	1 ○	2 ○	3 ○	4 ○
14. Trouble experiencing positive feelings (for example, being unable to feel happiness or have loving feelings for people close to you)?	0 ○	1 ○	2 ○	3 ○	4 ○
15. Irritable behavior, angry outbursts, or acting aggressively?	0 ○	1 ○	2 ○	3 ○	4 ○
16. Taking too many risks or doing things that could cause you harm?	0 ○	1 ○	2 ○	3 ○	4 ○
17. Being "superalert" or watchful or on guard?	0 ○	1 ○	2 ○	3 ○	4 ○
18. Feeling jumpy or easily startled?	0 ○	1 ○	2 ○	3 ○	4 ○
19. Having difficulty concentrating?	0 ○	1 ○	2 ○	3 ○	4 ○
20. Trouble falling or staying asleep?	0 ○	1 ○	2 ○	3 ○	4 ○

PCL-5 (18 August 2023) National Center for PTSD Page 3 of 3

The PCL-5: 20 self-report items mapped to the four DSM-5 clusters, each rated 0 to 4 over the past month (total 0 to 80); a provisional cut-off of about 31 to 33 suggests probable PTSD, but the National Center for PTSD states the cut-off as provisional and under review, so it is used to flag, not to diagnose.

PCL-5 (Weathers et al.); US National Center for PTSD, in the public domain (a work of the United States federal government).

Fig 14.15 The PTSD Checklist for DSM-5 (PCL-5). The standard self-report measure for PTSD symptom severity and monitoring: twenty items, one per DSM-5 symptom, each rated 0 (not at all) to 4 (extremely) over the past month, for a total of 0 to 80. A provisional cut-off of about 31 to 33 flags probable PTSD, but the National Center for PTSD holds the cut-off as provisional, so the score screens and tracks rather than diagnoses. Shown as the actual public-domain Veterans Affairs form.

21.1 The traumatic-stressor criterion: what counts as Criterion A

The gateway. PTSD is one of the few diagnoses that requires a specified *cause*. DSM-5-TR Criterion A demands exposure to actual or threatened death, serious injury or sexual violence in one of four ways: *directly experiencing* the event; *witnessing* it in person as it happened to others; *learning* that it happened to a close family member or friend (where the event was violent or accidental); or *repeated or extreme exposure to aversive details* of traumatic events, as in first responders or those handling human remains (DSM-5-TR 2022; Kaplan & Sadock CTP 2024). The fourth route does *not* apply to exposure through electronic media, television, films or pictures unless that exposure is work-related.

How the systems frame it. ICD-11 requires exposure to an event or situation of an *extremely threatening or horrific* nature, listing disasters, combat, serious accidents, torture, sexual violence, terrorism, assault or acute life-threatening illness, and includes witnessing the sudden violent injury or death of others and learning of the sudden violent death of a loved one (ICD-11 CDDR). A historically examinable point: DSM-5 *removed* the old DSM-IV Criterion A2 requirement that the person felt intense fear, helplessness or horror at the time, because many who later develop full PTSD (combat personnel, first responders) show muted emotion at the moment of trauma (Kaplan & Sadock CTP 2024).

WORKED EXAMPLE

A 34-year-old woman survives a bus accident in which two fellow passengers die. Over the following weeks she is ambushed by vivid images of the crushed vehicle that arrive unbidden and feel as if it is happening again; she cannot take a bus, detours around the accident road, sleeps two hours a night, startles violently at horns, and believes the world is now lethally dangerous and that she should have saved the others. This is Criterion A (directly experiencing a life-threatening accident) followed by re-experiencing, avoidance, negative cognitions and hyperarousal persisting beyond a month: post-traumatic stress disorder, not an understandable transient reaction.

21.2 The DSM-5 four symptom clusters (B, C, D, E)

Four groups, minimum counts. DSM-5-TR parses PTSD into four symptom clusters, each with a required minimum, all beginning or worsening after the trauma (DSM-5-TR 2022; Kaplan & Sadock CTP 2024). **Cluster B, intrusion** (one or more of five): intrusive distressing memories, traumatic nightmares, dissociative flashbacks, intense distress at reminders, and marked physiological reactivity to reminders. **Cluster C, avoidance** (one or more of two): avoidance of trauma-related thoughts or feelings, and avoidance of external reminders (people, places, activities). **Cluster D, negative alterations in cognitions and mood** (two or more of seven): dissociative amnesia for the event, persistent negative beliefs about self or the world, distorted blame, persistent negative emotional state, markedly diminished interest, detachment or estrangement, and an inability to feel positive emotions. **Cluster E, alterations in arousal and reactivity** (two or more of six): irritability or aggression, reckless or self-destructive behaviour, hypervigilance, exaggerated startle, concentration problems, and sleep disturbance.

The threshold criteria. On top of the four clusters, the full picture must last *more than one month* (Criterion F), cause clinically significant distress or functional impairment (Criterion G), and not be attributable to a substance or another medical condition (Criterion H) (DSM-5-TR 2022). The negative-cognitions cluster (D) is the one that was *new* in DSM-5, absent from DSM-IV, and it widens PTSD from a fear-based reaction into a disorder of altered worldview, mood and self-belief.

MNEMONIC

TRAUMA → IANA (1·1·2·2)

The four DSM-5 clusters and their minimum counts, in order B-C-D-E. **I**ntrusion / re-experiencing (need **1** of 5), **A**voidance (need **1** of 2), **N**egative alterations in cognitions and mood (need **2** of 7), **A**rousal and reactivity (need **2** of 6). Then the three threshold gates: over one month, distress/impairment, not substance or medical.

21.3 Cluster B in depth: re-experiencing in the here and now

The pathognomonic feature. What makes an intrusion a PTSD symptom rather than an ordinary bad memory is that it is lived **re-experiencing** in the present, not retrospective recall. The intrusive memory carries the emotional and physiological charge of the original event and is experienced as recurring and current, even while the person knows intellectually that the trauma is in the past (Kaplan & Sadock CTP 2024). At the extreme, a *dissociative flashback* (Criterion B3) transports the person back so completely that they lose awareness of present surroundings. Nightmares thematically related to the trauma and marked distress or bodily reactivity on encountering reminders complete the cluster.

Not sufficient. The reciprocal point, which discriminates PTSD from rumination and grief, is that merely reflecting on, ruminating about, or remembering the feelings of the event is *not* enough to meet the re-experiencing requirement; the event must be experienced as occurring again in the here and now (ICD-11 CDDR). This is the exact line that separates PTSD re-experiencing from the preoccupied recollection of prolonged grief disorder.

RULE **Present-tense, not past-tense.** The single discriminating feature of PTSD is that the trauma is re-experienced in the here and now (intrusive images, flashbacks, nightmares that feel current), not simply remembered as belonging to the past; ordinary distressing recall or rumination does not meet the re-experiencing criterion.

21.4 Clusters C, D and E: avoidance, negative cognitions, hyperarousal

Avoidance. Because the re-experiencing is so intolerable, the person makes effortful attempts to avoid its triggers, both external (people, places, conversations, activities) and internal (thoughts, feelings, bodily sensations tied to the event). This **avoidance** tends to *generalise* over time, new objects and situations progressively drawn into the avoided set, which can confine severely affected patients to a shrinking, no-surprises world (Kaplan & Sadock CTP 2024).

Negative cognitions. The Cluster D **negative cognitions** and mood run beyond the event itself into fixed, permanent-feeling beliefs, the world is *always* dangerous, other people are untrustworthy, the self is irreversibly damaged or to blame, alongside anhedonia, detachment, a persistent negative emotional state and, in some, dissociative amnesia for part of the event. These overlap with depression and mark how far PTSD reshapes the whole disposition, not just the trauma response.

Hyperarousal. Cluster E, the alterations in arousal and reactivity, is the state of a threat-detection system stuck on: **hyperarousal** with hypervigilance (unrelenting scanning for danger),

exaggerated startle, irritability and angry outbursts, poor concentration, sleep disturbance, and reckless or self-destructive behaviour (DSM-5-TR 2022; Kaplan & Sadock CTP 2024). The irritability and aggression are frequently aimed at family and close relationships, deepening the person's isolation.

PEARL

The four clusters have an inner logic worth stating in a viva. The trauma stays intolerably alive (*intrusion*); because it is intolerable it is walled off (*avoidance*); the effort to make sense of it corrodes belief about self, others and the world (*negative cognitions*); and a system that failed to keep the person safe once now never stands down (*hyperarousal*). Naming that chain shows you understand PTSD as a coherent post-exposure trap, not a checklist.

21.5 The ICD-11 three-cluster model and the DSM-5 divergence

ICD-11 6B40. Icd-11 ptsd deliberately narrows the picture to three core elements, all developing after the trauma and lasting *at least several weeks* (ICD-11 CDDR). First, *re-experiencing* the traumatic event in the present (vivid intrusive memories, flashbacks or nightmares experienced as occurring again in the here and now). Second, *deliberate avoidance* of reminders, whether internal (thoughts, memories) or external (people, situations). Third, *persistent perceptions of heightened current threat*, indicated for example by hypervigilance or an enhanced startle reaction. Function must be significantly impaired, or maintained only through significant extra effort.

Why the divergence is examinable. ICD-11 collapses DSM-5's negative-cognitions cluster and much of avoidance out of the core criteria, keeping only three tighter **symptom clusters**, and reserves the wider disturbances of affect regulation, self-concept and relationships for the separate diagnosis of complex PTSD. The consequence, repeatedly demonstrated in military and international samples, is that many people who meet DSM-5 PTSD do *not* meet ICD-11 PTSD and vice versa (Kaplan & Sadock CTP 2024). Neither system should therefore be used to exclude a distressed, impaired trauma survivor from care.

FEATURE	DSM-5-TR (309.81 / F43.10)	ICD-11 (6B40)
Number of clusters	**Four (B intrusion, C avoidance, D negative cognitions/mood, E arousal)**	**Three (re-experiencing in the present, avoidance, persistent sense of current threat)**
Re-experiencing	Intrusive memories, nightmares, flashbacks, cued distress, cued physiological reactivity (need 1 of 5)	Re-experienced in the here and now (not mere recall); required core element
Avoidance	Internal and/or external reminders (need 1 of 2)	Deliberate avoidance of reminders; required core element
Negative cognitions and mood	Separate required cluster D (need 2 of 7)	Not a core criterion; features moved to complex PTSD

FEATURE	DSM-5-TR (309.81 / F43.10)	ICD-11 (6B40)
Arousal / current threat	Cluster E arousal and reactivity (need 2 of 6)	Expressed as persistent perceptions of heightened current threat (e.g. hypervigilance, startle)
Duration threshold	More than 1 month	At least several weeks
Complex presentations	Handled within PTSD plus dissociative subtype	Separate diagnosis: complex PTSD (6B41)

The DSM-5-TR four-cluster and ICD-11 three-cluster architectures of PTSD side by side; the key divergence is that ICD-11 drops the negative-cognitions cluster from the core and spins complex reactions into complex PTSD, so a patient can meet one system and not the other (criteria verified against DSM-5-TR 2022 and the ICD-11 CDDR).

GOOD TO REMEMBER

- **Post-traumatic stress disorder (the syndrome):** the defining criterion is a qualifying trauma (Criterion A, actual or threatened death, serious injury or sexual violence, experienced, witnessed, learned of, or through repeated occupational exposure) followed by a characteristic syndrome lasting *more than one month* (DSM-5) or *at least several weeks* (ICD-11); the discriminator from ordinary distress is re-experiencing *in the here and now* plus a persistent sense of current threat, and the first step is to confirm the stressor and then map the clusters (DSM-5 four: intrusion, avoidance, negative cognitions, arousal; ICD-11 three: re-experiencing, avoidance, current threat).

21.6 The dissociative subtype and delayed-onset (delayed expression)

Dissociative subtype. DSM-5 recognises a **dissociative subtype** of PTSD: full PTSD criteria are met and, in addition, there are persistent or recurrent symptoms of *depersonalisation* (feeling detached from, or an outside observer of, one's own mind or body) or *derealisation* (a sense that surroundings are unreal, dreamlike or distorted) (DSM-5-TR 2022; Kaplan & Sadock CTP 2024). It marks a subgroup who respond to reminders not with hyperarousal but with dissociation, characterised biologically by *over*modulation of the amygdala; the World Mental Health Surveys estimated it at about **14.4%** of those with PTSD.

Delayed expression. The *with delayed expression* specifier applies when the full diagnostic criteria are not met until *at least 6 months* after the event, even though some symptoms may have appeared immediately (DSM-5-TR 2022). The examinable subtlety is that genuine delayed *onset* from a truly asymptomatic state is rare; most apparent delayed-onset cases are worsening of pre-existing subsyndromal symptoms or delayed help-seeking, often re-triggered by a reminder or new stressor (Kaplan & Sadock CTP 2024).

GOOD TO REMEMBER

- **Dissociative subtype:** full PTSD *plus* persistent depersonalisation or derealisation; the signature caution is that these patients dissociate rather than hyperarouse to reminders (amygdala overmodulation), and it accounts for about 14.4% of PTSD.
- **Delayed expression specifier:** full criteria first met at least 6 months after the trauma; true asymptomatic delayed onset is rare, so look for pre-existing subsyndromal symptoms rekindled by a reminder or fresh stressor.

21.7 Epidemiology and course

Common trauma, selective disorder. Lifetime trauma exposure is near-universal (roughly 50 to 89% in United States samples; about 70% in a 69,000-adult worldwide study), yet only a minority exposed develop PTSD (Kaplan & Sadock CTP 2024). The National Comorbidity Survey Replication put the *lifetime* prevalence of PTSD in United States adults at **6.8%** and past-year prevalence at 3.5%. The disorder is roughly twice to three times as common in women (lifetime 9.7% in women versus 3.6% in men), partly reflecting the very high conditional risk after sexual assault.

Course. Conditional risk after trauma varies sharply by trauma type (highest after sexual assault, lower after accidents). Symptoms in most trauma-exposed people wane over the first months; nearly half of those who develop PTSD recover within 3 months, but roughly a third run a *chronic* course persisting for months to years, with survivors of interpersonal violence taking longest to remit (DSM-5-TR 2022; ICD-11 CDDR; Kaplan & Sadock CTP 2024). Symptom severity can fluctuate, patients crossing in and out of formal diagnostic threshold in the early years.

21.8 The PCL-5: what it is and its verified provisional cut-off

What it is. The **pcl-5** (the PTSD Checklist for DSM-5, Weathers et al. 2013) is a 20-item self-report questionnaire, one item for each of the 20 DSM-5 PTSD symptoms, each rated 0 to 4 over the past month and summed to a total score of **0 to 80** (Kaplan & Sadock CTP 2024). It takes about 5 to 10 minutes, is free from the United States National Center for PTSD, and its items are ordered by DSM-5 cluster (items 1 to 5 = Cluster B, 6 to 7 = Cluster C, and so on), so it can also support a provisional cluster-based diagnosis by counting endorsed symptoms per domain.

The cut-off to memorise. The PCL-5 is a screen and severity monitor, *not* a diagnosis (the CAPS-5 or SCID structured interview remains the gold standard). A total-score cut of **31 to 33** has been suggested as indicative of *probable* PTSD, with the CAPS-5 or SCID structured interview remaining the diagnostic gold standard (Kaplan & Sadock CTP 2024). Refer to the accompanying scale plate for the reproduced instrument; the number to carry is the provisional cut-off of 31 to 33 on a 0 to 80 range, and the concept map of the clusters is set out in the figure alongside.

TRAP **Treating a PCL-5 score as a diagnosis.** A PCL-5 of 33 or more is *probable* PTSD and a prompt to assess, not a diagnosis; the diagnosis needs a clinical interview confirming Criterion A and the cluster pattern. Equally, do not miss complex PTSD hiding behind a borderline personality-disorder label, chronic interpersonal trauma with affect dysregulation, disturbed self-concept and relational difficulty on top of the core PTSD triad is complex PTSD (ICD-11 6B41), and mislabelling it forfeits trauma-focused treatment.

31 to 33	0 to 80	1 month	6.8%
PCL-5 PROVISIONAL CUT-OFF FOR PROBABLE PTSD	PCL-5 TOTAL RANGE (20 ITEMS, EACH 0 TO 4)	DSM-5 MINIMUM DURATION (OVER ONE MONTH)	LIFETIME PTSD PREVALENCE (NCS-R, DSM-IV)

21.9 The India device: the treatment gap, benzodiazepines, and the IPS line

Where PTSD lands in Indian practice. India carries a very wide anxiety/OCD/PTSD treatment gap: trauma is common (road-traffic and industrial accidents, interpersonal and domestic violence, disasters), but PTSD is under-recognised, frequently somatised, and reaches formal care late, with most sufferers never seeing a mental-health professional (echoing the international finding that over half of people with PTSD do not seek treatment). Into that gap has flowed the benzodiazepine over-prescription problem: distress after trauma is met with a long-term benzodiazepine (typically alprazolam), which touches none of the core clusters and is explicitly *not* a PTSD treatment. The Indian Psychiatric Society CPGs and every major guideline put trauma-focused psychotherapy first, then an SSRI or the SNRI venlafaxine, with prazosin (Minipress, Prazopress) for trauma nightmares and propranolol (Ciplar, Inderal) in the peri-trauma setting; the benzodiazepine has no role. Indian brands of the anchor drugs are named where they arise, escitalopram as Nexito or Rexipra, clomipramine as Anafranil, in the accompanying management note.

INDIA

The single highest-yield Indian point is that a benzodiazepine is the wrong answer for PTSD twice over: it is not a treatment for any PTSD cluster, and early post-trauma benzodiazepine use may actually *increase* the risk of developing PTSD (CANMAT 2014). Against India's wide trauma treatment gap and its benzodiazepine over-prescription problem, the IPS-aligned answer is trauma-focused psychotherapy first, then paroxetine, sertraline or venlafaxine, with prazosin (Minipress, Prazopress) reserved for nightmares, never alprazolam as maintenance.

HOLD THIS

PTSD needs a Criterion-A trauma followed, for more than one month (DSM-5) or at least several weeks (ICD-11), by the cluster pattern: DSM-5 has FOUR clusters (intrusion 1/5, avoidance 1/2, negative cognitions and mood 2/7, arousal and reactivity 2/6) while ICD-11 has THREE (re-experiencing in the here and now, deliberate avoidance, a persistent sense of current threat); the pathognomonic feature is re-experiencing *in the present* not mere recall; specifiers are the dissociative subtype (depersonalisation/derealisation, ~14.4%) and delayed expression (full criteria first met at least 6 months on); lifetime prevalence is 6.8% (women ~2 to 3x men); and the PCL-5 is a 20-item, 0 to 80 self-report screen with a probable-PTSD provisional cut of 31 to 33, never a substitute for the CAPS-5/SCID interview.

22 · The evidence-based treatment of PTSD

The **evidence-based treatment of ptsd** is one of the cleanest algorithms in the anxiety and trauma syllabus, and examiners reward the candidate who states its two hard rules in the first sentence: *trauma-focused psychotherapy is first-line, and a benzodiazepine is never used*. Everything else, the choice of SSRI, the role of venlafaxine, prazosin for nightmares, antipsychotic augmentation for the refractory case, hangs off that spine. This is a management topic, so the marks are in the lines of treatment, the licensed agents, the doses, the monitoring and the sequence, not in re-describing the clusters (those sit in the separate PTSD clinical-features note).

Why it matters clinically. Every major guideline converges: BAP (BAP 2014), NICE (NICE 2018), CANMAT (CANMAT 2014), the WFSBP (WFSBP 2022) and the United States VA/DoD (VA/DoD 2023) all place a manualised **trauma-focused psychotherapy** ahead of any drug, and reserve pharmacotherapy for the patient who declines, cannot access, or does not respond to that psychotherapy. The **first-line ptsd** drugs are a tight list, sertraline and paroxetine (both licensed for PTSD), and venlafaxine, with **prazosin** added specifically for trauma-related nightmares. The deep antidepressant pharmacology of these agents, their doses, adverse effects and interactions, is developed in the Mood disorders: pharmacotherapy notes, and the general exposure/CBT model in the Psychotherapies, clinical assessment, MSE and nosology notes; this note assembles them into the PTSD algorithm and keeps to what the guidelines actually say.

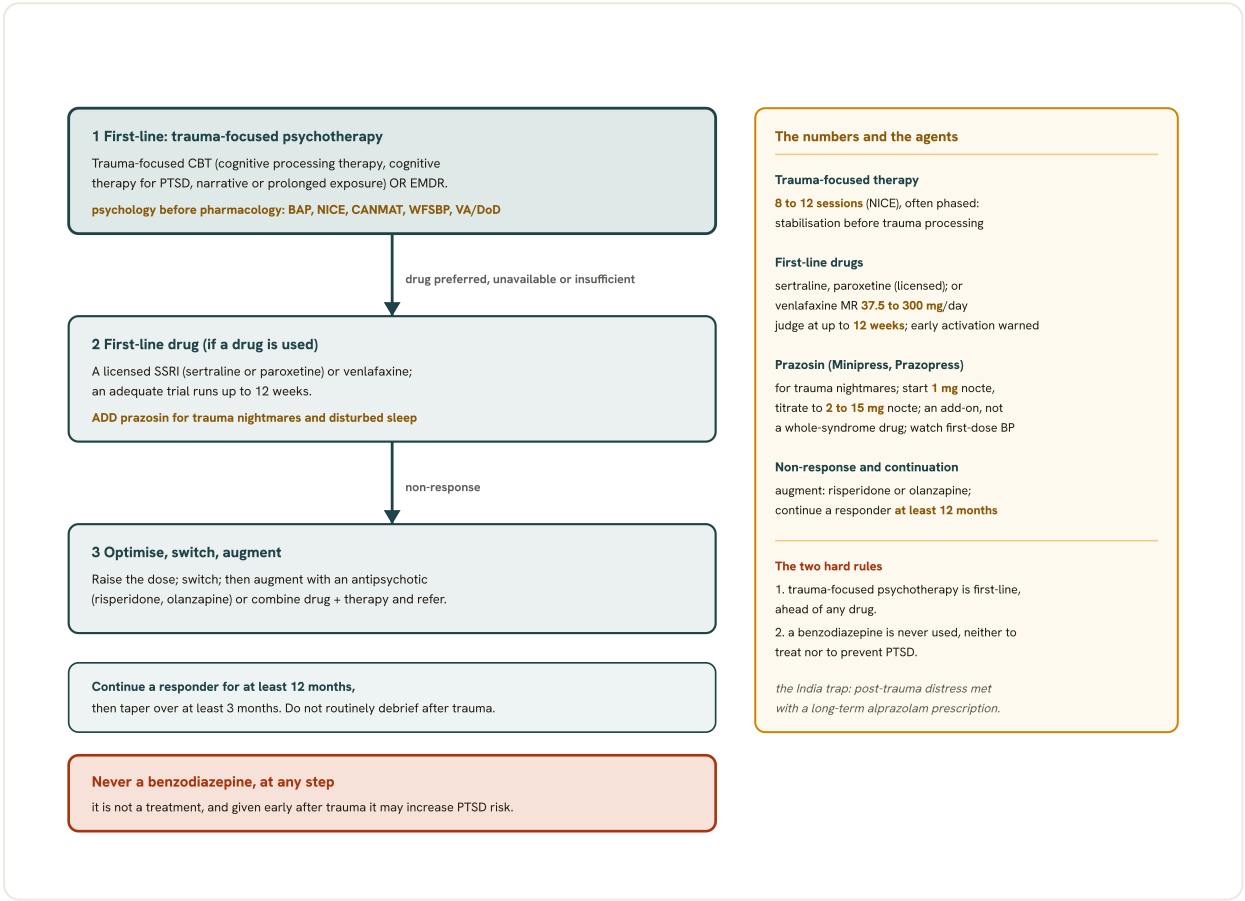


Fig 14.16 The PTSD treatment algorithm. Its two hard rules open every answer: trauma-focused psychotherapy is first-line, and a benzodiazepine is never used. First-line is a manualised trauma-focused therapy, trauma-focused CBT or EMDR over 8 to 12 sessions, placed ahead of any drug by BAP, NICE, CANMAT, WFSBP and VA/DoD. Where a drug is used because the patient prefers it or therapy is unavailable or insufficient, the first-line agents are a licensed SSRI (sertraline or paroxetine) or venlafaxine (37.5 to 300 mg modified release), trialled up to 12 weeks, with prazosin (Minipress or Prazopress) added at 1 mg nocte and titrated to 2 to 15 mg for trauma nightmares. The non-responder has the dose raised, then a switch, then antipsychotic augmentation (risperidone, olanzapine) or a drug-plus-therapy combination with referral, and a responder continues for at least twelve months. The benzodiazepine is excluded throughout, a rule that collides directly with the Indian habit of meeting post-trauma distress with long-term alprazolam.

22.1 The governing principle: trauma-focused psychotherapy is first-line

Psychology before pharmacology. The single most examinable statement in PTSD management is that a trauma-focused psychological therapy, not a drug, is the first-line treatment. BAP instructs the clinician to "choose an evidence-based acute psychological treatment for chronic

PTSD: trauma-focused individual CBT or EMDR" (strength A) (BAP 2014). NICE goes further and makes it a *strong* recommendation to offer individual **trauma-focused cbt** or **emdr** in preference to drug treatment (NICE 2018), and the VA/DoD guideline states the point most explicitly of all: "recommend specific manualized trauma-focused psychotherapies over pharmacotherapy as first-line treatment for PTSD" (strong recommendation) (VA/DoD 2023). Drug treatment is offered where psychotherapy is declined, unavailable, or insufficient, not as an equal first option.

What "trauma-focused" means. The therapies that carry this recommendation are the ones that process the traumatic memory directly, cognitive processing therapy, cognitive therapy for PTSD, narrative exposure therapy and prolonged exposure therapy (the **tf-cbt** family), and eye movement desensitisation and reprocessing (**emdr**) (NICE 2018; VA/DoD 2023). Generic supportive counselling or non-trauma-focused CBT does not qualify. The WFSBP names CBT as "the psychotherapy with the best evidence for PTSD" (WFSBP 2022), and WHO mhGAP, the guideline that matters most for low-resource Indian settings, likewise puts individual or group trauma-focused CBT or EMDR first for adults and for children and adolescents (WHO mhGAP 2023).

RULE **Trauma-focused therapy first.** In PTSD the first-line treatment is a manualised trauma-focused psychotherapy, trauma-focused CBT (cognitive processing therapy, cognitive therapy for PTSD, narrative exposure, prolonged exposure) or EMDR; pharmacotherapy is second, offered only when psychotherapy is declined, unavailable or insufficient.

GOOD TO REMEMBER

- **Trauma-focused CBT / TF-CBT (the psychotherapy):** the mechanism is deliberate processing of the traumatic memory (cognitive processing, cognitive therapy for PTSD, narrative exposure, prolonged exposure) so the event is refiled as past rather than relived as present; it is FIRST-LINE for PTSD (offered before drugs), typically delivered over 8 to 12 sessions, more where there are multiple traumas, comorbid depression or dissociation (NICE 2018).
- **EMDR / eye movement desensitisation and reprocessing (the psychotherapy):** structured recall of the trauma paired with bilateral (eye-movement) stimulation to reprocess the memory; it is a first-line trauma-focused therapy alongside TF-CBT, and NICE offers it for PTSD presenting more than three months after a non-combat trauma over 8 to 12 sessions (NICE 2018; CANMAT 2014).

22.2 When to reach for drugs, and the two licensed SSRIs

The indication for pharmacotherapy. A drug is offered when the patient has a preference for medication over therapy, when a trauma-focused psychotherapy is not available or not acceptable, or when psychotherapy alone has been insufficient (NICE 2018; BAP 2014). NICE frames it precisely: "consider venlafaxine or an SSRI such as sertraline for adults with a diagnosis of PTSD if the person has a preference for drug treatment" (NICE 2018). Note the strength, this is a *weak* ("consider") recommendation, whereas the trauma-focused therapy is a *strong* ("offer") one.

The ssri ptsd answer. Of the SSRIs, two are licensed specifically for PTSD and are the drugs to name: sertraline and paroxetine. BAP identifies "paroxetine, sertraline or venlafaxine" as the first-

line pharmacological choice for chronic PTSD (strength A) (BAP 2014); CANMAT lists fluoxetine, paroxetine, sertraline and venlafaxine XR as first-line pharmacotherapy for core PTSD symptoms (CANMAT 2014); and VA/DoD, when a drug is used, offers "paroxetine, sertraline or venlafaxine" (strong) (VA/DoD 2023). The Maudsley concurs, an SSRI (paroxetine, sertraline or fluoxetine preferred) up to the maximum licensed dose is first-line drug treatment, and it repeats the rider that psychological approaches should be used before drugs (Maudsley 2021). The generic is primary in the note; the shared antidepressant brand list (fluoxetine, sertraline, fluvoxamine, paroxetine, escitalopram) is developed in the Mood disorders: pharmacotherapy notes.

WORKED EXAMPLE

A 40-year-old lorry driver, six months after a fatal highway collision, has nightly nightmares, cannot drive past the accident stretch and is hypervigilant and irritable. He declines "talking therapy" and asks for tablets. The evidence-based response is not a benzodiazepine and not reassurance. It is to explain that a trauma-focused psychotherapy would be the first choice, but that since he prefers medication, sertraline (starting low, titrating to the maximum tolerated licensed dose over several weeks) or paroxetine is appropriate; because trauma nightmares are prominent, prazosin can be added at night; and he is warned that a therapeutic effect may take up to 12 weeks to assess.

22.3 Venlafaxine: the SNRI first-line alternative

Equal footing with the SSRIs. The SNRI venlafaxine sits alongside the two licensed SSRIs as a first-line pharmacological option. BAP names it in the same breath as paroxetine and sertraline, noting that on meta-analysis "only paroxetine, sertraline and venlafaxine were superior to placebo" (strength A) (BAP 2014); the WFSBP recommends "SSRIs or the SNRI venlafaxine as first-line pharmacological treatment for PTSD" (WFSBP 2022); and NICE lists venlafaxine as the drug alternative to an SSRI (NICE 2018). On non-response to an SSRI, BAP's first step is to raise the dose (venlafaxine has post-hoc efficacy across trauma types), and only then to switch to another evidence-based treatment (BAP 2014).

The dose to carry. The Maudsley gives venlafaxine modified release **37.5 to 300 mg** daily for PTSD, recommended by NICE (Maudsley 2021). As with all these agents, an adequate trial is needed before declaring failure, guidelines advise that up to **12 weeks** may be required to assess pharmacological efficacy in PTSD (BAP 2014).

GOOD TO REMEMBER

- **Sertraline / paroxetine (SSRI, PTSD):** the two SSRIs licensed for PTSD and the first-line drug answer once psychotherapy is set aside; mechanism is serotonin re-uptake inhibition, the signature caution is that a full trial takes up to 12 weeks and early SSRI activation can transiently worsen symptoms, and continuation after response is for at least 12 months (BAP 2014; NICE 2018).
- **Venlafaxine (SNRI, PTSD):** the first-line SNRI alternative to the SSRIs, dosed as modified release 37.5 to 300 mg/day; the mechanism is dual serotonin-noradrenaline re-uptake inhibition, the caution is dose-related blood-pressure rise so monitor BP at higher doses, and on SSRI non-response raising the dose or switching to venlafaxine is the BAP-endorsed next step (BAP 2014; Maudsley 2021).

22.4 Prazosin: the targeted add-on for trauma nightmares

What it treats and how. Prazosin (Minipress, also marketed in India as Prazopress and Minipress XL) is a selective alpha-1 adrenergic blocker used *specifically* for trauma-related nightmares and sleep disturbance in PTSD, not for the disorder as a whole. It reduces central noradrenergic tone, damping the sympathetic surge that drives nightmares and the hyperaroused sleep of PTSD. CANMAT states it plainly: "for PTSD-associated trauma nightmares and poor sleep quality, use prazosin" (CANMAT 2014), and BAP notes that "prazosin augmentation reduces nightmares and other PTSD symptoms" (strength A) (BAP 2014). It is an *add-on* to a first-line SSRI or SNRI (or to psychotherapy), targeting one symptom cluster.

The dose and the caution. The Maudsley dose is **2 to 15 mg nocte**: initiate at 1 mg at night and titrate the dose gradually to reduce the risk of first-dose hypotension (Maudsley 2021). Because it is an antihypertensive, blood pressure and dizziness must be monitored (BAP 2014). Lead the drug with the Indian brand: prazosin is *Minipress* (and Prazopress) in Indian practice.

TRAP **Prazosin is not a PTSD cure-all.** Prazosin treats trauma nightmares and disturbed sleep, one symptom domain, and is an add-on, not a first-line agent for the whole disorder; do not offer it as monotherapy for core PTSD in place of a trauma-focused psychotherapy or a licensed SSRI/SNRI, and always start at 1 mg nocte to avoid first-dose hypotension.

GOOD TO REMEMBER

- **Prazosin (Minipress / Prazopress, alpha-1 blocker):** the targeted add-on for PTSD trauma nightmares and sleep disturbance; mechanism is alpha-1 adrenergic blockade lowering central noradrenergic tone, the signature caution is first-dose hypotension so start at 1 mg nocte and titrate to 2 to 15 mg nocte, and it augments (never replaces) first-line psychotherapy or an SSRI/SNRI (CANMAT 2014; Maudsley 2021).

22.5 The hard rule: no benzodiazepine in PTSD

Not a treatment, and possibly harmful. The most heavily tested negative rule in the whole topic is that a benzodiazepine is *not* used for PTSD, neither as treatment nor as prophylaxis. The VA/DoD makes it a strong recommendation "against the use of benzodiazepines for the treatment of PTSD" (VA/DoD 2023). CANMAT is equally firm and adds the mechanism of harm: "do not use benzodiazepines early after trauma to prevent PTSD; early benzodiazepine use may *increase* PTSD risk" (CANMAT 2014). NICE states that no drug treatment, "including

benzodiazepines", should be offered to prevent PTSD (NICE 2018), and BAP's do-not-use list for PTSD includes alprazolam (with citalopram, tiagabine and divalproex), which were not efficacious in placebo-controlled trials (BAP 2014).

Why the error is so common. Benzodiazepines touch none of the PTSD symptom clusters, they do not process the traumatic memory, do not reduce re-experiencing or avoidance, and blunt the emotional engagement that trauma-focused therapy depends on. Their apparent early calming effect is what makes the trap seductive, and their risk of dependence in a chronically distressed, often substance-comorbid population makes the error costly.

INDIA

This rule collides directly with Indian prescribing reality. Against a very wide anxiety/OCD/PTSD treatment gap, post-trauma distress is routinely met with a long-term benzodiazepine (typically alprazolam), the benzodiazepine over-prescription problem in Indian practice in one line. The guideline-anchored, IPS-aligned answer is the opposite: trauma-focused psychotherapy first, then sertraline, paroxetine or venlafaxine, with prazosin (Minipress, Prazopress) for nightmares, and no benzodiazepine, which is not merely ineffective but may raise the risk of PTSD when given acutely after trauma (CANMAT 2014). WHO mhGAP, designed for exactly these low-resource settings, keeps trauma-focused CBT or EMDR first (WHO mhGAP 2023).

22.6 The guideline-by-guideline algorithm

Convergence across five guidelines. The value of holding the guidelines side by side is that their agreement is the exam answer. Leading with BAP and NICE: first-line is trauma-focused psychotherapy (TF-CBT or EMDR); first-line drug, where a drug is used, is a licensed SSRI (sertraline or paroxetine) or venlafaxine; prazosin is added for nightmares; and the benzodiazepine is excluded. CANMAT, the WFSBP and VA/DoD add nothing that contradicts this and reinforce every element. The table alongside sets out the primary recommendations verbatim in structure so the concordance is visible.

GUIDELINE (YEAR)	FIRST-LINE TREATMENT	FIRST-LINE DRUG (IF USED)	KEY ADD-ON / NOT-USED
BAP (2014)	Trauma-focused individual CBT or EMDR (strength A)	**Paroxetine, sertraline or venlafaxine (strength A)**	Prazosin for nightmares; do NOT use alprazolam, citalopram
NICE (2018)	Individual trauma-focused CBT or EMDR (strong "offer")	**Venlafaxine or an SSRI such as sertraline (weak "consider")**	Risperidone add-on if refractory; do NOT offer benzodiazepines, even to prevent PTSD
CANMAT (2014)	Individual trauma-focused CBT or EMDR (first-line)	**Fluoxetine, paroxetine, sertraline or venlafaxine XR (first-line)**	Prazosin for nightmares/sleep; do NOT use benzodiazepines (may increase risk)

GUIDELINE (YEAR)	FIRST-LINE TREATMENT	FIRST-LINE DRUG (IF USED)	KEY ADD-ON / NOT-USED
WFSBP (2022)	CBT (best-evidenced psychotherapy)	**SSRIs or the SNRI venlafaxine (first-line)**	Antipsychotic augmentation of an SSRI if unresponsive
VA/DoD (2023)	Manualised trauma-focused psychotherapy over pharmacotherapy (strong); PE / CPT / EMDR	**Paroxetine, sertraline or venlafaxine (strong)**	Recommend AGAINST benzodiazepines and against cannabis

The evidence-based PTSD treatment algorithm across five guidelines: trauma-focused psychotherapy first everywhere, a licensed SSRI (sertraline/paroxetine) or venlafaxine as the first-line drug, prazosin added for nightmares, and the benzodiazepine excluded (recommendations verified against BAP 2014, NICE 2018, CANMAT 2014, WFSBP 2022 and VA/DoD 2023). The complete stepped algorithm is drawn in the accompanying figure.

22.7 The non-responder: augmentation and second-line agents

Optimise, then switch, then augment. When a first-line drug fails at an adequately tolerated dose, the BAP sequence is: first raise the dose, then switch to another evidence-based treatment (pharmacological or psychological), and only then, for the treatment-refractory case after dose optimisation and switching, combine an evidence-based drug with a trauma-focused psychotherapy and refer to specialist services (BAP 2014). The Maudsley second-line list (no fixed order, weaker evidence) is mirtazapine, phenelzine, amitriptyline, and the antipsychotics (Maudsley 2021).

Antipsychotic augmentation. For the disabling, unresponsive case, NICE says to "consider an antipsychotic such as risperidone in addition to psychological therapy" where symptoms have not responded and there is severe hyperarousal or psychotic symptoms (NICE 2018); the WFSBP endorses augmenting an SSRI with an antipsychotic for treatment-unresponsive PTSD (WFSBP 2022); and BAP notes RCT efficacy for risperidone and olanzapine as alternatives, with olanzapine or risperidone (or prazosin) as antidepressant-augmentation options in refractory PTSD (BAP 2014). Antipsychotics tend to help the intrusion symptoms (flashbacks, nightmares) more than avoidance or hyperarousal (Maudsley 2021).

PEARL

State the ladder as a single ordered line and you own the management viva: trauma-focused psychotherapy (TF-CBT or EMDR) first; if a drug is used, a licensed SSRI (sertraline, paroxetine) or venlafaxine, given an adequate trial of up to 12 weeks; add prazosin for nightmares; on non-response raise the dose, then switch, then augment with an antipsychotic (risperidone, olanzapine) or combine drug plus psychotherapy and refer; continue a responding drug for at least 12 months; and never a benzodiazepine at any step.

22.8 Prevention, early intervention and continuation

Do not debrief. A classic negative point: routine single-session or multiple-session psychological debriefing is *not* recommended to prevent PTSD after trauma, it does not help and may harm (BAP 2014; NICE 2018). For subthreshold symptoms within a month of the trauma, NICE advises active monitoring with follow-up within a month rather than immediate treatment (NICE

2018). Where preventive action is warranted after major trauma, BAP notes that propranolol (Ciplar, Inderal in India) or sertraline, or trauma-focused CBT, may be considered to reduce the emergence of post-traumatic symptoms (BAP 2014).

How long to continue. A drug that produces a response should be continued for at least **12 months** using a relapse-prevention approach (BAP 2014), with fluoxetine and sertraline having RCT evidence for longer-term relapse prevention. When stopping, taper gradually over an extended period (BAP suggests a minimum three-month taper) to avoid discontinuation and rebound symptoms (BAP 2014).

12 weeks	12 months	1 to 15	8 to 12
TIME UP TO WHICH A PTSD DRUG TRIAL MAY BE NEEDED TO ASSESS EFFICACY (BAP)	MINIMUM CONTINUATION OF A RESPONDING DRUG	PRAZOSIN NOCTE RANGE, MG (START 1, TITRATE)	SESSIONS OF TRAUMA-FOCUSED CBT OR EMDR (NICE)

22.9 The India device and the treatment gap

Where the algorithm meets Indian practice. Trauma is common in India (road-traffic and industrial accidents, interpersonal and domestic violence, disasters), yet PTSD is under-recognised, frequently somatised, and reaches formal care late. Trauma-focused psychotherapy, the first-line treatment everywhere, is scarce outside tertiary centres, which is precisely why the WHO mhGAP framing matters: it keeps trauma-focused CBT or EMDR first even in low-resource settings (WHO mhGAP 2023). The Indian Psychiatric Society clinical practice guidelines for the anxiety and stress-related disorders align with the international consensus, an SSRI as the first-line pharmacotherapy and a structured psychotherapy as the first-line psychological treatment, and the benzodiazepine reserved out of the PTSD pathway. Indian brands of the anchor drugs are named where they arise: prazosin as Minipress or Prazopress, propranolol as Ciplar or Inderal, with the shared SSRI antidepressant brand list carried in the Mood disorders: pharmacotherapy notes.

TRAP **Under-dosing and stopping too early.** A PTSD SSRI/SNRI trial must run to an adequate dose for long enough, up to 12 weeks may be needed before judging efficacy; abandoning the trial at three or four weeks, or never titrating past a token starting dose, manufactures a false "treatment failure" and pushes the prescriber toward the wrong answer (a benzodiazepine).

HOLD THIS

The evidence-based treatment of PTSD, in one line: trauma-focused psychotherapy FIRST (trauma-focused CBT, that is cognitive processing therapy / cognitive therapy for PTSD / narrative exposure / prolonged exposure, or EMDR), across BAP, NICE, CANMAT, WFSBP and VA/DoD; where a drug is used, a licensed SSRI (sertraline or paroxetine) or venlafaxine, trialled up to 12 weeks and continued at least 12 months if it responds; prazosin (Minipress/Prazopress) 1 mg nocte titrated to 2 to 15 mg for trauma nightmares; antipsychotic augmentation (risperidone, olanzapine) for the refractory case; and NEVER a benzodiazepine, which is not a treatment and may increase PTSD risk if given early after trauma.

23 · Complex PTSD

Complex PTSD is the diagnosis ICD-11 created for the survivor of trauma that was not a single event but a captivity: prolonged, repeated, inescapable harm, most damagingly in childhood. On top of the ordinary post-traumatic triad it adds a deeper wound, to the way the person regulates emotion, holds themselves in their own mind, and relates to other people. The examiner's target here is almost never the whole criterion list; it is one discrimination done cleanly. cptsd is the disorder most often mislabelled as a personality disorder, above all emotionally unstable (borderline) personality disorder, and the person who can hold the **distinction from personality disorder** in a viva is the person who will not forfeit a trauma survivor's access to trauma-focused treatment.



Fig 14.17 ICD-11 complex PTSD contains the core PTSD triad, re-experiencing, avoidance and persistent current threat, plus affect dysregulation, negative self-concept and relational disturbance.

Why it matters clinically. **icd-11 complex** PTSD (6B41) is a *new* category, absent from DSM-5, built on Judith Herman's 1992 description of a syndrome in survivors of prolonged and repeated trauma. Its architecture is deliberately simple to state: the three core elements of PTSD *plus* three

disturbances in self-organisation (often abbreviated DSO), namely **affect dysregulation**, a persistent negative self-concept, and interpersonal difficulties. Two facts anchor every answer. First, you cannot have complex PTSD without first meeting PTSD; the DSO clusters sit on top of, never instead of, re-experiencing, avoidance and a sense of current threat. Second, the differential that examiners want is not PTSD versus complex PTSD (that is a severity-and-breadth step) but complex PTSD versus a personality disorder, because that is where real patients are misrouted. The core PTSD phenomenology is developed in the PTSD notes; the amygdala and fear-circuit substrate in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the general exposure principle in the Psychotherapies, clinical assessment, MSE and nosology notes; the reactive attachment and disinhibited engagement disorders that can co-occur in maltreated under-5s in the Child behavioural, emotional and other disorders notes and the Child psychiatry: assessment, treatment, services and protection notes.

Shared: affective dysregulation
the emotional instability both show, which is exactly why complex PTSD gets mislabelled as a personality disorder

The four splits read each row across	Complex PTSD ICD-11 6B41	Borderline personality disorder the emotionally unstable pattern
Trauma avoidance and current threat the deciding line	**Core diagnostic features** the trauma fingerprint: present by definition	**Not diagnostic features** not part of the personality-disorder picture
Sense of self	**Stable but negative** a settled, chronically low self-view	**Unstable identity** an oscillating, disturbed sense of self
Relationships	**Avoidance, disconnection** pulls away, keeps others at a distance	**Fear of abandonment** frantic push-pull, clings and lashes
Suicidality	**Less frequent, less impulsive** but of higher lethality	**Frequent and impulsive** recurrent self-harm and attempts

Both share affective dysregulation (top). The shaded row is the deciding one: the trauma fingerprint is present in complex PTSD and absent in the personality disorder.

Fig 14.18 Complex PTSD against borderline personality disorder. The two share their most visible symptom, affective dysregulation (the banner), which is exactly why a trauma survivor is so often mislabelled as borderline and the trauma missed. ICD-11 gives four lines that separate them. The deciding one, shaded, is the trauma fingerprint: trauma-reminder avoidance and a persistent sense of current threat are core to complex PTSD and are not diagnostic features of a personality disorder. Beneath it, the self-view is stable but negative in complex PTSD versus an unstable identity in the personality disorder; relationships are marked by avoidance and disconnection versus a fear of abandonment and push-pull instability; and suicidality is less frequent and less impulsive but of higher lethality, against the frequent, impulsive self-harm of the borderline pattern. Getting the label right unlocks trauma-focused treatment.

23.1 The definition: PTSD core plus three disturbances in self-organisation

The whole diagnosis in one sentence. Following the traumatic exposure, the person develops, for *at least several weeks*, all three core elements of PTSD *and* all three disturbances in self-organisation, with significant functional impairment (ICD-11 CDDR 6B41). The complex PTSD label is earned only when both halves are present; meet the PTSD triad alone and the diagnosis is PTSD (6B40), not complex PTSD.

The two halves. The *PTSD half* is the familiar triad: re-experiencing the event in the here and now (not mere recall), deliberate avoidance of reminders, and persistent perceptions of heightened current threat. The *self-organisation half* is the added signature of chronic entrapment: **affect dysregulation**, a persistent negative self-concept, and persistent difficulties in relationships. A single verbal-recall handle for the three DSO clusters is that the person cannot regulate feeling, cannot hold a workable view of the self, and cannot sustain closeness to others.

MNEMONIC

PTSD + A S R

Complex PTSD = the PTSD triad PLUS three disturbances in self-organisation. **A** = **A**ffect dysregulation (heightened reactivity, outbursts, reckless or self-destructive behaviour, dissociation under stress, emotional numbing). **S** = negative **S**elf-concept (persistent beliefs of being diminished, defeated or worthless, with pervasive shame, guilt or failure). **R** = **R**elationship difficulties (persistent trouble feeling close to or sustaining relationships with others). All three DSO clusters, on top of all three PTSD clusters.

23.2 The traumatic exposure: prolonged, repeated, inescapable

The typical stressor. Complex PTSD is generally a function of trauma that is *chronic, repeated and difficult or impossible to escape*, continuing over months or years: childhood physical, sexual or emotional abuse and severe neglect, domestic violence, torture, being trafficked, prolonged captivity or being a child soldier (ICD-11 CDDR; Herman 1992; Kaplan & Sadock CTP 2024). Exposure in early development carries a greater risk of complex PTSD (rather than PTSD) than does adult-onset trauma. Kaplan & Sadock frame simple PTSD as arising from a single or circumscribed event and complex PTSD from prolonged, inescapable stress, particularly in early childhood, complex precisely because of its extensive impact on all areas of development and functioning.

The threshold caution. Exposure to an extreme, prolonged or repetitive stressor from which escape is difficult does *not* in itself indicate complex PTSD; many people endure such stressors without developing any disorder (ICD-11 CDDR, boundary with normality). The presentation must meet all the diagnostic requirements. The stressor is the setting, not the diagnosis.

RULE **Two halves, both required.** Complex PTSD = the full PTSD triad PLUS all three disturbances in self-organisation (affect dysregulation, negative self-concept, interpersonal difficulty); no PTSD core, no complex PTSD, and DSO clusters without the PTSD triad point elsewhere.

23.3 Disturbance one: affect dysregulation

What it looks like. The presentation is characterised by severe and pervasive problems in **affect dysregulation** (ICD-11 CDDR). This runs in both directions on the arousal dial: *hyper*-regulation failure, showing as heightened emotional reactivity to minor stressors, violent outbursts, and reckless or self-destructive behaviour; and *hypo*-regulation, showing as emotional numbing, an inability to feel pleasure or positive emotion, and dissociative symptoms when under stress. A

telling ICD-11 detail is that, unlike in PTSD, the startle reaction in complex PTSD may be *diminished* rather than enhanced, the system shuts down rather than fires.

Where affect dysregulation misleads. This is the cluster that most resembles the affective instability of borderline personality disorder, and the overlap is genuine: affective dysregulation is a feature of both (ICD-11 CDDR). It is therefore the single cluster you must *not* read in isolation, because it is the shared ground on which the misdiagnosis is built. The discrimination lives in the accompanying figure, the complex-PTSD discriminator grid, and is unpacked in 23.6.

23.4 Disturbance two: a persistent negative self-concept

What it looks like. There are persistent beliefs about oneself as *diminished, defeated or worthless*, accompanied by deep and pervasive feelings of shame, guilt or failure related to the stressor (ICD-11 CDDR). The survivor of prolonged abuse may feel guilty for not having escaped, for having succumbed, or for not having prevented the suffering of others. The key adjective is *persistent*: this is a settled, stable, chronically low self-view, not a mood that swings across an afternoon.

The discriminating quality. Contrast this with the *unstable* sense of self of borderline personality disorder, where identity itself oscillates. In complex PTSD the self-view is bad but *steady*; in borderline PD it is bad and *unstable*. Stability of a negative self-concept is one of the cleanest single discriminators from a personality disorder (ICD-11 CDDR, boundary with personality disorder), and worth saying in exactly those words.

23.5 Disturbance three: interpersonal difficulties

What it looks like. There are persistent difficulties in sustaining relationships and in feeling close to others (ICD-11 CDDR). The characteristic pattern is *withdrawal*: the person consistently avoids, derides, or has little interest in relationships and social engagement. Where relationships do form they may be occasionally intense but hard to sustain. The organising theme is disconnection and avoidance of closeness.

The discriminating quality. This is the interpersonal cluster's crucial split from borderline PD. In complex PTSD, relationships are dominated by *avoidance and a general sense of disconnection*; they are *less* likely to be driven by fear of abandonment and the frantic, unstable, push-pull attachment that defines the borderline pattern (ICD-11 CDDR). Complex PTSD pulls away; borderline PD clings and lashes. That contrast (disconnection versus abandonment-driven instability) is the second clean discriminator.

GOOD TO REMEMBER

- **Complex PTSD (the syndrome, ICD-11 6B41):** the defining requirement is the full PTSD triad (re-experiencing in the here and now, deliberate avoidance, persistent sense of current threat) PLUS all three disturbances in self-organisation, affect dysregulation, a persistent negative self-concept, and interpersonal difficulties, lasting at least several weeks after prolonged/repeated/inescapable trauma, with functional impairment; the discriminator from PTSD is the added DSO clusters, and the first step is to confirm the PTSD core is present before adding the complex label.

23.6 The critical distinction: complex PTSD versus personality disorder

Why the confusion is real. Many people with a personality disorder have a history of childhood trauma, and affective dysregulation is a feature of both complex PTSD and personality disorder, particularly the borderline pattern (ICD-11 CDDR). The two therefore share their most visible symptom, emotional instability, which is exactly why the borderline label gets reached for and the trauma gets missed. ICD-11 lists four specific ways the profiles diverge, and these are the examinable discriminators.

The four discriminators. First, *avoidance of trauma reminders and a heightened sense of current threat* are core to complex PTSD and are *not* diagnostic features of a personality disorder, they are the trauma-specific fingerprint. Second, the *self-view*: complex PTSD shows a stable but persistently negative self-view, whereas an *unstable* sense of self is more typical of personality disorder. Third, *relationships*: complex PTSD is marked by avoidance and disconnection, personality disorder (borderline) by fear of abandonment and relationship instability. Fourth, *suicidality*: in personality disorder it tends to be frequent and impulsive, whereas in complex PTSD it tends to be less frequent, less impulsive, and of *higher lethality* (ICD-11 CDDR).

FEATURE	COMPLEX PTSD (ICD-11 6B41)	PERSONALITY DISORDER, BORDERLINE PATTERN
Trauma-reminder avoidance and heightened current threat	**Core diagnostic features (the PTSD fingerprint)**	**Not diagnostic features**
Sense of self	**Stable but persistently negative self-view**	**Unstable sense of self / identity disturbance**
Relationships	Avoidance and general disconnection	Fear of abandonment, relationship instability (push-pull)
Suicidality	Less frequent, less impulsive, higher lethality	Frequent, often impulsive
Affective dysregulation	Present (shared feature)	Present (shared feature)
Origin required for diagnosis	Prolonged/repeated/inescapable trauma is typical, but the syndrome must be met	Enduring personality pattern; trauma frequent but not required

The complex-PTSD-versus-borderline-personality-disorder discriminator grid; affective dysregulation is the shared feature that drives the misdiagnosis, and the four rows above it (trauma avoidance/current threat, stable-negative versus unstable self, disconnection versus abandonment, lethality pattern) are the ICD-11 lines that separate them (verified against ICD-11 CDDR 6B41, boundary with personality disorder). The concept map is set out in the figure alongside.

TRAP **Complex PTSD mislabelled as a personality disorder.** A childhood-abuse survivor with affective instability, low self-worth and stormy relationships is reflexively called borderline; the trauma-reminder avoidance, the persistent sense of current threat, the *stable* negative self-view and the disconnection (not abandonment-driven) pattern are the ICD-11 lines that make it complex PTSD, and the label change unlocks trauma-focused treatment.

WORKED EXAMPLE

A 27-year-old woman with a documented history of chronic childhood sexual abuse presents with intrusive flashbacks of the abuse that feel as if it is happening now, avoidance of anything that reminds her of it, and constant hypervigilance. On top of this she has explosive anger at trivial provocations alternating with numb emptiness, a fixed conviction that she is worthless and to blame, and a pattern of keeping everyone at arm's length. A previous clinician had labelled her borderline personality disorder on the emotional instability alone. The re-experiencing, the trauma-specific avoidance, the persistent current threat, the *stable* (not oscillating) negative self-view and the *avoidant* (not abandonment-driven) relational style make this complex PTSD (ICD-11 6B41), not a personality disorder, and reframe the whole treatment plan around the trauma.

GOOD TO REMEMBER

- **Complex PTSD versus personality disorder (the discrimination):** both share affective dysregulation, but complex PTSD is marked by trauma-reminder avoidance and a persistent sense of current threat (absent in PD), a *stable* negative self-view (versus an unstable sense of self), relationships dominated by avoidance/disconnection (versus fear of abandonment), and suicidality that is less frequent, less impulsive but of higher lethality; the trauma fingerprint is the deciding feature.

23.7 Management: trauma-focused psychotherapy first, guideline-anchored

The management principle. As for PTSD, the first-line treatment for complex PTSD is *trauma-focused psychotherapy*, not a drug (NICE 2018; BAP 2014). NICE 2018 covers complex presentations explicitly and directs an *urgent referral for specialist trauma assessment* when PTSD presents with severe dissociation or complex-PTSD features (pervasive affect dysregulation, severely disturbed self-concept, profound interpersonal difficulties), or when first-line trauma-focused therapy has failed or worsened symptoms. The evidence-based psychological treatments are individual trauma-focused CBT (cognitive processing therapy, cognitive therapy for PTSD, narrative exposure therapy or prolonged exposure) and EMDR (eye-movement desensitisation and reprocessing), each delivered over about **8 to 12 sessions**, extended where there are multiple traumas, comorbid depression or significant dissociation (NICE 2018). Clinically, complex PTSD often needs a *phased* approach: stabilisation and affect-regulation skills before trauma processing, because a poorly timed exposure can destabilise a dysregulated survivor.

Where drugs sit. Pharmacotherapy is an adjunct, not the spine. Where a drug is used, the first-line agents are the same evidence-based antidepressants as in PTSD: sertraline, paroxetine or the SNRI venlafaxine (BAP 2014; NICE 2018; CANMAT 2014). Adequate response can take up to **12 weeks** to judge, and responders should continue for at least **12 months** (BAP 2014). For trauma nightmares and disturbed sleep, prazosin (Minipress, Prazopress) is the targeted agent, an alpha-1 antagonist added for the nightmare symptom, not a whole-syndrome treatment (CANMAT 2014; BAP 2014). Where disabling hyperarousal or psychotic-level symptoms resist first-line care, NICE allows adjunctive risperidone alongside psychological therapy. The detailed SSRI/SNRI pharmacology (doses, adverse effects, interactions) sits in the Mood disorders: pharmacotherapy notes and is not re-derived here.

GOOD TO REMEMBER

- **Trauma-focused psychotherapy (the first-line treatment):** the principle is that complex PTSD, like PTSD, is treated *psychologically first*, with trauma-focused CBT or EMDR (about 8 to 12 sessions, often phased with stabilisation before processing); the signature caution is that a drug is an adjunct, and NICE 2018 directs urgent specialist referral for complex-PTSD features or when first-line therapy has failed or worsened.
- **Prazosin (Minipress, Prazopress):** an alpha-1 adrenergic antagonist; the one indication to anchor is trauma-related *nightmares* and sleep disturbance, added on to a first-line antidepressant, with blood pressure and dizziness the signature cautions, never a stand-alone PTSD treatment.

23.8 The India device: the trauma treatment gap, benzodiazepines, and the IPS line

Where complex PTSD lands in Indian practice. India carries a very wide anxiety, OCD and PTSD treatment gap, and complex PTSD sits at its blindest point. The precipitating traumas, chronic childhood abuse and neglect, prolonged domestic and interpersonal violence, are precisely those that are under-reported, stigmatised and reach formal care late, and the presentation, emotional instability with self-loathing and stormy relationships, is the one most readily misfiled as a personality disorder or dismissed. Into that gap flows the benzodiazepine over-prescription problem: a long-term benzodiazepine (typically alprazolam) is handed to a distressed survivor, touching none of the six clusters and, given early after trauma, potentially *increasing* the risk of PTSD (CANMAT 2014). The Indian Psychiatric Society CPGs, aligned with NICE and BAP, put trauma-focused psychotherapy first, then an SSRI (sertraline, paroxetine) or venlafaxine, with prazosin (Minipress, Prazopress) reserved for nightmares; the benzodiazepine has no maintenance role. Indian brands of the anchor antidepressants (sertraline, paroxetine, escitalopram) are named in the Mood disorders: pharmacotherapy notes.

INDIA

The highest-yield Indian point is that complex PTSD is doubly failed in Indian practice: the chronic-abuse trauma is under-recognised, and the affective-instability presentation is misrouted to a personality-disorder label (or an alprazolam prescription) instead of trauma-focused care. Against India's wide trauma treatment gap and its benzodiazepine over-prescription problem, the IPS-aligned answer is to name the complex PTSD, treat it psychologically first (trauma-focused CBT or EMDR), add an SSRI or venlafaxine only as an adjunct, use prazosin for nightmares, and never a benzodiazepine as maintenance.

6B41	3 + 3	8 to 12	12 months
ICD-11 CODE FOR COMPLEX PTSD (PTSD IS 6B40)	PTSD CORE CLUSTERS PLUS DISTURBANCES IN SELF-ORGANISATION	TRAUMA-FOCUSED CBT / EMDR SESSION RANGE (NICE 2018)	MINIMUM CONTINUATION OF DRUG IN RESPONDERS (BAP 2014)

HOLD THIS

Complex PTSD (ICD-11 6B41, NOT in DSM-5) = the full PTSD triad (re-experiencing in the here and now, deliberate avoidance, persistent current threat) PLUS all three disturbances in self-organisation (affect dysregulation, a persistent negative self-concept, interpersonal difficulties), after prolonged/repeated/inescapable trauma; the critical discrimination is from borderline personality disorder, and although affective dysregulation is shared, complex PTSD is set apart by trauma-reminder avoidance and a persistent sense of current threat (absent in PD), a STABLE (not unstable) negative self-view, relationships driven by avoidance/disconnection (not fear of abandonment), and suicidality that is less impulsive but higher-lethality; treatment is trauma-focused psychotherapy FIRST (trauma-focused CBT or EMDR), with an SSRI or venlafaxine as adjunct and prazosin for nightmares, never a benzodiazepine.

24 · Acute stress reaction and acute stress disorder

These two labels sit in the hours-to-weeks window immediately after a terrifying event, and the whole examinable point is that they are *not* the same kind of thing. **Acute stress reaction** is the ICD-11's name for a **transient stress response**, a normal reaction to an exceptional stressor that the classification deliberately keeps *outside* the mental disorders; **acute stress disorder** is the DSM-5's *diagnosable* disorder in the first month after trauma. Getting the framing right, which is a disorder and which is not, which classification owns which, and how each relates to **ptsd**, is exactly what a viva examiner probes.

Why it matters clinically. Most people exposed to horror react and then recover; a minority stay ill. The early window is where clinicians must decide who is having an expectable acute stress reaction that needs support and time, and who is developing a disorder that needs treatment, without medicalising the first or missing the second. The trap that runs through the whole area is reflexively reaching for a benzodiazepine in the acute aftermath, which is not a treatment and may actually worsen the trajectory. The amygdala and fear-circuit anatomy that drives the acute autonomic storm is developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the full-blown syndrome and its clusters belong to the PTSD notes and are not re-derived here.

24.1 The core distinction: a reaction that is not a disorder versus a disorder

Two different objects. The single most tested fact is definitional. ICD-11 acute stress reaction (code **QE84**) is *not* considered a mental disorder: it is placed in Chapter 24, on factors influencing health status or contact with health services, precisely to signal that a transient response to an extreme stressor is normal (ICD-11 CDDR). It is only secondary-parented into the grouping of disorders specifically associated with stress to aid differential diagnosis. DSM-5-TR acute stress disorder (F43.0), by contrast, is a full trauma- and stressor-related *disorder* with operational criteria, a symptom threshold and a duration window (DSM-5-TR 2022; Kaplan & Sadock CTP 2024).

The consequence for the two systems. ICD-11 therefore has *no* "acute stress disorder" among its disorders: its stress grouping runs PTSD, complex PTSD, prolonged grief disorder and adjustment disorder, with acute stress reaction sitting outside as a non-disorder (ICD-11 CDDR).

DSM-5 *does* carry acute stress disorder as a diagnosis. So the same distressed trauma survivor in the first weeks may be given an ICD-11 "acute stress reaction" (a health-status factor, no disorder) or a DSM-5 "acute stress disorder" (a diagnosis), depending entirely on which manual is used.

RULE **Reaction is normal; disorder is diagnosable.** ICD-11 acute stress reaction is a transient normal response classified *outside* the mental disorders (Chapter 24, QE84); DSM-5 acute stress disorder is a diagnosable disorder in the first month. If the manual is ICD-11 there is no "acute stress disorder" to give.

24.2 Acute stress reaction: what it is and its time frame

The ICD-11 description. Acute stress reaction is the development of transient emotional, somatic, cognitive or behavioural symptoms after exposure to an event or situation, short- or long-lasting, of an *extremely threatening or horrific* nature (natural or human-made disasters, combat, serious accidents, sexual violence, assault) (ICD-11 CDDR). The picture is mixed and shifting: autonomic signs of anxiety (tachycardia, sweating, flushing), being in a daze, confusion, sadness, anxiety, anger, despair, over-activity, inactivity, social withdrawal, or at the extreme a stupor. Crucially, "the response to the stressor is considered to be normal given the severity of the stressor, and usually begins to subside within a few days after the event or following removal from the threatening situation".

The classic ICD-10 timings to carry. The older ICD-10 acute stress reaction, still the version most exam stems use, sets sharp temporal anchors: symptoms appear *within minutes* of the exceptional stressor and resolve rapidly, typically within a few hours once the stressor is removed, and within **1 to 3 days** even if it is not, so that a transient reaction lasts considerably less than **48 hours** (Companion to Psychiatric Studies; ICD-10). It is more likely to develop, and to be more severe, in the presence of physical exhaustion or at the extremes of age. The point that unifies both editions is transience: this is a storm that passes.

WORKED EXAMPLE

A previously well 40-year-old man is pulled from a collapsed scaffold at a construction site. For the next couple of hours he is dazed and disoriented, cannot recall parts of the rescue, is tremulous, tachycardic and sweating, alternates between agitation and withdrawal, and briefly cannot take in what is said to him. By the evening, moved to a quiet ward and reassured, he is oriented, calmer and communicative, and by the following morning he is largely settled. This is an *acute stress reaction*, a transient stress response that subsided once he was removed from the threat, not a disorder; the correct management was safety, orientation and support, not a benzodiazepine drip.

GOOD TO REMEMBER

- **Acute stress reaction (the syndrome):** the defining criterion is a transient, mixed, rapidly shifting emotional/autonomic/dissociative reaction beginning within minutes of an *exceptional* stressor and resolving fast (within hours to 1 to 3 days, typically under 48 hours); the discriminator is that it is judged *normal given the severity of the stressor* and is classified *outside* the mental disorders in ICD-11 (QE84, Chapter 24), so the first step is support and safety, not diagnosis or a drug.

24.3 Acute stress disorder: the DSM-5-TR criteria and the 9-of-14 rule

The gateway and the threshold. DSM-5-TR acute stress disorder requires the same Criterion A traumatic stressor as PTSD (exposure to actual or threatened death, serious injury or sexual violence, experienced, witnessed, learned of, or through repeated occupational exposure to aversive details), and then a symptom threshold that is distinctive: the presence of **nine (or more) of 14** symptoms drawn from *any* of five categories, all beginning or worsening after the trauma (DSM-5-TR 2022). The five categories are *intrusion*, *negative mood*, *dissociation*, *avoidance* and *arousal*. Because the nine can come from any mix of the five, the symptom profile of two people with the same diagnosis can look very different.

The 14 symptoms, by category. Intrusion (four): intrusive distressing memories, distressing dreams, dissociative flashback reactions, and intense/prolonged distress or marked physiological reactivity to reminders. Negative mood (one): a persistent inability to experience positive emotions. Dissociation (two): an altered sense of reality of self or surroundings (derealisation/depersonalisation), and inability to remember an important aspect of the event (dissociative amnesia). Avoidance (two): effortful avoidance of internal reminders (memories, thoughts, feelings) and of external reminders. Arousal (five): sleep disturbance, irritability or angry outbursts, hypervigilance, concentration problems, and exaggerated startle (DSM-5-TR 2022).

> **COMMON TRAP**
>
> Assuming acute stress disorder still *requires* dissociation. DSM-IV demanded a set number of dissociative symptoms, so ASD was historically taught as "the dissociative early trauma reaction". DSM-5 deliberately dropped that requirement: dissociation is now just *one of five* symptom categories, and the nine symptoms can be reached with none from the dissociation category at all (DSM-5-TR 2022; Kaplan & Sadock CTP 2024). Marking a survivor as "not ASD because they did not dissociate" is a DSM-IV-era error.

24.4 The time frames that separate acute stress disorder from PTSD

The window is the whole point. Acute stress disorder is a diagnosis of the *first month*. DSM-5-TR fixes the duration of the disturbance at **3 days to 1 month** after trauma exposure: symptoms typically begin immediately, but persistence for at least three days is needed before the label applies, and the diagnosis cannot outlive the first month (DSM-5-TR 2022). This is the mirror image of PTSD, whose duration criterion is *more than* one month. The two are, by construction, temporally exclusive: before the third day, neither applies; from three days to a month it is ASD; beyond a month it is PTSD.

The floor and the ceiling. The *floor* of three days exists so that the transient acute stress *reaction* of the first hours and days is not over-diagnosed as a disorder. The *ceiling* of one month exists because at that point the diagnostic question changes: if the full syndrome is still present after a month, the correct label is PTSD, and ASD is retired. A patient who is symptomatic at five weeks does not "still have ASD"; they have crossed into PTSD (or another diagnosis) (DSM-5-TR 2022; Tasman Psychiatry).

FEATURE	ACUTE STRESS REACTION (ICD-11 QE84)	ACUTE STRESS DISORDER (DSM-5-TR F43.0)	PTSD
Status	**Not a mental disorder (Chapter 24, factors influencing health)**	**A diagnosable disorder**	A diagnosable disorder
Owning system	ICD-11 (also ICD-10 F43.0)	DSM-5 (no ASD exists in ICD-11)	Both DSM-5 and ICD-11
Onset	Within minutes of the stressor	May begin immediately; label needs at least 3 days	Any time; delayed expression if first met after 6 months
Duration	Hours to 1 to 3 days (typically under 48 hours)	3 days to 1 month	More than 1 month
Symptom rule	Transient, mixed, shifting; no operational count	9 or more of 14 across 5 categories	DSM-5 four clusters (or ICD-11 three)
Framing	Normal response given stressor severity	Early diagnosable syndrome; imperfect predictor of PTSD	Established disorder of persistent re-experiencing

The three labels placed on one timeline from the exceptional event outward; the load-bearing points are that ICD-11 acute stress reaction is a non-disorder, DSM-5 acute stress disorder occupies the 3-day-to-1-month window with a 9-of-14 rule, and PTSD takes over beyond a month (verified against ICD-11 CDDR, DSM-5-TR 2022 and Tasman Psychiatry).

GOOD TO REMEMBER

- **Acute stress disorder (the syndrome):** the defining criterion is a Criterion-A trauma followed by *9 or more of 14* symptoms from any of five categories (intrusion, negative mood, dissociation, avoidance, arousal), lasting *3 days to 1 month*; the discriminator from PTSD is purely the time window (ASD under a month, PTSD over a month) and from ICD-11 acute stress reaction is that ASD is a diagnosable *disorder*, while dissociation is no longer mandatory (contrast DSM-IV); the first step is to confirm the stressor, then count symptoms across the five categories.

24.5 The relationship to PTSD: who progresses, and the sensitivity problem

The asd trauma pathway. Acute stress disorder was introduced partly to flag people early on the road to PTSD, and it does carry predictive weight: roughly **half of those meeting ASD criteria go on to develop PTSD** (Tasman Psychiatry; Bryant et al. 2011). That is a clinically meaningful signal, and a positive ASD diagnosis in the first month should prompt monitoring and access to care.

Why it is a poor screen. The examinable subtlety is the other direction: *many people who develop PTSD never met criteria for ASD* in the first month (Tasman Psychiatry; Bryant et al. 2011). Some progress to PTSD from subthreshold early symptoms, and some show a delayed course. So ASD has reasonable positive predictive value but *poor sensitivity* as a screen for eventual PTSD: a clean first month does not rule out PTSD later, which is why guidelines favour active monitoring over reassurance-and-discharge for symptomatic trauma survivors (NICE 2018). ASD prevalence itself

varies by trauma type, estimated at about **13 to 25%** of motor-vehicle-accident survivors (Tasman Psychiatry).

TRAP **Treating absent ASD as reassurance.** A survivor who did not meet acute stress disorder criteria in the first month is *not* safe from PTSD; many who develop PTSD never had ASD. Do not discharge with false reassurance; use active monitoring with follow-up within a month for subthreshold symptoms (NICE 2018).

3 days to 1 month DSM-5 ACUTE STRESS DISORDER DURATION WINDOW	**9 of 14** DSM-5 ASD SYMPTOM THRESHOLD (ACROSS 5 CATEGORIES)	**~50%** OF ASD CASES PROGRESS TO PTSD	**under 48 hours** TYPICAL DURATION OF AN ICD ACUTE STRESS REACTION

24.6 Early management: what to do, and the benzodiazepine and debriefing traps

Support first, drugs rarely. The evidence-based early response is psychological first aid, safety, orientation, practical support and reconnection, with active monitoring and follow-up within a month for anyone with subthreshold symptoms (NICE 2018). Where the early syndrome is established, an *individual trauma-focused CBT* intervention is the treatment of choice, not a drug (NICE 2018). Two things are explicitly *not* to be done routinely: single-session psychological debriefing is ineffective at preventing PTSD and may increase the risk of developing it (BAP 2014; NICE 2018; Companion), and drug treatments, including benzodiazepines, should not be offered to *prevent* PTSD after trauma (NICE 2018).

The benzodiazepine point, stated twice over. A benzodiazepine is the wrong reflex in the acute aftermath for two separate reasons: it treats none of the core trauma symptoms, and early post-trauma benzodiazepine use may actually *increase* the risk of subsequently developing PTSD (CANMAT 2014). Where a specific peri-trauma preventive is considered at all, the guideline-supported options are trauma-focused CBT, or, more tentatively, propranolol (Ciplar, Inderal) or sertraline, never an early anxiolytic (BAP 2014). For established PTSD later, prazosin (Minipress, Prazopress) is the anchor for trauma nightmares (CANMAT 2014), but that belongs to the management of the persistent disorder, not the acute reaction.

GOOD TO REMEMBER

- **Early trauma management (the principle):** the mechanism is that recovery is the norm, so the first-line move is psychological first aid plus active monitoring, with individual trauma-focused CBT if an early syndrome is established (NICE 2018); the signature caution is that routine single-session debriefing may *increase* PTSD risk and a benzodiazepine both fails to treat trauma symptoms and may raise PTSD risk (CANMAT 2014), so the one thing not to do is sedate-and-debrief.

24.7 The India device: the treatment gap, benzodiazepine over-prescription and the IPS line

Where this lands in Indian practice. India carries a wide anxiety, OCD and PTSD treatment gap, and the early trauma window is exactly where it shows. Trauma is common (road-traffic and industrial accidents, disasters, interpersonal and domestic violence), distress after it is frequently somatised, and the reflex in over-stretched settings is a short course, then a long course, of a

benzodiazepine, usually alprazolam. Against that benzodiazepine over-prescription problem, the acute stress reaction is precisely the presentation that should *not* be medicalised: it is a transient normal response, best met with support and safety, and any benzodiazepine given past marked acute agitation risks doing harm rather than good (CANMAT 2014). The Indian Psychiatric Society CPGs, in line with NICE and BAP, put psychological first aid and active monitoring first, trauma-focused psychotherapy for established syndromes, and reserve pharmacotherapy for the persistent disorder, where the anchors are the SSRIs and the SNRI, with prazosin (Minipress, Prazopress) for nightmares and no maintenance benzodiazepine.

INDIA

The highest-yield Indian point: an acute stress reaction is a *non-disorder* that needs support, not a prescription, yet it is a common trigger for the benzodiazepine over-prescription seen across Indian practice. Set against India's wide trauma treatment gap, the IPS-aligned answer is psychological first aid and active monitoring first, trauma-focused CBT for an established early syndrome, and an SSRI (not alprazolam) only if the illness persists into PTSD, with prazosin (Minipress, Prazopress) reserved for nightmares.

PEARL

Line the whole area up on one clock and it becomes un-confusable. Minutes-to-hours after the event, mixed and settling: acute stress reaction (a normal response, not a disorder, ICD-11 QE84). Three days to a month, 9 of 14 symptoms: acute stress disorder (a DSM-5 diagnosis; ICD-11 has none). Beyond a month, the cluster syndrome: PTSD. Reaction, disorder-in-the-month, disorder-past-the-month, in that order.

HOLD THIS

Acute stress reaction is a *transient normal response* to an exceptional stressor, coded QE84 in ICD-11 *outside* the mental disorders (Chapter 24), beginning within minutes and settling within hours to 1 to 3 days (under 48 hours); acute stress disorder is a *DSM-5 diagnosable disorder* requiring a Criterion-A trauma plus 9 or more of 14 symptoms across five categories (intrusion, negative mood, dissociation, avoidance, arousal) lasting 3 days to 1 month, with dissociation no longer mandatory (unlike DSM-IV); ICD-11 has no acute stress disorder at all; about half of ASD cases progress to PTSD but many who develop PTSD never had ASD (poor sensitivity); and the acute management is psychological first aid plus active monitoring, never routine debriefing and never a benzodiazepine, which may raise PTSD risk.

25 · Adjustment disorder

Adjustment disorder is the diagnosis for a **maladaptive reaction** to an identifiable life event that is more than an expectable upset but less than a full syndrome such as a depressive episode or generalised anxiety disorder. The whole examinable tension sits in that middle ground: the reaction is real and can carry genuine morbidity (including suicide risk), yet the same clinical picture, in a slightly milder form, is simply *normal human distress* that must *not* be labelled a disorder. Getting the frame right, that a stressor is necessary but not sufficient, is exactly what a viva examiner probes.

Why it matters clinically. Adjustment disorder is one of the most frequently used diagnoses in consultation-liaison, primary-care and emergency settings, and it is also one of the most easily misused. The icd-11 changes reconceptualised it around two positive features, preoccupation with the stressor and a *failure to adapt*, moving it away from being a pure residual "not-quite-anything-else" category. The examinable traps run in two opposite directions at once: over-diagnosing a normal, self-limiting adaptive reaction as a disorder, and under-recognising that a genuine adjustment disorder carries a real, impulsive self-harm risk that can be greater per-episode than in major depression. The amygdala and fear-circuit anatomy that underpins the stress response is developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the wider CBT and problem-solving model that anchors treatment belongs to the Psychotherapies, clinical assessment, MSE and nosology notes and is not re-derived here.

25.1 The core concept: a maladaptive reaction bounded by a stressor at one end and another disorder at the other

The sine qua non. A precipitating stressor is the one non-negotiable requirement: adjustment disorder is the development of emotional or behavioural symptoms *in response to* an identifiable psychosocial stressor (Kaplan & Sadock CTP 2024). The stressor can be single (a relationship ending, job loss, a new medical diagnosis) or multiple, acute or continuous, and of *any* severity, it need not be extreme or life-threatening (DSM-5-TR 2022; ICD-11 CDDR). Unlike almost every other DSM-5-TR disorder, there is *no* defined symptom checklist; the diagnosis is defined by its relationship to the stressor, not by a signature symptom profile.

Bounded on both sides. The diagnosis is squeezed between two thresholds. At the lower boundary it must be more than normality: a **maladaptive reaction** with marked distress out of proportion to the stressor, *or* significant functional impairment (DSM-5-TR 2022). At the upper boundary it must be less than another disorder: if the picture meets criteria for a depressive episode, an anxiety disorder, PTSD or acute stress disorder, that diagnosis is made *instead*, and adjustment disorder is not given (ICD-11 CDDR; DSM-5-TR 2022). This is why it has historically read as a residual category, the diagnosis you reach when the reaction is clearly abnormal but fits no better-defined box.

RULE **Stressor necessary, but never sufficient.** No identifiable stressor, no adjustment disorder; but a stressor plus a full syndrome (depressive episode, an anxiety disorder, PTSD) means you diagnose *that* disorder, not adjustment disorder.

25.2 The ICD-11 reconceptualisation: preoccupation and failure to adapt as the positive core

From residual to defined. The single most testable point of the icd-11 changes is that adjustment disorder was given a *positive* core rather than being left as a leftover category. ICD-11 defines it as a **maladaptive reaction** to an identifiable psychosocial stressor whose two defining features are preoccupation with the stressor (excessive worry, recurrent distressing thoughts about the stressor, or constant rumination about its implications) and a *failure to adapt* that

produces significant impairment (ICD-11 CDDR). Symptoms of preoccupation characteristically worsen with reminders of the stressor and can drive avoidance of those reminders.

What this changes in practice. Because the core is now preoccupation-plus-failure-to-adapt, ICD-11 does *not* require the old affective subtypes: depressive and anxiety symptoms are listed as common *additional* features, not as the defining substance (ICD-11 CDDR). Two further ICD-11-specific anchors are examinable. First, ICD-11 tightens the onset window: symptoms usually emerge **within one month** of the stressor, tighter than the DSM-5-TR three-month window (ICD-11 CDDR; Kaplan & Sadock CTP 2024). Second, ICD-11 explicitly places adjustment disorder inside the grouping of "disorders specifically associated with stress" (code **6B43**) alongside PTSD, complex PTSD and prolonged grief disorder, all of which require a stressor by definition.

PEARL

The ICD-11 mnemonic for the core is simply *preoccupation plus failure to adapt*. If a candidate can only name one ICD-11 change, name that the diagnosis is now built on those two positive features rather than being a residual "everything else after a stressor" bin, with onset within one month rather than three.

GOOD TO REMEMBER

- **Adjustment disorder (the syndrome):** the defining criterion is a *maladaptive reaction to an identifiable psychosocial stressor* whose ICD-11 core is *preoccupation with the stressor* (worry, recurrent distressing thoughts, rumination) plus a *failure to adapt* causing significant impairment; the discriminators are that a stressor is *necessary* (below) and that it must not meet criteria for any better-defined disorder (above); the first step is to establish the stressor, confirm the reaction is out of proportion or impairing, and exclude a full depressive/anxiety/PTSD syndrome (ICD-11 CDDR; DSM-5-TR 2022).

25.3 The time frame: the onset window and the 6-month resolution rule

Onset and resolution. The temporal architecture is heavily examined. DSM-5-TR requires onset **within 3 months** of the stressor; ICD-11 tightens this to usually **within one month** (DSM-5-TR 2022; ICD-11 CDDR). Both systems agree the exit rule: once the stressor *or its consequences* have terminated, symptoms resolve **within 6 months** (DSM-5-TR 2022; ICD-11 CDDR). If symptoms outlast the stressor by more than six months, the diagnosis should generally be changed to a more appropriate one.

Acute versus persistent. DSM-5-TR carries two duration specifiers: *acute* (symptoms under six months) and *persistent (chronic)* (six months or longer). The persistent specifier applies only when the stressor itself is ongoing or has enduring consequences, a chronic disabling illness, or the lasting financial and emotional sequelae of a divorce, so that the diagnosis can legitimately run longer than six months *because the stressor has not actually ended* (DSM-5-TR 2022). The rule is not contradicted: what resolves within six months is the reaction after the stressor terminates.

FEATURE	ICD-11 (6B43)	DSM-5-TR
Onset after stressor	**Usually within one month**	**Within 3 months**
Defining core	Preoccupation with the stressor + failure to adapt	Emotional/behavioural symptoms, marked distress out of proportion or functional impairment
Resolution	Within 6 months of stressor/consequences ending	Within 6 months of stressor/consequences ending
Subtypes / specifiers	No affective subtypes; depression/anxiety are additional features	Five specifiers; plus acute vs persistent (chronic)
Relation to other disorders	Not diagnosed if another disorder accounts for symptoms	Must not meet criteria for another disorder; not merely an exacerbation of a pre-existing one

The two classifications side by side; the load-bearing contrasts are the tighter one-month ICD-11 onset window versus the DSM-5-TR three-month window, the shared six-month resolution rule, and ICD-11's positive preoccupation-plus-failure-to-adapt core replacing the DSM affective subtypes (verified against ICD-11 CDDR and DSM-5-TR 2022).

25.4 The DSM-5-TR subtypes: six specifiers by predominant symptom

The five plus one. Where ICD-11 dropped subtypes, DSM-5-TR retains a specifier for the *predominant* disturbance (DSM-5-TR 2022): *with depressed mood* (F43.21, low mood, tearfulness, hopelessness); *with anxiety* (F43.22, nervousness, worry, jitteriness, or in children separation anxiety); *with mixed anxiety and depressed mood* (F43.23); *with disturbance of conduct* (F43.24, e.g. rule-breaking, reckless behaviour); *with mixed disturbance of emotions and conduct* (F43.25); and *unspecified* (F43.20) for maladaptive reactions not classifiable as one of the above. The most common subtypes in adults carry prominent depressive symptoms.

Why the conduct subtypes matter. The conduct and mixed-conduct subtypes are the examinable reminder that adjustment disorder is not only an affective category: in adolescents it may present as acting-out, risk-taking or a rise in substance use, and in children the preoccupation is often not verbalised but somatised (stomach pains, headaches) or shown as regression, oppositional behaviour, tantrums or increased clinginess (ICD-11 CDDR; DSM-5-TR 2022). The reactive attachment and disinhibited engagement disorders that also follow adverse early environments are covered in the Child behavioural, emotional and other disorders notes and the Child psychiatry: assessment, treatment, services and protection notes.

MNEMONIC

DAMCU

DSM-5-TR adjustment disorder specifiers: **D**epressed mood, **A**nxiety, **M**ixed anxiety and depressed mood, **C**onduct disturbance, mixed emotions-and-conduct (the sixth being **U**nspecified). Five named subtypes plus unspecified.

25.5 Do not over-diagnose: the boundary with a normal adaptive reaction

The lower threshold is the hard part. The central clinical skill, and the most tested single caution, is distinguishing a diagnosable disorder from an expectable, self-limiting response to a hard event. A precipitant plus some distress is *not* a disorder: emotional reactions to negative life events that are *not* markedly out of proportion and do *not* cause significant impairment should not be diagnosed as adjustment disorder (ICD-11 CDDR). Transient responses that settle within a few days do not warrant the label at all, and where a reaction is judged normal given the severity of an extreme stressor, ICD-11 directs you to the non-disorder category *acute stress reaction* (QE84) rather than any diagnosis (ICD-11 CDDR).

The bereavement carve-out. Ordinary grief is explicitly excluded: DSM-5-TR requires that the symptoms do not represent normal bereavement and are not better explained by *prolonged grief disorder* (DSM-5-TR 2022). Adjustment disorder may still be diagnosed after a death when the intensity, quality or persistence of the grief exceeds what age, cultural and religious norms would expect and the picture does not meet prolonged grief criteria, but the default assumption is that grief is normal. Over-medicalising life's difficulties, treating "problems of daily living" as illness because families, community and religious supports have thinned, is the error the diagnosis most invites (Kaplan & Sadock CTP 2024).

TRAP **Labelling normal distress a disorder.** A stressor plus understandable upset is *not* adjustment disorder unless the reaction is markedly out of proportion *or* functionally impairing; transient distress settling in days, and ordinary bereavement, are normal, not diagnoses.

25.6 The self-harm signal: why "minor" is a dangerous word here

The other-direction error. Set against the over-diagnosis trap is its mirror image, dismissing a genuine adjustment disorder as trivial. Several studies link adjustment disorder to significant suicidal ideation and behaviour that belies its "minor and self-limiting" reputation (Kaplan & Sadock CTP 2024). Among emergency-department self-harm presentations, patients with adjustment disorder made *more impulsive* acts, were more often associated with alcohol use, and reached self-harm *earlier* in the course of illness than patients with major depression; poisoning is the commonest method (Kaplan & Sadock CTP 2024). Subthreshold conditions can therefore carry high morbidity, including death.

The clinical consequence. This is why ongoing suicide risk assessment is written into management, and why acuity, not the size of the stressor, drives the decision to intervene. A rapidly escalating reaction with impulsivity and alcohol involvement warrants crisis intervention and case management on a short-term basis to preclude suicide attempts and, where necessary, to avoid hospitalisation (Kaplan & Sadock CTP 2024).

HOLD THIS

Adjustment disorder is a *maladaptive reaction to an identifiable stressor* with, in ICD-11, *preoccupation with the stressor plus failure to adapt* at its core; onset is within one month (ICD-11) or three months (DSM-5-TR) and it resolves within six months of the stressor ending; it requires a stressor but is trumped by any full disorder (depression, an anxiety disorder, PTSD) and must be more than normal distress or grief; treatment is *predominantly psychological* (supportive, problem-solving, CBT) with drugs only complementary and symptom-targeted, and, despite its "minor" reputation, it carries a real impulsive self-harm risk that mandates active suicide-risk assessment.

25.7 Management: the predominantly psychological approach

Psychosocial strategies are the mainstay. The guiding principle is that adjustment disorder is treated *predominantly psychologically*: understand the meaning of the stressor to the patient, minimise its day-to-day impact, and mobilise adaptive coping (Kaplan & Sadock CTP 2024). The evidence base is thin, and the first formal systematic review appeared only in 2018, but the psychotherapeutic options that have been used are supportive psychotherapy, cognitive-behavioural and behavioural approaches, *problem-solving* techniques, relaxation training and brief psychodynamic work. Treatment is often short-term, with crisis intervention and case management layered on where acuity or self-harm risk demands it. Notably, in a Cochrane meta-analysis, *problem-solving therapy* was the intervention that reduced the time for patients to return to work.

The India device. Adjustment disorder is a high-volume presentation in Indian consultation-liaison and primary-care practice, exactly the settings where the benzodiazepine over-prescription problem is most entrenched: the reflex to reach for alprazolam or another short-acting benzodiazepine for a distressed patient after a life event. That reflex is doubly wrong here, the disorder is predominantly psychological, and even short-term benzodiazepine use in adjustment disorder can produce withdrawal (Kaplan & Sadock CTP 2024). Against India's wide anxiety, OCD and PTSD treatment gap, and in line with the Indian Psychiatric Society clinical practice guidelines, the answer is psychological support and problem-solving first, with medication reserved and symptom-targeted, never a benzodiazepine as the default.

INDIA

The highest-yield Indian point: adjustment disorder is one of the commonest reasons a distressed patient after a life event is handed a benzodiazepine (typically alprazolam) in Indian outpatient and consultation-liaison practice. It is precisely the presentation that should *not* be medicalised by reflex: the mainstay is psychological (supportive work, problem-solving, brief CBT), and even short-term benzodiazepine use risks withdrawal. The IPS-aligned line is support and problem-solving first, and any drug used briefly and only for a specific symptom such as severe insomnia or anxiety.

GOOD TO REMEMBER

- **Psychological treatment (the principle):** the mechanism is to help the patient process the *meaning* of the stressor and mobilise adaptive coping, so the first-line move is a brief, predominantly psychological intervention, supportive psychotherapy, problem-solving therapy (the option shown to speed return to work) or brief CBT; the signature caution is that adjustment disorder carries a real impulsive self-harm risk, so ongoing suicide-risk assessment and, where acuity demands, crisis intervention are built in; the first-line indication is essentially every case, with drugs kept complementary (Kaplan & Sadock CTP 2024).

25.8 Pharmacotherapy: complementary, symptom-targeted, and benzodiazepine-sparing

Where drugs fit. Medication is a *complementary*, not a primary, treatment, and the evidence is limited: Stein's 2018 systematic review of adjustment-disorder pharmacotherapy could identify only 11 randomised trials (Kaplan & Sadock CTP 2024). The sensible practice is to target specific symptoms in the short run, for example treating severe insomnia or severe anxiety, and to use an antidepressant for moderate-to-severe depressive symptoms. SSRI agents (fluoxetine, sertraline, escitalopram, and the others) have been found useful for some subthreshold depressive symptoms and certain subtypes, but the evidence for improving depressive symptoms in adjustment disorder is genuinely scant, and psychosocial strategies remain the mainstay.

The benzodiazepine problem. Benzodiazepines carry particular caution: even short-term use in adjustment disorder can result in withdrawal, and the harms are magnified in older adults and those with a substance use disorder (Kaplan & Sadock CTP 2024). Comparator studies in the anxiety subtype found the non-benzodiazepine GABA-A modulator etifoxine (a European agent) at least as effective as, and better tolerated than, lorazepam or alprazolam, with less rebound anxiety on discontinuation, a useful teaching point on why a benzodiazepine is not the natural first drug even when anxiety predominates. The deeper anxiolytic and hypnotic pharmacology, benzodiazepines, buspirone (Buspin), pregabalin and dependence, is developed in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes; the SSRI pharmacology and dosing sit in the Mood disorders: pharmacotherapy notes.

COMMON TRAP

Reaching for a benzodiazepine as the default treatment for adjustment disorder because the patient is anxious after a life event. It is not first-line, the disorder is predominantly psychological; and even short-term benzodiazepine use here can cause withdrawal, especially in older adults and those with substance use disorder (Kaplan & Sadock CTP 2024). Target the specific symptom briefly if you must, but the mainstay is psychological, not sedative.

1 month	3 months	6 months	5 to 20%
ICD-11 USUAL ONSET WINDOW AFTER THE STRESSOR	DSM-5-TR ONSET WINDOW AFTER THE STRESSOR	RESOLUTION ONCE THE STRESSOR/CONSEQUENCES END	OF OUTPATIENT MENTAL-HEALTH CASES (PRINCIPAL DIAGNOSIS)

WORKED EXAMPLE

A previously well woman in her forties, redeployed under sustained pressure during a public-health crisis, presents after a low-lethality overdose. She has no prior psychiatric history. Over the preceding weeks she has been unable to sleep, tearful at work and at home, withdrawing from family meals, and consumed by worry about the risk she poses to an immunosuppressed spouse, clear *preoccupation with the stressor* and a failing effort to adapt, but she does not meet full criteria for a depressive episode. This is an adjustment disorder. Management was crisis intervention in the emergency setting, then individual psychotherapy and a peer-support group over about six months, with an antidepressant added as a *complement* and planned to taper once the stressor eased, not a standing benzodiazepine. She reached full remission. The example carries the whole topic: preoccupation-plus-failure-to-adapt below the depressive-episode threshold, a real self-harm risk, and psychological treatment first with medication complementary.

26 · The neurobiology of trauma and fear conditioning

The **neurobiology of trauma** is the story of a normal survival-learning system pushed past its design limits by an overwhelming event. A trauma is, in learning terms, an intensely aversive experience that teaches the brain, fast and durably, that a set of previously neutral cues now predict catastrophe. The machinery that does this learning is the same amygdala-centred fear circuit that underlies ordinary anxiety, but in post-traumatic stress disorder (PTSD) the learning is too strong, the context that should contain it fails, the stress-hormone axis that should switch off the alarm is dysregulated, and the prefrontal brake that should teach safety again is too weak to do so. Examiners test this as a four-part story, and the candidate who can name the four parts in order, amygdala over-learning, hippocampal context failure, HPA-axis dysregulation and impaired prefrontal extinction, has the answer.

Why it matters clinically. The neurobiology is not decoration; it is the rationale for every effective treatment. Trauma-focused psychotherapy works because it drives **fear extinction** through the prefrontal cortex, the very process that is impaired; a beta-blocker was trialled to blunt the noradrenergic consolidation of the traumatic memory; prazosin dampens the noradrenergic hyperarousal that fires the nightmares. Two ideas anchor the whole answer. First, PTSD is a disorder of fear learning that will not extinguish, an over-consolidated fear memory in the **amygdala** that the prefrontal cortex cannot teach the brain to switch off. Second, the disorder is maintained, not merely triggered, so the neurobiology explains why symptoms persist for years after the threat is gone. The detailed fear-circuit anatomy and the receptor systems are developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; this topic applies that anatomy to trauma and refers to the accompanying figure for the fear-conditioning map.

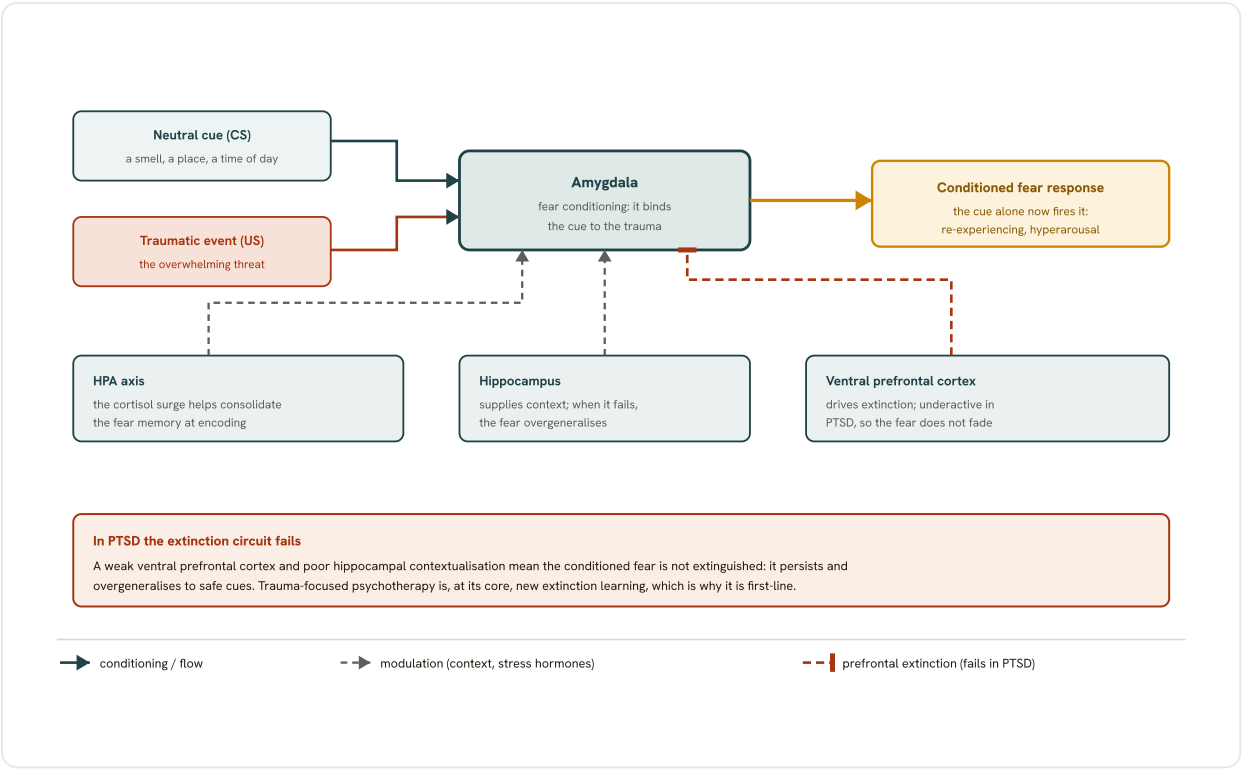


Fig 14.19 The neurobiology of trauma: fear conditioning and its failed extinction. At the moment of trauma the amygdala binds a neutral cue (the conditioned stimulus) to the overwhelming event (the unconditioned stimulus), so that afterwards the cue alone fires the conditioned fear response, the re-experiencing and hyperarousal of PTSD. The HPA-axis cortisol surge helps consolidate that memory, and the hippocampus normally tags it with a safe context. Recovery depends on extinction, new learning driven by the ventral prefrontal cortex that the cue is now safe. In PTSD the prefrontal extinction circuit is underactive and the hippocampus contextualises poorly, so the fear neither fades nor stays tied to its original context but overgeneralises; trauma-focused psychotherapy works precisely because it is new extinction learning. The pathway anatomy is taught in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

26.1 Fear conditioning: how a neutral cue becomes a trauma trigger

The learning paradigm to state first. **fear conditioning** is Pavlovian associative learning applied to threat. In the laboratory paradigm an animal meets an intrinsically neutral cue, the conditioned stimulus (CS, for example a tone), paired repeatedly with an inherently aversive **unconditioned stimulus** (UCS, for example a shock); after conditioning, the cue that was paired with the shock (the CS+) alone provokes the defensive response, freezing and a heightened startle, while the cue never paired with shock (the CS-) does not (Kaplan & Sadock CTP 2024). The neutral cue has acquired threat value.

The clinical translation. This is exactly what trauma does. The horn, the smell of diesel, the particular light of the time of day, whatever neutral cue happened to be present at the moment of the trauma (the UCS), becomes a conditioned fear cue (the CS+) that thereafter fires the full alarm on its own. The intrusive re-experiencing and the cue-driven panic of PTSD are conditioned fear responses to CS+ cues laid down at the time of the event; naming the trauma as the UCS and the trigger as the CS+ is the cleanest way to explain a flashback in circuit terms.

WORKED EXAMPLE

A survivor of a road collision hears a car horn (a neutral cue, present at the crash) and is instantly flooded with terror, a pounding heart and a vivid sense of the impact. In conditioning language the crash was the UCS, the horn was a co-occurring cue that became the CS+, and the terror is the conditioned fear response the CS+ now evokes on its own. The lateral amygdala is where that horn-to-terror association was welded, and it is why an apparently trivial sound reliably reproduces the alarm.

26.2 The amygdala: where the trauma memory is welded

The site of the plasticity. The amygdala, specifically its lateral nucleus, is the convergence point where the conditioned cue (CS) and the aversive trauma (UCS) meet; single lateral-nucleus neurons receive both streams, and the strengthening of that synapse (long-term potentiation) is the physical substrate of the acquired fear (Kaplan & Sadock CTP 2024). The central nucleus is the output that broadcasts the fear response to the hypothalamus, brainstem and periaqueductal grey. In trauma this plasticity is excessive: an overwhelming UCS produces an over-consolidated, easily reactivated fear memory.

The imaging signature. The consequence is an amygdala set on a hair trigger. Functional imaging in PTSD shows amygdala *hyper*-responsivity to trauma-related and even to generally threatening or fearful stimuli, the neural correlate of the exaggerated startle and the sense of current threat (Kaplan & Sadock CTP 2024; New Oxford Textbook of Psychiatry). The amygdala is the hub whose over-reactivity the whole rest of the circuit is meant to, and in PTSD fails to, restrain.

RULE **PTSD is over-consolidated fear learning the brain cannot extinguish.** A hyper-responsive amygdala holds an over-strong trauma memory (excessive fear conditioning), a failing hippocampus lets the fear generalise out of its context, a dysregulated HPA axis fails to shut the alarm down, and a weak ventromedial prefrontal cortex cannot drive the extinction that would teach safety; the fear therefore persists.

26.3 The hippocampus: encoding the context, and why it fails

Context is the hippocampus's job. The hippocampus supplies the *context* of a fear memory, the where and when that tells the brain whether a cue is dangerous *here and now* or only in the original setting; it is central to contextual fear conditioning and to telling a safe context apart from a dangerous one (Kaplan & Sadock CTP 2024). Intact hippocampal gating is what normally keeps a conditioned fear tied to its proper situation.

How the failure produces PTSD symptoms. When hippocampal contextual processing fails, the fear *over-generalises*: cues that merely resemble the trauma, or occur in plainly safe settings, trigger the full response, which is the over-generalisation that characterises PTSD (Kaplan & Sadock CTP 2024; New Oxford Textbook of Psychiatry). The hippocampus is also uniquely vulnerable to the very stress hormones the trauma unleashes: the dentate-gyrus to CA3 system is delicately balanced, and chronic stress lasting longer than about three weeks impairs hippocampal-dependent function while it *enhances* amygdala-dependent fear conditioning, a

double hit that reduced hippocampal volume in PTSD may reflect (New Oxford Textbook of Psychiatry). A weaker context signal and a stronger fear memory pull in the same maladaptive direction.

PEARL

Read the amygdala and the hippocampus as a pair of opposing dials that trauma turns the wrong way. Stress *up*-regulates amygdala fear conditioning and *down*-regulates hippocampal contextual function at the same time. The result is a fear memory that is both too strong (amygdala) and untethered from its context (hippocampus), so it fires everywhere. That single sentence answers "why does PTSD generalise?"

26.4 The HPA axis: the stress-hormone response and its dysregulation

The axis and its normal job. The **hpa axis** (hypothalamic-pituitary-adrenal axis) is the body's neuroendocrine stress response: the amygdala drives the hypothalamic paraventricular nucleus to release corticotropin-releasing hormone, which drives pituitary ACTH, which drives adrenal cortisol; cortisol then normally feeds back to terminate the stress response (Kaplan & Sadock CTP 2024; New Oxford Textbook of Psychiatry). Cortisol's job is, in part, to switch the alarm *off* once the threat has passed.

The dysregulation in PTSD, and its counter-intuitive direction. The examinable, counter-intuitive fact is that PTSD is associated with *low* or normal, not high, basal cortisol, together with an *enhanced* negative-feedback sensitivity of the axis (an exaggerated cortisol suppression to dexamethasone), a pattern distinct from the high-cortisol picture of melancholic depression (Kaplan & Sadock CTP 2024). Because glucocorticoids are thought to facilitate extinction learning and to constrain the over-consolidation of a traumatic memory, an inadequate cortisol response at the time of trauma is one proposed reason the fear memory is laid down too strongly and extinguishes too poorly; consistent with this, giving stress-dose hydrocortisone around a major stressor has been trialled to reduce later PTSD, hypothesised to work by facilitating extinction and impairing consolidation of the traumatic event (New Oxford Textbook of Psychiatry). The HPA story is thus not "too much stress hormone" but a dysregulated axis that fails to do its off-switch and extinction-facilitating work.

TRAP **Assuming PTSD means high cortisol.** Unlike melancholic depression, chronic PTSD is classically associated with *low or normal* basal cortisol and *enhanced* glucocorticoid negative feedback (exaggerated dexamethasone suppression); writing "raised cortisol" is the reflex error that loses the mark. The maladaptive point is a failure of the axis to regulate and to facilitate extinction, not a simple excess.

26.5 Fear extinction: the safety learning that is meant to switch the alarm off

What extinction is, and is not. **fear extinction** is the learned reduction of a conditioned fear when the CS+ is presented repeatedly *without* the UCS, so the cue no longer predicts the threat (Kaplan & Sadock CTP 2024). The crucial point, and a favourite examiner distinction, is that extinction does *not* erase the original fear memory; it creates a new, competing "safety" memory that *inhibits* the fear response. Because the original memory persists, extinguished fears can

return (spontaneous recovery, renewal in a new context, reinstatement after a stressor), which is exactly why PTSD relapses under stress and why treatment is safety-learning rather than deletion.

The prefrontal driver. Extinction is driven by the ventromedial prefrontal cortex (the infralimbic region in the rodent), which acts through the amygdala's GABAergic intercalated cells to inhibit central-nucleus output; a strong ventromedial prefrontal brake means a fear that can be extinguished (Kaplan & Sadock CTP 2024). This is the mechanism that trauma-focused exposure therapy recruits: repeated exposure to trauma-related cues in a safe environment leads to extinction of the fear response, and agents such as D-cycloserine (an NMDA partial agonist) have been trialled to enhance that extinction learning (New Oxford Textbook of Psychiatry).

MNEMONIC

A-H-H-E: the four-hit story of trauma

Run the neurobiology of trauma in four beats. **A**mygdala over-learns the fear (excessive conditioning, hyper-responsivity). **H**ippocampus loses the context, so fear over-generalises. **H**PA axis is dysregulated (low/normal cortisol, over-sensitive feedback, extinction not facilitated). **E**xtinction fails because the ventromedial prefrontal brake is too weak. Naming A-H-H-E in order is the fastest route to the "neurobiology of PTSD" marks.

26.6 Impaired prefrontal extinction: the lesion that maintains PTSD

The core maintaining lesion. The single circuit abnormality that best explains why PTSD *persists* is impaired prefrontal-mediated extinction. In PTSD the ventromedial prefrontal cortex is *hypo*-active and structurally reduced, while the amygdala is hyperactive; a weak prefrontal brake over a hot amygdala means the fear cannot be taught to switch off, and the conditioned response keeps firing to trauma cues long after any real danger has gone (Kaplan & Sadock CTP 2024; New Oxford Textbook of Psychiatry). Where ordinary recovery from a frightening event is spontaneous extinction, PTSD is the failure of that extinction.

Why this is the treatment target. This is why trauma-focused psychotherapy, not sedation, is the first-line treatment: exposure-based and cognitive trauma therapies work by driving successful extinction and safety learning through the prefrontal cortex, correcting the very process that is impaired. It is also why a benzodiazepine is the wrong tool, it sedates the alarm and can actually impair the extinction learning on which recovery depends, and why it has no place in PTSD treatment. The general exposure principle and the CBT model are developed in the Psychotherapies, clinical assessment, MSE and nosology notes; the licensed drugs, doses and the trauma-focused-first algorithm sit in the PTSD-treatment material.

WORKED EXAMPLE

Two soldiers survive the same ambush. Weeks later one no longer startles at a slammed door: repeated safe exposures let his ventromedial prefrontal cortex extinguish the conditioned fear. The other still dives for cover, has nightly nightmares and cannot enter a car park: his amygdala holds an over-consolidated fear his under-active prefrontal cortex cannot extinguish, his hippocampus has let the fear generalise to any enclosed space, and his HPA axis is not doing its off-switch work. The difference between recovery and PTSD is, in circuit terms, whether prefrontal extinction succeeds.

26.7 Noradrenaline and the consolidation of the traumatic memory

The amplifier that also fixes the memory. The noradrenergic system, driven by the locus coeruleus, does two things in trauma: it produces the peripheral hyperarousal (tachycardia, hypervigilance, exaggerated startle) that the patient feels, and, because noradrenaline released during a highly emotional event enhances the amygdala consolidation of that memory, it helps weld the traumatic memory in *more* strongly (Kaplan & Sadock CTP 2024; New Oxford Textbook of Psychiatry). A trauma is remembered vividly in part because it was encoded under a noradrenergic surge.

The pharmacological corollary. This gives two rational, noradrenergically targeted interventions. Peri-traumatic propranolol (Ciplar, Inderal), a beta-blocker, was trialled to blunt amygdala fear conditioning and the noradrenergic consolidation of the memory, though the evidence is insufficient to recommend it routinely for prevention (New Oxford Textbook of Psychiatry). And prazosin (Minipress, Prazopress), an alpha-1 antagonist, dampens the central noradrenergic hyperarousal that drives PTSD nightmares, which is why it is the targeted add-on for trauma-related nightmares. Both are the neurobiology cashed out as treatment; the prescribing detail sits in the PTSD-treatment material.

GOOD TO REMEMBER

- **Propranolol / prazosin (the noradrenergic handles on trauma):** noradrenaline released during trauma both drives the hyperarousal and strengthens amygdala consolidation of the memory; propranolol (Ciplar, Inderal), a beta-blocker, was trialled peri-traumatically to blunt that consolidation but is not routinely recommended for prevention, whereas prazosin (Minipress, Prazopress), an alpha-1 blocker, is the established add-on for trauma nightmares by lowering central noradrenergic tone, the signature caution for prazosin being first-dose hypotension.

26.8 Putting the trauma circuit together

One loop, four failures. The neurobiology of trauma is a single fear-learning loop failing at four nodes at once. The amygdala over-learns the fear (excessive conditioning, hyper-responsivity); the hippocampus loses the context, so fear generalises; the HPA axis is dysregulated and fails to facilitate the extinction and shut-down it should; and the ventromedial prefrontal cortex cannot drive the extinction that would teach safety. The result is a conditioned fear response, laid down under a noradrenergic surge, that fires to trauma cues indefinitely. Every effective treatment targets one of these nodes, and trauma-focused psychotherapy targets the most important, the failed prefrontal extinction.

NODE / PROCESS	WHAT IT DOES NORMALLY	THE FAILURE IN TRAUMA / PTSD
Amygdala (lateral nucleus)	Welds the CS-UCS association; site of fear conditioning (LTP)	Over-consolidated fear memory; amygdala hyper-responsive to threat
Amygdala (central nucleus)	Broadcasts the fear response to hypothalamus, brainstem, PAG	Drives exaggerated startle and sense of current threat
Hippocampus	**Supplies the context of the fear memory**	Context fails, so fear over-generalises to safe cues; reduced volume
HPA axis	Cortisol terminates the stress response; facilitates extinction	**Low/normal cortisol, enhanced feedback; extinction not facilitated**
Ventromedial prefrontal cortex	**Drives fear extinction via GABAergic intercalated cells**	Hypo-active and reduced; extinction fails, fear persists
Locus coeruleus / noradrenaline	Arousal; enhances emotional memory consolidation	Hyperarousal and over-strong memory encoding; nightmares
Extinction learning	New safety memory inhibits the conditioned fear	**Impaired; the target of trauma-focused psychotherapy**

The trauma fear-learning loop node by node, mapped to its normal role and its PTSD failure; the accompanying figure draws the fear-conditioning sequence (neutral cue paired with the trauma UCS becomes a CS+ that fires the amygdala, with the hippocampal context signal and the prefrontal extinction brake shown as the two systems that fail). Grounded in Kaplan & Sadock CTP 2024 and the New Oxford Textbook of Psychiatry.

26.9 Definitions to fix the vocabulary

Fear conditioning

Pavlovian learning in which a neutral cue (CS), paired with an aversive event (UCS), acquires the power to evoke a fear response.

Conditioned stimulus (CS+)

The cue that was paired with the trauma and now triggers the conditioned fear on its own; the CS- is the unpaired cue that does not.

Unconditioned stimulus (UCS)

The intrinsically aversive event, the trauma itself, that gives the cue its threat value.

Fear extinction

Learned reduction of a conditioned fear when the CS+ is met without the UCS; a new safety memory that inhibits, not erases, the fear.

HPA axis

Hypothalamic-pituitary-adrenal stress axis (CRH to ACTH to cortisol); cortisol normally terminates the stress response and facilitates extinction.

Contextual fear

Fear tied by the hippocampus to a specific setting; its failure produces the over-generalisation of PTSD.

GOOD TO REMEMBER

- **PTSD (the syndrome, in circuit terms):** the defining neurobiology is a conditioned fear memory over-consolidated in a hyper-responsive amygdala, stripped of its context by a failing hippocampus (fear over-generalises), against a dysregulated HPA axis (low/normal cortisol, enhanced negative feedback) and a hypo-active ventromedial prefrontal cortex that cannot drive extinction; the discriminator from ordinary recovery is that recovery *is* spontaneous extinction while PTSD is its failure, and the first therapeutic step is trauma-focused psychotherapy to re-drive prefrontal extinction (never a benzodiazepine, which impairs it).

INDIA

Trauma is abundant in India, road-traffic collisions, interpersonal and gender-based violence, disasters and displacement, yet PTSD is under-recognised and under-treated, folded into vague "tension" or somatic complaints and rarely reaching a psychiatrist; the trauma treatment gap is wide. Into that gap steps the country's **benzodiazepine over-prescription** problem: alprazolam and clonazepam are handed out freely, often long-term, for post-trauma distress and insomnia, which is precisely the wrong move on this circuit, because a benzodiazepine sedates the alarm and can *impair* the prefrontal extinction learning on which real recovery depends, while breeding dependence. The neurobiology gives the corrective the Indian Psychiatric Society CPG endorses: trauma-focused psychotherapy first (it drives the failed extinction), an SSRI or SNRI where a drug is needed, and prazosin (Minipress, Prazopress) for nightmares, with no role for a benzodiazepine. The correct answer treats the fear circuit, not merely the sleeplessness.

4	2	21
FAILING NODES TO NAME (AMYGDALA, HIPPOCAMPUS, HPA AXIS, PREFRONTAL EXTINCTION)	TRAUMA-CONDITIONING TERMS (CS+ TRIGGER, UCS TRAUMA)	DAYS OF STRESS BEYOND WHICH HIPPOCAMPAL FUNCTION IS IMPAIRED AND AMYGDALA CONDITIONING ENHANCED

HOLD THIS

PTSD is a fear-conditioning disorder: an overwhelming trauma (UCS) welds an over-strong conditioned fear to neutral cues (CS+) in a hyper-responsive amygdala, a failing hippocampus lets that fear generalise out of its context, a dysregulated HPA axis (low or normal cortisol, over-sensitive feedback) fails to facilitate extinction, and a hypo-active ventromedial prefrontal cortex cannot drive the fear extinction that would teach safety, so the alarm keeps firing, which is why trauma-focused psychotherapy (re-driving prefrontal extinction) is first-line and a benzodiazepine, which impairs extinction, is never used.

27 . Prolonged grief disorder

A new diagnosis, and an examiner's favourite trap. **Prolonged grief disorder** is the pathological grief syndrome added to DSM-5-TR (2022) and codified in ICD-11 (6B42). It sits in the trauma- and stress-related grouping alongside PTSD and adjustment disorder, and its whole diagnostic weight rests on one judgement: has grief persisted, and become impairing, *beyond* what this person's social, cultural and religious context would expect. The syndrome the DSM once parked in an appendix as **persistent complex bereavement disorder** is now a full disorder.

The examiner is rarely testing whether you can list the symptoms. They are testing whether you know the **time thresholds**, whether you can separate this from a depressive episode and from PTSD, and above all whether you resist the reflex to medicalise ordinary mourning. Grief is not a disease; only a grief response that is atypically prolonged, pervasive and disabling earns the label.

27.1 What the entity is

Persistent grief. Both classifications describe a **persistent and pervasive grief response** following the death of someone close, dominated by yearning or longing for the deceased, or by persistent preoccupation with them, and carrying intense emotional pain (sadness, guilt, anger, denial, difficulty accepting the death, emotional numbness, a sense that part of the self has died). This is **persistent grief** that has not moved through the normal arc of adaptation. The phrase to memorise is that the response **markedly exceeds expected social, cultural or religious norms** for that person's context.

27.2 The time thresholds (where marks are won and lost)

Two systems, two numbers. The single highest-yield discriminator is duration, and the two manuals differ. ICD-11 requires the response to have persisted for an atypically long time, giving a floor of at least **6 months** (longer in some cultural contexts). DSM-5-TR sets a higher adult bar: the death must have occurred at least **12 months** ago for adults (at least **6 months** for children and adolescents), and the symptoms must have been present nearly every day for at least the last month. Do not conflate the two.

FEATURE	ICD-11 (6B42)	DSM-5-TR
Minimum time since death	**at least 6 months**	**12 months adult; 6 months child/adolescent**
Core (one or both)	yearning/longing OR preoccupation with the deceased	intense yearning OR preoccupation, nearly every day, last month
Accompanying symptoms	intense emotional pain features (not a fixed count)	at least 3 of 8 (identity disruption, disbelief, avoidance of reminders, intense emotional pain, difficulty reintegrating, emotional numbness, life feels meaningless, intense loneliness)
Threshold clause	exceeds cultural/religious norms; impairment	exceeds social/cultural/religious norms; distress or impairment

The ICD-11 versus DSM-5-TR criteria for prolonged grief disorder; the duration cells are the ones examiners probe.

RULE **Duration is the discriminator.** ICD-11 says at least 6 months; DSM-5-TR says at least 12 months in adults. Anchor every answer to the number for the system being asked.

27.3 Do not pathologise normal grief too early

The threshold is cultural, not just temporal. Normal bereavement is protective, self-limiting and does not need psychiatric treatment. Both manuals build in a boundary-with-normality clause: a grief reaction within the normative period for the person's cultural and religious context

is *normal*, and it is often decisive to ask whether family, friends and community who share that perspective regard the duration or intensity as abnormal. Some traditions prescribe grieving that lasts a year or is deliberately reawakened at the first anniversary; a mourning ritual that runs its expected course is not a disorder.

TRAP **Labelling grief as disorder from the outset.** Applying the diagnosis before the time threshold, or against the person's own cultural norm, medicalises normal mourning; the community's reading of what is abnormal is part of the criterion.

27.4 Discriminating from depression and PTSD

Circumscribed versus pervasive. Prolonged grief disorder and a depressive episode share sadness, loss of interest, social withdrawal, guilt and suicidal ideation, but grief is *focused on the loss*: the yearning, the difficulty accepting the death, the sense that part of the self has died, feeling bitter about the loss. Depressive cognitions spread across many areas of life and pervasive low mood dominates. Against PTSD, the person with prolonged grief may be preoccupied with the circumstances of the death but does **not re-experience** them as happening again in the here and now; intrusive re-experiencing, flashbacks and hyperarousal point to PTSD. All three can co-occur, and each should be diagnosed where full criteria are met.

WORKED EXAMPLE

A widow, 14 months after her husband's death, still lays out his belongings untouched, longs for him nearly every day, cannot re-engage with friends and feels life is meaningless, yet finds joy in her grandchildren and has no pervasive anhedonia. The distress is circumscribed to the loss and the death is more than 12 months past: this meets DSM-5-TR prolonged grief disorder, not a depressive episode. Had she instead relived the moment of his death as if it were happening now, PTSD would move up the list.

27.5 Where it fits in the Indian setting

An old idea with a new name. Indian teaching has long distinguished normal grief from a **morbid grief reaction** (Gurmeet Singh's classification), where symptoms of grief are exaggerated or run prolonged beyond about 6 months without spontaneous recovery. Bowlby's three phases of response to loss, protest then despair then detachment, remain the standard developmental scaffold. The clinical caution matters in Indian practice: with the anxiety, OCD and PTSD treatment gap already leaving most common mental disorders untreated, scarce specialist time should not be spent converting culturally sanctioned mourning into a prescription, and the reflex to reach for a **benzodiazepine** for an acutely grieving person, a real over-prescription problem in Indian outpatient settings, is exactly the wrong move.

INDIA

Gurmeet Singh's normal-versus-morbid grief distinction predates the ICD-11 entity and is the classification most likely quoted by Indian examiners. Frame prolonged grief disorder as the formalised successor to morbid/pathological grief, hold the cultural-norm clause front and centre in a society with elaborate, lengthy mourning customs, and keep benzodiazepines off the acute-grief prescription.

27.6 Management: grief-targeted psychotherapy first

Talk before pills. Uncomplicated grief needs no drug. For prolonged grief disorder the evidence base points to a grief-targeted psychotherapy as first-line, most notably complicated grief treatment (the manualised approach developed by Shear), a structured therapy that combines processing the reality of the loss with re-engaging in life, and family-focused grief therapy in palliative and bereavement settings. Antidepressants are **not** routinely indicated for the grief itself: trials of SSRIs for grief have been largely negative, and drug treatment is reserved for a co-occurring depressive episode or another comorbid disorder diagnosed in its own right. If an antidepressant is used for comorbid depression, it is an SSRI (for example sertraline; Indian brands include the generic across many manufacturers), not a benzodiazepine.

RULE **Grief-targeted psychotherapy is the treatment; drugs treat comorbidity.** Complicated grief treatment first; reserve an SSRI for a diagnosed comorbid depression, and never a benzodiazepine for the grief.

6	12	3 of 8	9 to 25%
ICD-11 MINIMUM MONTHS SINCE DEATH	DSM-5-TR ADULT MINIMUM MONTHS	DSM-5-TR ACCOMPANYING SYMPTOMS	BEREAVED OLDER ADULTS DEVELOPING PGD

MNEMONIC

GRIEF-TOO-LONG

Grief that is persistent and pervasive; **R**eaction exceeds cultural/**R**eligious norms; **I**ntense yearning or preoccupation is the core; **E**motional pain plus impairment; **F**ocused on the loss (not pervasive like depression, not re-experienced like PTSD); **TOO LONG** = past the threshold (6 months ICD-11, 12 months DSM-5-TR adult). The unpacking is the diagnosis.

PEARL

The term you will meet under several names points to one construct: **complicated grief**, morbid/pathological grief, persistent complex bereavement disorder (the old DSM-5 appendix name) and prolonged grief disorder (the current entity) are the historical layers of the same idea. When an examiner uses any of these, answer with the current ICD-11/DSM-5-TR criteria.

GOOD TO REMEMBER

- **Prolonged grief disorder (syndrome):** defining criterion is a persistent, pervasive grief response with intense **yearning** or preoccupation with the deceased that exceeds the person's cultural/religious norm; time floor is at least 6 months (ICD-11) or at least 12 months in adults (DSM-5-TR); the first discriminator against depression is that grief is circumscribed to the loss, and against PTSD that the death is not re-experienced in the here and now.
- **Complicated grief treatment (psychotherapy):** the grief-targeted, manualised first-line therapy (Shear); principle is to process the reality of the loss while restoring engagement with life; signature caution is that antidepressants do not treat the grief itself and are reserved for comorbid depression, never a benzodiazepine for acute grief.

HOLD THIS

Prolonged grief disorder = persistent yearning/preoccupation exceeding the cultural norm, at least 6 months (ICD-11) or at least 12 months in adults (DSM-5-TR) after the death; treat with grief-targeted psychotherapy, and do not pathologise normal mourning too early.

28 · Reactive attachment and disinhibited social engagement disorders

Two disorders of early, severe neglect. These are the trauma- and stressor-related disorders of the very young child. **Reactive attachment disorder** (RAD) is the emotionally withdrawn, inhibited pattern toward caregivers; **disinhibited social engagement disorder** (DSED, formerly disinhibited attachment disorder of childhood) is indiscriminate, over-familiar behaviour toward strangers. Both are named here briefly and criterion-led; the fuller developmental and services detail belongs to the child-psychiatry chapters. The exam hook is that both require the same aetiology, **early neglect** so severe it prevents normal attachment forming, yet they express in opposite behavioural directions.

Keep two nosological facts in front of you. First, DSM-5-TR and ICD-11 agree in splitting the old single "attachment disorder" into these two distinct disorders, both classed as trauma- and stressor-related, not as childhood-onset residuals. Second, both need a developmental age of at least **9 months** (the level at which selective attachment becomes possible) and onset before **5 years**. This note stays deliberately short: the point is the criterion, the discrimination, and the fact that treatment is psychosocial, never a drug.

28.1 Shared aetiology: pathogenic care

Insufficient care is the gateway criterion for both. Neither disorder is diagnosed without a documented history of a pattern of extremes of insufficient care: persistent social neglect or deprivation of basic emotional needs, repeated changes of primary caregiver that limit stable attachment (for example serial foster placements), or rearing in unusual settings with high child-to-caregiver ratios (institutions) that severely limit selective attachment. This "grossly insufficient care" is presumed causative, so the history of **early neglect** is not optional context, it is a criterion. Absent such a history the diagnoses are rare and, if made, are likely wrong.

28.2 Reactive attachment disorder: the withdrawn, inhibited child

Minimal comfort-seeking and minimal response to comfort. The child with RAD shows a consistent pattern of emotionally withdrawn, inhibited behaviour toward adult caregivers: rarely or minimally seeking comfort when distressed, and rarely or minimally responding to comfort when it is offered. Layered on this is a persistent social and emotional disturbance, reduced positive affect, and episodes of unexplained irritability, sadness or fearfulness even during non-threatening interactions. It is, in effect, the absence of an organised attachment where one should have formed. RAD is diagnosed only when the child does not meet criteria for autism spectrum disorder.

28.3 Disinhibited social engagement disorder: the over-familiar child

Indiscriminate over-familiarity with unfamiliar adults. The child with DSED actively approaches and engages unfamiliar adults with a striking lack of the normal stranger wariness that emerges between **7 to 9 months**. DSM-5-TR requires at least **two** of: reduced or absent reticence in approaching unfamiliar adults; overly familiar verbal or physical behaviour beyond age-appropriate and culturally sanctioned bounds; diminished or absent checking back with the caregiver after venturing away, even in unfamiliar settings; and willingness to go off with an unfamiliar adult with little or no hesitation. The behaviour is sometimes called "indiscriminate friendliness," but it is intrusive, boundary-crossing, and self-endangering rather than sociable.

28.4 RAD versus DSED versus their mimics

Two discriminators carry the marks. First, the direction of behaviour: RAD is under-social and withdrawn, DSED is over-social and disinhibited. Second, the exclusion pattern: **autism spectrum disorder** excludes RAD (both show diminished social reciprocity, but the ASD child has restricted, repetitive behaviours and a history without required neglect), whereas ASD does not exclude DSED. DSED must also be more than the behavioural impulsivity of **ADHD**, which may co-occur; the DSED behaviour is specifically social disinhibition toward strangers, not general impulsivity. The table alongside sets out the split.

AXIS	REACTIVE ATTACHMENT DISORDER (RAD)	DISINHIBITED SOCIAL ENGAGEMENT DISORDER (DSED)
Core behaviour	**Emotionally withdrawn, inhibited toward caregivers**	**Indiscriminate over-familiarity with unfamiliar adults**
Comfort	Minimal seeking and minimal response to comfort	Reduced checking-back with the caregiver
Required threshold	Full withdrawn pattern plus social/emotional disturbance	**At least 2 disinhibited behaviours**
Developmental age / onset	At least 9 months; before age 5	At least 9 months; before age 5
Autism spectrum disorder	**Excludes the diagnosis**	**Does NOT exclude the diagnosis**
Response to good care	Signs typically recede within weeks of adequate caregiving	**May persist even after a stable attachment forms**

Same neglectful root, opposite behavioural expression; the autism exclusion and the response to remediation are the two most-tested discriminators.

28.5 Course: why the two diverge under good care

RAD tends to remit, DSED can stick. This is the highest-yield prognostic point. In children moved from institutional to adequate caregiving (the Bucharest Early Intervention Project randomised foster care against continued institutional care), RAD signs typically recede within weeks of an adequate caregiving environment. DSED behaviours improve but can persist in a minority even after the child forms a selective attachment to a foster or adoptive parent, which is why some argue the core deficit in DSED is not simply the absence of an attachment relationship. Earlier placement helps: signs of DSED are not reported when deprivation begins only after age 2, and attachment disorders are very rare in children adopted before **6 months** of age.

28.6 Management: the intervention is the caregiving environment

Change the care, not the child, and never a drug. There is no established pharmacotherapy for RAD or DSED; the treatment is a stable, sensitive, individualised caregiving relationship, delivered by placing the child with a committed caregiver (foster or adoptive) and coaching that caregiver to respond to the child's distress as if it had been requested, so the child learns comfort is available. The clinician also protects the child (DSED carries real danger from going off with strangers). Critically, the coercive "attachment therapies", holding, restraint and rebirthing, are unproven and dangerous, having caused child deaths, and are formally discredited (AACAP practice parameter). This is the one point where the benzodiazepine over-prescription theme becomes a pure trap: there is nothing to prescribe here.

RULE **No neglect, no diagnosis.** A documented history of grossly insufficient care is a criterion for both RAD and DSED, not background colour; without it, look elsewhere.

TRAP **Do not reach for medication.** There is no drug treatment for RAD or DSED; prescribing a sedative or antipsychotic for the "difficult" neglected child treats the clinician's discomfort, not the disorder, and misses that the intervention is the caregiving environment.

WORKED EXAMPLE

A boy of nearly four, adopted at 30 months from an orphanage with rotating caregivers, is brought for "hyperactivity." He approaches and chats with complete strangers, has more than once followed a stranger willingly, tolerates injury with an oddly high pain threshold, and his warmth toward adults feels shallow rather than selective. Teachers find him charming yet attention-seeking. The history of institutional early neglect plus at least two disinhibited-approach behaviours, beyond ADHD-type impulsivity, gives disinhibited social engagement disorder. Management is protective and relational, focused on curbing self-endangering approach and rewarding age-appropriate social hesitance; his approach to strangers persists at a reduced, more manageable level.

INDIA

Institutional care of orphaned, abandoned and maltreated young children remains widely used across Asia, India included, which is exactly the pathogenic-care setting that produces RAD and DSED; child-protection and alternative-care law (the Juvenile Justice framework and CARA-regulated foster care and adoption) is the practical lever, since the treatment is the caregiving environment, not a prescription. This is also the sharpest place to name the **benzodiazepine over-prescription** problem by its absence: the temptation to sedate a "hyperactive" or "withdrawn" neglected child must be resisted, because no anxiolytic or antipsychotic treats an attachment disorder, and the wider Indian pattern of handing out clonazepam or alprazolam against the IPS Clinical Practice Guidelines has no foothold here at all.

9 mo	before 5 yr	2	12 mo
MINIMUM DEVELOPMENTAL AGE FOR EITHER DIAGNOSIS	REQUIRED AGE OF ONSET	DISINHIBITED BEHAVIOURS NEEDED FOR DSED	PERSISTENCE FOR THE "PERSISTENT" SPECIFIER

MNEMONIC

IN versus OUT

RAD turns IN (withdrawn, inhibited, minimal comfort-seeking, and autism is excluded); **DSED turns OUT** (over-familiar, approaches strangers, checks back less, and autism is NOT excluded). Same neglect at the root, opposite direction of travel.

PEARL

The clean way to remember the prognosis split: RAD, being about the missing relationship, largely repairs when a good relationship arrives; DSED, being about missing stranger-wariness and inhibitory control, can outlast the arrival of a secure attachment.

GOOD TO REMEMBER

- **Reactive attachment disorder (RAD):** defining criterion is a consistent emotionally withdrawn, inhibited pattern toward caregivers, minimal comfort-seeking and minimal response to comfort, on a history of grossly insufficient care, developmental age at least 9 months and onset before 5 years; autism spectrum disorder excludes it, and the first step is to confirm the neglect history and check the child is not autistic.
- **Disinhibited social engagement disorder (DSED):** defining criterion is at least two disinhibited behaviours toward unfamiliar adults (over-familiarity, reduced reticence, diminished checking-back, willingness to go off with a stranger) beyond ADHD impulsivity, on the same neglect history and same age window; autism does NOT exclude it, and the discriminator from RAD is the outward, over-social direction of behaviour.
- **Caregiving intervention (the "therapy"):** the principle is that a stable, sensitive, individualised caregiving relationship is itself the treatment; there is no established medication, and coercive holding or "attachment" therapies are dangerous and discredited, so the first-line move is protective placement with a committed caregiver plus coaching of responsive care.

HOLD THIS
RAD (withdrawn, autism excluded) and DSED (over-familiar, autism not excluded) are the two trauma-related disorders of early neglect, both needing a developmental age of at least 9 months and onset before 5, and both treated by fixing the caregiving environment, never with a drug.

For the wider childhood picture and the child-protection and services detail, see the Child behavioural, emotional and other disorders notes and the Child psychiatry: assessment, treatment, services and protection notes; for the amygdala and fear-circuit anatomy touched on in the brain-imaging work, the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

Apply and consolidate

29 · Worked cases

The anxiety, OCD and trauma syllabus rewards a candidate who can *reason* a case from the door to the discharge letter, not one who recites lists. This note is the arc closer: four **worked cases**, each taken as a **vignette** and reasoned aloud, so that the diagnostic discriminator, the criterion that clinches it, and the guideline-anchored management fall out in the right order. Read each as the examiner reads it, the story first, then "which disorder, and is it even a psychiatric disorder at all?", then "what, in what order, at what dose, for how long?".

Why it matters, and how to use this note. Every fact here is developed at depth elsewhere in the chapter; this note only assembles them into four reasoned walk-throughs and ends each named syndrome and each named drug or psychotherapy with an anchored Good-to-remember box. The Clark cognitive loop behind the first case lives in the Clark cognitive model note; the OCD algorithm behind the second in the OCD management note; the PTSD algorithm behind the third in the PTSD treatment note; and the organic-mimic grid behind the fourth in the anxiety differential note. The deep antidepressant pharmacology (SSRIs, SNRIs, clomipramine, doses, interactions) sits in the Mood disorders: pharmacotherapy notes; the anxiolytic and benzodiazepine pharmacology in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes; the general CBT and exposure principle in the Psychotherapies, clinical assessment, MSE and nosology notes; and the deep brain stimulation option for refractory OCD in the ECT and neurostimulation notes. Each case refers to a *case:* line so you can find it fast on revision.

29.1 Case one, the presentation: panic disorder with agoraphobia

case: the vignette. A 28-year-old teacher gives a several-month history of episodes that begin from a calm state with a pounding heart, breathlessness and a lurching certainty that she is having a heart attack; the surge crests within about **10 minutes** and subsides. Two cardiology work-ups have been normal. She now avoids crowded markets, buses and being far from home alone, in case an attack strikes where she "cannot get out or get help", and she carries an alprazolam tablet "just in case". **The reasoning.** The fear is of the *attacks themselves* (anticipatory

anxiety about the next surge), which names panic disorder; the fear of situations where escape is difficult or help unavailable names the comorbid agoraphobia. Normal cardiac work-up and the out-of-the-blue onset from calm exclude an arrhythmia driving it.

29.2 Case one, the criterion that clinches panic disorder and agoraphobia

Panic disorder. The defining criterion is *recurrent unexpected panic attacks* not restricted to a particular stimulus or situation, followed by persistent concern about further attacks or a maladaptive change in behaviour to avoid them (ICD-11 6B01; DSM-5-TR 2022). The word that does the work is *unexpected*: the attack arrives from a calm state, which is exactly what separates panic disorder from the cued surges of a phobia. **Agoraphobia.** The defining criterion is marked fear or anxiety about *multiple* situations where escape might be difficult or help unavailable should a panic-like or incapacitating symptom occur (crowds, public transport, open or enclosed spaces, being alone outside the home), consistently avoided or endured with dread (ICD-11 6B02; DSM-5-TR 2022). The focus is on escape and rescue, not on the place itself.

GOOD TO REMEMBER

- **Panic disorder (the syndrome):** defining criterion is *recurrent unexpected* panic attacks (from a calm state, not cued) plus persistent concern about further attacks or behavioural change to avoid them; the discriminator is the "out-of-the-blue" onset, and the first step is to exclude an organic mimic (arrhythmia, thyrotoxicosis) before the label (ICD-11 6B01; DSM-5-TR 2022).
- **Agoraphobia (the syndrome):** defining criterion is fear of *multiple* situations where escape is difficult or help unavailable (crowds, transport, open or enclosed spaces, being alone out), avoided or endured with dread; the discriminator is that the fear is of being unable to escape or get help, not of the place itself (ICD-11 6B02; DSM-5-TR 2022).

29.3 Case one, the formulation: Clark's cognitive model applied

The loop, drawn on this patient. Clark's model formulates her disorder as the *catastrophic misinterpretation of benign bodily sensations*: a benign internal trigger (a fleeting palpitation) is read as an imminent catastrophe ("heart attack"), which produces fear, which drives more autonomic arousal, which is again misinterpreted, tightening a self-amplifying vicious cycle until a full attack crests (the accompanying figure lays out the loop). Her carried alprazolam and her habit of sitting down and gripping a companion's arm are safety behaviours: they feel protective but prevent the belief from ever being *disconfirmed*, because she attributes surviving each attack to the prop rather than to the harmlessness of the sensation. That is the engine of chronicity and of the widening agoraphobic avoidance.

GOOD TO REMEMBER

- **Clark cognitive model (the formulation):** the mechanism is catastrophic misinterpretation of benign bodily sensations feeding a vicious cycle; the signature principle is that *safety behaviours* (the pocketed benzodiazepine, sitting down, gripping) block disconfirmation and maintain the disorder; the first therapeutic move is to drop the safety behaviour and let the sensation prove itself harmless (Clark 1986).

29.4 Case one, the management: an SSRI plus CBT, and the activation warning

What the guidelines say. First-line is an SSRI licensed for panic (escitalopram, sertraline, paroxetine or citalopram) or venlafaxine, *with* CBT built on Clark's protocol; combination of CBT and an antidepressant has the best outcomes (IPS 2025; NICE 2011; BAP 2014). CBT for panic is delivered in the optimal range of **7 to 14 hours**, typically weekly over about **4 months** (NICE 2011), using cognitive restructuring, interoceptive exposure and the dropping of safety behaviours. **The activation caution to state.** An SSRI started for panic must carry an explicit warning about *early activation* and a transient worsening of anxiety in the first days, because in Clark's terms the initial jitteriness supplies fresh bodily sensations to misinterpret; start low and titrate. A responder continues the drug for at least six months (BAP 2014). **The benzodiazepine is not the answer.** NICE explicitly advises *against* benzodiazepines in panic disorder, associated with a worse long-term outcome; her carried alprazolam is a chemical safety behaviour to be withdrawn, not the treatment.

RULE **SSRI plus CBT, never a standing benzodiazepine.** First-line panic disorder is an SSRI licensed for panic (escitalopram, sertraline, paroxetine, citalopram) or venlafaxine combined with Clark-protocol CBT; benzodiazepines are advised against because they worsen long-term outcome and act as a safety behaviour (NICE 2011; BAP 2014).

TRAP **Starting the SSRI without the activation warning.** Beginning an SSRI in panic disorder without warning of early activation invites the patient to misread the first-week jitteriness as "the tablets are giving me attacks", abandon treatment, and reach back for the benzodiazepine; start low, titrate, and forewarn from the outset.

GOOD TO REMEMBER

- **SSRI (first-line, panic disorder):** serotonin re-uptake inhibitor; the one first-line indication is an SSRI licensed for panic (escitalopram Nexito, sertraline Daxid/Zosert, paroxetine Paxidep, citalopram) with CBT; the signature caution is early activation, so start low, titrate, and warn from the outset; continue at least six months in a responder (BAP 2014; NICE 2011).
- **CBT for panic (first-line psychotherapy):** the mechanism is breaking the Clark vicious cycle by cognitive restructuring, interoceptive exposure and dropping safety behaviours; the one dose to quote is 7 to 14 hours over about 4 months; it is co-equal first-line with an SSRI and combination gives the best outcomes (NICE 2011; IPS 2025).

29.5 Case two, the presentation: OCD worked up the management algorithm

case: the vignette. A 26-year-old man has intrusive contamination thoughts he recognises as his own and as excessive, and washes his hands until they crack, spending four hours a day on rituals; his baseline Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) is 28, in the *severe* band. His wife has taken over "clean" tasks to keep the peace (family accommodation). **The reasoning.** Ego-dystonic, recognised-as-own intrusive obsessions plus repetitive neutralising compulsions that consume more than an hour a day and impair function name OCD; the Y-BOCS objectifies severity and will govern every rung of the algorithm. This is a *worked example* of the four-rung ladder.

GOOD TO REMEMBER

- **Obsessive-compulsive disorder (the syndrome):** defining criterion is persistent *obsessions* (intrusive, unwanted, recognised as one's own) and/or *compulsions* (repetitive behaviours or mental acts the person feels driven to perform) that are time-consuming (conventionally more than an hour a day) or cause marked distress or impairment; the discriminator from a psychotic disorder is preserved insight that the thoughts are excessive, and the first step is to rate the Y-BOCS (ICD-11 6B20; DSM-5-TR 2022).

29.6 Case two, rung one: a high-dose SSRI for a long trial, plus ERP

The governing principle. OCD is *under-treated by default* because the doses are timid and the trials cut short; the first rung is a high-dose SSRI for a long trial, together with CBT incorporating exposure and response prevention (ERP) (BAP 2014; IPS 2025). **Applied to him.** He is started on fluoxetine (Fludac, Prodep) and escalated to **60 mg** over about five to six weeks, the OCD target being roughly the 60 to 80 mg fluoxetine-equivalent, higher than the depression dose (IPS 2025; Maudsley). It is held at the maximum tolerated dose for a *long trial*: continue for at least **12 weeks** (about 10 to 12 weeks at ceiling, with at least 6 of those weeks at the maximum) before judging efficacy (IPS 2025; New Oxford Textbook). Alongside, therapist-guided ERP works up a graded hierarchy, exposing him to a "contaminated" object and preventing the washing ritual so anxiety habituates and the belief that the ritual averts catastrophe is disconfirmed; his wife's accommodation is assessed and reduced, since high accommodation predicts poor outcome (IPS 2025).

RULE **High dose, long trial, with ERP.** First-line OCD is an SSRI pushed to the maximum tolerated dose above the depression range (fluoxetine 60 mg equivalent) for about 10 to 12 weeks, combined with CBT incorporating exposure and response prevention; this is unanimous across BAP, IPS, NICE, CANMAT and WFSBP.

TRAP **Calling the SSRI a failure too early or at too low a dose.** An OCD trial is not adequate until roughly 10 to 12 weeks at the maximum tolerated dose, with at least 6 weeks at the ceiling; switching or augmenting on a depression-range dose stopped at six weeks mislabels a slow-but-real responder as treatment-resistant.

GOOD TO REMEMBER

- **Y-BOCS (the scale):** clinician-rated 10-item scale, each item 0 to 4, total **0 to 40**; bands 0-7 subclinical, 8-15 mild, 16-23 moderate, 24-31 severe, 32-40 extreme; response is a 25 to 35% reduction and remission a score of 12 or below; it is rated at baseline and every 4 weeks and governs every rung of the OCD algorithm (Goodman 1989; IPS 2025).
- **CBT with ERP (first-line psychotherapy, OCD):** the mechanism is graded exposure to the feared stimulus with prevention of the neutralising ritual, driving habituation and belief disconfirmation; the signature principle is that exposure and response prevention must be delivered *together* (either alone is inferior, Foa); the first-line indication is mild-to-moderate OCD as monotherapy and severe OCD combined with a high-dose SSRI (IPS 2025; CANMAT 2014).

29.7 Case two, the next rungs: switch, augment, then refer

Reading the trial. At 12 weeks his Y-BOCS is 25, under a 25% reduction, so despite an adequate high-dose long trial this is *non-response*. The dose is optimised toward 80 mg for a further period;

he remains a partial responder. **Rung two, switch.** The next step is to switch, either to a second SSRI or to clomipramine (Anafranil), the one tricyclic with genuine anti-obsessional efficacy and historically the first drug shown to work in OCD, at **150 to 225 mg/day** under ECG monitoring (IPS 2025; BAP 2014). Clomipramine sits at the margins of superiority over the SSRIs but is *less well tolerated* (anticholinergic burden, cardiac conduction effects, seizure risk in overdose), which is exactly why an SSRI is tried first and clomipramine held in reserve. **Rung three, augment.** On continued partial response, low-dose antipsychotic augmentation is added to the continuing serotonergic drug: risperidone **1 to 3 mg/day** (strongest augmentation evidence) or low-dose aripiprazole, continued for at least 8 weeks, with intensive ERP throughout (IPS 2025; BAP 2014). Antipsychotics are augmentation only, never monotherapy for OCD (NICE 2005). **Rung four, refer.** Only after this whole sequence, with each trial genuinely adequate, is he refractory; the refractory rung is intensive therapist-led ERP and, at a specialist centre such as NIMHANS, IV clomipramine then deep brain stimulation or ablative neurosurgery (cross-referenced to the ECT and neurostimulation notes).

RUNG	STEP FOR THIS PATIENT	DOSE / DURATION
1 First-line	**High-dose SSRI (fluoxetine) + ERP**	60 (up to 80) mg for at least 12 weeks at ceiling
2 Switch	Optimise dose, then another SSRI or clomipramine	Clomipramine 150 to 225, ECG-monitored
3 Augment	**Add low-dose risperidone or aripiprazole to the SRI**	Risperidone 1 to 3, at least 8 weeks
4 Refer	Intensive ERP, then IV clomipramine, DBS, neurosurgery	Specialist centre only

The OCD management algorithm worked through case two; doses are bare numbers in the cells with the unit in the header (BAP 2014; IPS 2025; NICE 2005). The full ladder is drawn in the accompanying figure.

GOOD TO REMEMBER

- **Clomipramine (Anafranil):** the most serotonergic tricyclic and the original anti-obsessional drug; mechanism is potent serotonin (and noradrenaline) re-uptake inhibition; the one dose is 150 to 225 mg/day in OCD; the signature caution is poorer tolerability than an SSRI (anticholinergic, cardiac conduction, seizure in overdose) requiring ECG monitoring, so it is the switch after an adequate SSRI trial fails, not the first drug (BAP 2014; IPS 2025).
- **Antipsychotic augmentation (risperidone / aripiprazole, OCD):** low-dose dopamine blockade *added* to a continuing SSRI or clomipramine for treatment-resistant OCD; the one dose is risperidone 1 to 3 mg/day for at least 8 weeks (strongest evidence risperidone); the signature caution is that antipsychotics are augmentation only and never monotherapy for OCD (IPS 2025; NICE 2005).

29.8 Case three, the presentation: PTSD, and choosing psychotherapy first

case: the vignette. A 40-year-old lorry driver, six months after a fatal highway collision he survived, has nightly nightmares of the crash that feel as if it is happening again, cannot drive past the accident stretch, startles violently at horns and is convinced the world is now lethally dangerous. He asks for "something to calm the nerves". **The reasoning.** A qualifying trauma

(directly experiencing a life-threatening event, Criterion A) followed by re-experiencing *in the present*, avoidance of reminders and a persistent sense of current threat, all lasting more than one month, names PTSD (ICD-11 6B40; DSM-5-TR 2022). The pathognomonic feature is that the crash is re-lived here-and-now, not merely remembered, which is the line that separates PTSD from ordinary painful recollection.

GOOD TO REMEMBER

- **Post-traumatic stress disorder (the syndrome):** defining criterion is a qualifying trauma (Criterion A) followed by the ICD-11 triad, *re-experiencing in the present*, deliberate avoidance of reminders, and a persistent sense of current threat, lasting more than one month; the single discriminator is that the event is re-lived here-and-now (flashbacks, nightmares that feel current), not simply recalled; the first management step is to offer a trauma-focused psychotherapy, not a drug (ICD-11 6B40; DSM-5-TR 2022).

29.9 Case three, the management: trauma-focused therapy first, SSRI and prazosin considered

The governing rule. The single most examinable statement in PTSD management is that a trauma-focused psychotherapy, not a drug, is first-line: trauma-focused CBT (cognitive processing therapy, cognitive therapy for PTSD, narrative exposure, prolonged exposure) or EMDR, typically over **8 to 12** sessions, offered in preference to medication (NICE 2018; BAP 2014; VA/DoD 2023). Drugs are second, offered when psychotherapy is declined, unavailable or insufficient. **Applied to him.** He is told that trauma-focused psychotherapy would be the first choice; because he presses for medication, a licensed SSRI, sertraline (Daxid, Zosert) or paroxetine (Paxidep), or the SNRI venlafaxine, is appropriate, titrated to the maximum tolerated dose, with the warning that a therapeutic effect may take up to **12 weeks** to assess and a responder continues for at least **12 months** (BAP 2014; NICE 2018). Because trauma nightmares are prominent, prazosin (Minipress, Prazopress), a selective alpha-1 blocker, is *considered* as a targeted add-on for the nightmares, started at 1 mg nocte and titrated to **2 to 15 mg** nocte to avoid first-dose hypotension (CANMAT 2014; Maudsley). **The hard negative.** The "something to calm the nerves" he wants must *not* be a benzodiazepine: it treats none of the PTSD clusters, blunts the emotional engagement trauma-focused therapy needs, and may *increase* PTSD risk if given early after trauma (VA/DoD 2023; CANMAT 2014).

RULE **Trauma-focused therapy first; never a benzodiazepine.** In PTSD the first-line treatment is a manualised trauma-focused psychotherapy (TF-CBT or EMDR); where a drug is used it is a licensed SSRI (sertraline, paroxetine) or venlafaxine, with prazosin for nightmares; the benzodiazepine is excluded at every step (NICE 2018; VA/DoD 2023).

GOOD TO REMEMBER

- **Trauma-focused psychotherapy (first-line, PTSD):** the mechanism is deliberate processing of the traumatic memory so the event is refiled as past rather than relived as present (TF-CBT or EMDR); the one indication is that it is offered *before* drugs, typically over 8 to 12 sessions; the signature principle is that generic supportive counselling does not qualify, only memory-processing therapies (NICE 2018; VA/DoD 2023).
- **Sertraline / paroxetine (SSRI, PTSD):** the two SSRIs licensed for PTSD and the first-line drug once psychotherapy is set aside; mechanism is serotonin re-uptake inhibition; the signature caution is that a full trial takes up to 12 weeks and early activation can transiently worsen symptoms; continuation after response is at least 12 months (BAP 2014; NICE 2018).
- **Prazosin (Minipress / Prazopress, alpha-1 blocker):** the targeted add-on for PTSD trauma nightmares and sleep disturbance; mechanism is alpha-1 blockade lowering central noradrenergic tone; the one dose is 1 mg nocte titrated to 2 to 15 mg; the signature caution is first-dose hypotension, and it augments, never replaces, first-line psychotherapy or an SSRI/SNRI (CANMAT 2014; Maudsley).

29.10 Case four, the presentation: anxiety versus a medical mimic

case: the vignette. A 45-year-old man is referred with "treatment-resistant panic": episodic palpitations, pounding headache, drenching sweats and a surge of dread, several times a week, unresponsive to an SSRI. He drinks six cups of coffee a day and takes an over-the-counter decongestant. **The reasoning, in the right order.** Before any anxiety label, ask "is this organic?". The *tempo* is the pivot: these are *episodic, paroxysmal* autonomic storms, which mimic panic rather than GAD, and the pounding headache plus recorded blood-pressure spikes point away from a primary disorder. The work-up must clear the body first, and only then, if all negative, settle on a primary anxiety disorder. This is a *worked example* of "exclude the body before you name the disorder".

29.11 Case four, excluding the three mimics: hyperthyroidism, phaeochromocytoma, substance

Hyperthyroidism, the sustained mimic of GAD. Thyrotoxicosis reproduces the somatic tail of anxiety (irritability, tremor, tachycardia), but because the thyroid drive is *continuous* it mimics *sustained* GAD, not his episodic picture; still, it is the commonest organic mimic and is screened with thyroid function (a suppressed TSH with raised free T4), looking for goitre, exophthalmos, atrial fibrillation and weight loss with a preserved appetite (Shorter Oxford Textbook). **Phaeochromocytoma, the paroxysmal mimic of panic.** This catecholamine-secreting tumour releases adrenaline and noradrenaline in *bursts*, producing exactly his paroxysmal palpitations, pounding headache and sweating; because the secretion is episodic it mimics panic. The pointing feature is *paroxysmal hypertension*, blood pressure spiking with each attack, and the screening test is plasma or 24-hour urinary metanephrines and catecholamines; the discriminator is the recorded hypertensive surge and the headache, which panic disorder does not produce (Shorter Oxford Textbook; New Oxford Textbook). **The substance cause.** His six coffees and the sympathomimetic decongestant are a substance mimic: DSM defines caffeine intoxication as recent intake usually over **250 mg** with **five or more** autonomic and neuropsychiatric symptoms, and the discriminator is that the anxiety settles on cutting the load (DSM-5-TR 2022). Only with thyroid function, metanephrines and the substance history all clear would a primary panic disorder be diagnosed, and the SSRI failure re-read as a mislabelled organic case.

MIMIC IN THIS CASE	POINTING FEATURE	SCREENING TEST
Hyperthyroidism	Goitre, exophthalmos, AF, weight loss with appetite (sustained, mimics GAD)	Thyroid function (TSH, free T4)
Phaeochromocytoma	**Paroxysmal hypertension, pounding headache (episodic, mimics panic)**	Plasma/urinary metanephrines, catecholamines
Substance (caffeine / sympathomimetic)	High caffeine load, decongestant, intoxication signs	Substance history; caffeine over 250 mg + 5 or more symptoms

Case four, the three mimics excluded before settling on a primary anxiety disorder; the tempo (episodic vs sustained) tells you which physical test to send (Shorter Oxford Textbook; New Oxford Textbook; DSM-5-TR 2022).

COMMON TRAP

The exam-fatal error in case four is to accept "treatment-resistant panic" at face value and add a second psychotropic while an organic lesion sits in plain sight. Episodic autonomic storms with paroxysmal hypertension and a pounding headache are a phaeochromocytoma until proven otherwise; a high caffeine and decongestant load is a substance mimic; each is treated at its source, not with another SSRI or, worse, a benzodiazepine.

GOOD TO REMEMBER

- **Phaeochromocytoma (the mimic):** a catecholamine-secreting tumour producing paroxysmal palpitations, pounding headache and sweating that mimic panic; the discriminator is paroxysmal hypertension with a recorded blood-pressure surge in the attack; the screening test is plasma or urinary metanephrines and catecholamines; the first step is that episodic autonomic storms mean "exclude phaeochromocytoma" before a panic label (Shorter Oxford Textbook; New Oxford Textbook).
- **Hyperthyroidism (the mimic):** the sustained organic mimic of GAD (tremor, tachycardia, restlessness); the discriminator is the physical thyroid signs (goitre, exophthalmos, weight loss with appetite) and resolution on treating the thyroid; the screening test is thyroid function (suppressed TSH, raised free T4) (Shorter Oxford Textbook).

INDIA

All four cases sit inside the same Indian reality: a wide anxiety, OCD and PTSD treatment gap (these disorders are common, heavily somatised as palpitations, tremor and "gas", and under-recognised), and an entrenched benzodiazepine over-prescription problem, typically alprazolam, prescribed long-term in primary care against every guideline. Case one's carried alprazolam, case three's request to "calm the nerves", and case four's referral as "treatment-resistant panic" are each the habit in miniature; a large number of Indian patients labelled "anxiety" are actually in daily alprazolam micro-withdrawal, itself an iatrogenic mimic. The Indian Psychiatric Society clinical practice guidelines correct all of this, exclude the organic causes, treat the primary disorder with an SSRI or SNRI and a structured psychotherapy first, and keep the benzodiazepine a short, time-limited bridge rather than a standing prescription. Indian brands are available across the board, fluoxetine (Fludac, Prodep), sertraline (Daxid, Zosert), escitalopram (Nexito), paroxetine (Paxidep), clomipramine (Anafranil), prazosin (Minipress, Prazopress) and propranolol (Ciplar, Inderal), so the limiting factor is recognition and adequate dosing, not access.

10 to 12 weeks	28	2 to 15	250 mg
ADEQUATE OCD SSRI TRIAL AT MAXIMUM TOLERATED DOSE	Y-BOCS OF CASE TWO (SEVERE BAND, 24 TO 31)	PRAZOSIN NOCTE RANGE, MG (START 1, TITRATE)	CAFFEINE INTOXICATION THRESHOLD (PLUS 5 OR MORE SYMPTOMS)

MNEMONIC

READ THE TEMPO, THEN THE FOCUS, THEN THE LADDER

Across the four cases: **READ THE TEMPO** (episodic storms mean exclude phaeochromocytoma, hypoglycaemia, a substance; sustained tremor with weight loss means thyrotoxicosis) → **THEN THE FOCUS** of the fear names the anxiety disorder (the next attack = panic; escape/rescue = agoraphobia; re-lived here-and-now = PTSD; ego-dystonic obsessions = OCD) → **THEN THE LADDER** (SSRI + CBT for panic; high-dose SSRI + ERP then switch/augment/refer for OCD; trauma-focused therapy first then SSRI + prazosin for PTSD), never a standing benzodiazepine.

PEARL

Every one of these four vignettes has the same wrong answer hiding in it, the benzodiazepine: the pocketed alprazolam in case one, the "calm the nerves" request in case three, the reflex add-on in case four's mislabelled panic. Name why it is wrong in each (safety behaviour in panic, harmful in PTSD, masking an organic lesion in the mimic case) and you have shown the examiner the single thread that runs through the whole anxiety, OCD and trauma management syllabus.

HOLD THIS

Work every anxiety, OCD or trauma case in the same order, exclude the organic mimic by tempo first (episodic storms = phaeochromocytoma/hypoglycaemia/substance, sustained = thyrotoxicosis), then name the disorder by the focus of the fear, then climb the guideline ladder (SSRI plus CBT for panic; high-dose SSRI plus ERP then clomipramine then risperidone/aripiprazole augmentation for OCD; trauma-focused psychotherapy first then a licensed SSRI plus prazosin for PTSD), and at no step reach for a standing benzodiazepine.

30 · Consolidation

The whole chapter now sits in front of you, and this closing topic is not new content but the machinery that turns reading into recall. The examination does not reward the candidate who has *read* the anxiety, OCD and trauma block; it rewards the one who can, cold and under pressure, state the discriminating criterion for each syndrome, the one first-line agent for each disorder, the OCD ladder in order, the scale bands to the number, and the PTSD algorithm in a single line. Those retrievals are what this topic drills. The single most robust finding in the science of learning is that **active recall** (pulling an answer out of an empty page) and **retrieval practice** (repeatedly testing yourself rather than re-reading) beat every passive method for durable memory, so the design here is deliberately answer-sparse: prompts first, and the answers held elsewhere in the chapter so you must fetch them.

Why it matters, and what this note owns. This note owns three things: the **mnemonic** that ties the chapter together, paid off from where it was seeded at the generalised-anxiety-disorder opener; a set of answer-free prompt lists for **active recall** across the anxiety disorders and their

first-line agents, the OCD ladder, the Y-BOCS bands, the PTSD algorithm and the trauma-disorder discriminators; and a whole-chapter **synthesis map** you are meant to **redraw from memory**. It re-derives no criteria, doses or bands of its own; every number quoted here is a pointer back to the topic that verified it. The deep pharmacology behind the drug names lives in the Mood disorders: pharmacotherapy notes and the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes; the fear-circuit substrate in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the general CBT and exposure model in the Psychotherapies, clinical assessment, MSE and nosology notes. The synthesis map that carries the whole block is drawn in the accompanying figure, framed cover-the-branches so it can be used as a retrieval test.

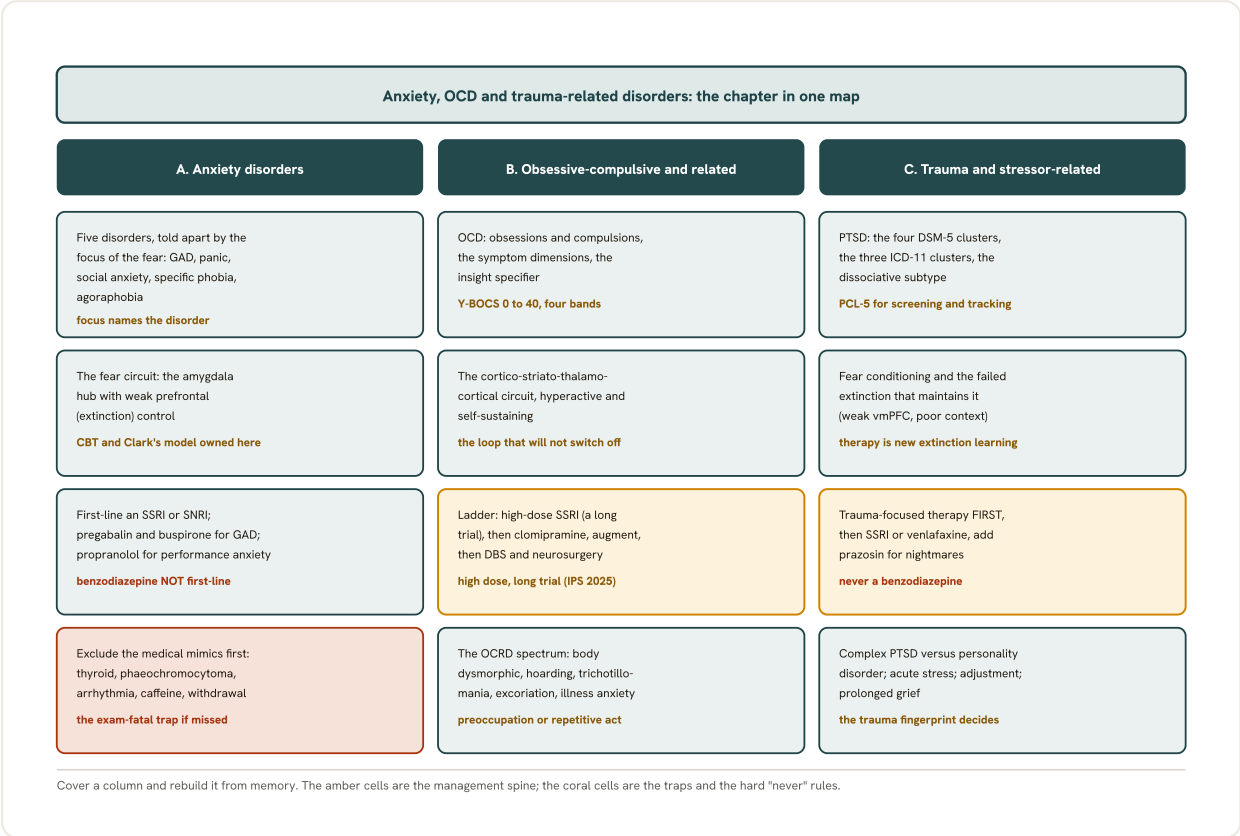


Fig 14.20 The whole chapter in one synthesis map, built for retrieval. Three columns, one per band: the anxiety disorders (told apart by the focus of the fear, treated with an SSRI or SNRI, the medical mimics excluded first); the obsessive-compulsive and related disorders (OCD and its cortico-striato-thalamo-cortical circuit, the high-dose long-trial ladder, the OCRD spectrum); and the trauma and stressor-related disorders (PTSD and its clusters, the fear-conditioning neurobiology, the trauma-focused-therapy-first algorithm, and the complex-PTSD discrimination). The amber cells are the management spine and the coral cells the traps and the hard rules. Cover a column and redraw it from memory, then check it against the note.

30.1 The master mnemonic, paid off: WORRIED FEARS

Seeded at the opener, closed here. The chapter opened by seeding the master mnemonic **"WORRIED FEARS"** at generalised anxiety disorder, and this is where it is paid off, because its two halves are not really about GAD alone: they encode the *template* that repeats across the whole anxiety block. **WORRIED** is the anxiety *picture* (worry that is free-floating and uncontrollable, on-edge restlessness, rumination and poor concentration, relaxation made impossible by muscle tension, irritability, easy fatigue, disturbed sleep). **FEARS** is the anxiety *management* template:

First-line SSRI or SNRI, **E**valuate for a long enough trial before judging failure, **A**lternatives such as pregabalin and buspirone, **R**efer to CBT as a co-equal first-line, and **S**hun the benzodiazepine as long-term monotherapy. If you can expand both halves without looking, you hold the spine of the entire block.

MNEMONIC

WORRIED FEARS

The chapter master mnemonic, paid off. **WORRIED** = the picture: **W**orry (free-floating, uncontrollable), **O**n edge/restless, **R**umination/poor concentration, **R**elaxation impossible (muscle tension), **I**rritability, **E**asily fatigued, **D**isturbed sleep. **FEARS** = the management template that repeats across the anxiety disorders: **F**irst-line SSRI/SNRI, **E**valuate over a long enough trial, **A**lternatives pregabalin and buspirone, **R**efer/CBT co-equal first-line, **S**hun the benzodiazepine long-term. Two further chapter mnemonics ride alongside it: **TIDRC** for the five Y-BOCS parameters, and **PTSD + A S R** for complex PTSD (the PTSD triad plus affect dysregulation, negative self-concept, relationship difficulty).

RULE **One template, many disorders.** For every anxiety disorder the default answer is SSRI (or SNRI) first-line plus CBT/exposure, with the benzodiazepine never the long-term monotherapy; learn the template once and vary only the twist (propranolol for performance, prazosin for nightmares, high-dose-long-trial for OCD).

30.2 Active-recall prompt list: the anxiety disorders and their first-line agents

Cover the answers and pull each one. This is a **retrieval practice** list, not a summary. For each disorder below, say aloud (or write) the one discriminating criterion and the first-line treatment before you check it against the topic that verified it. The point is the effort of retrieval: the harder the pull, the stronger the trace.

- **Generalised anxiety disorder.** Prompt: the discriminator from normal worry? The two numbers in DSM-5-TR? First-line drug and the two options? (Answers in the GAD topic: uncontrollable free-floating worry; **6 months**, 3 of 6; SSRI/SNRI first-line, pregabalin and buspirone as options.)
- **Panic disorder.** Prompt: what makes an attack diagnostic, and the one prescribing warning? (Recurrent *unexpected* attacks peaking within minutes plus a month of anticipatory anxiety; SSRI first-line started *low and slow* with a warning about early activation.)
- **Agoraphobia.** Prompt: the cognitive core, and is it tied to panic? (Fear that escape is difficult or help unavailable in at least two of five situations; a stand-alone disorder now, *irrespective* of panic disorder; exposure-based CBT core, SSRI for the panic component.)
- **Social anxiety disorder.** Prompt: the object of the fear, the one specifier, and the twist in treatment? (Fear of negative evaluation; the *performance-only* specifier; SSRI plus CBT for the generalised form, a situational beta-blocker for discrete performance anxiety.)
- **Specific phobia.** Prompt: the treatment of choice, and the drug trap? (Graded in-vivo exposure; a benzodiazepine is *not* first-line and blunts the extinction learning exposure

depends on.)

- **Separation anxiety disorder.** Prompt: the fear, and how it is easily missed? (Fear of separation from an attachment figure; presents as school refusal in a child or is sedated rather than diagnosed in an adult; exposure-based CBT, SSRI if needed.)

GOOD TO REMEMBER

- **The anxiety first-line map:** every one of GAD, panic disorder, agoraphobia, social anxiety and separation anxiety is SSRI (or SNRI) plus CBT/exposure first-line; specific phobia is *exposure-first* with drugs not first-line; the two disorder-specific twists are the situational beta-blocker (propranolol) for performance anxiety and starting the SSRI low-and-slow in panic; the benzodiazepine is never the long-term answer for any of them.

30.3 Active-recall prompt list: the OCD ladder and the trial rules

Recite the staircase in order. OCD management is a four-rung ladder governed by one idea, that OCD is under-treated by default because doses are timid and trials are cut short. Retrieve the rungs and the numbers before checking them against the OCD management topic.

- **Rung one.** Prompt: the first-line, and what makes it different from depression prescribing? (A *high-dose* SSRI for a *long* trial of about **10 to 12 weeks** plus CBT with exposure and response prevention; target roughly the 60 to 80 mg fluoxetine-equivalent.)
- **Rung two.** Prompt: what to do on partial or no response, and the classic contrast? (Optimise the dose, then switch SSRI or to clomipramine; the clomipramine-versus-SSRI point is that clomipramine sits at the margins of superiority but is *less tolerated*, so it is held in reserve, under ECG monitoring.)
- **Rung three.** Prompt: the augmentation step? (Low-dose antipsychotic augmentation, aripiprazole or risperidone, added to the continuing serotonergic drug for at least 8 weeks; augmentation only, never monotherapy.)
- **Rung four.** Prompt: the refractory options? (Intensive therapist-led ERP and, at a specialist centre only, intravenous clomipramine, then deep brain stimulation and ablative neurosurgery, cross-referenced to the ECT and neurostimulation notes.)
- **The judging rule.** Prompt: how is failure judged, and over what window? (By a less-than-25-to-35% fall on the Y-BOCS after a full high-dose trial of at least **12 weeks**, not by the patient's gestalt.)

TRAP **Calling an OCD trial a failure too early.** The commonest error is switching or augmenting before a high-dose SSRI has run about 10 to 12 weeks at the maximum tolerated dose, or judging on a depression-range dose; a slow-but-real responder is then mislabelled treatment-resistant and the ladder is climbed prematurely.

GOOD TO REMEMBER

- **The OCD ladder:** high-dose SSRI (about 60 to 80 mg fluoxetine-equivalent) for a long trial of roughly 10 to 12 weeks with ERP, then clomipramine (Anafranil) on failure, then aripiprazole or risperidone augmentation, then intensive ERP and specialist neurosurgery/DBS; judge response by a 25 to 35% Y-BOCS fall, continue a responder for at least 1 to 2 years, and the benzodiazepine has no place at any rung.

30.4 Active-recall prompt list: the Y-BOCS bands and the other scales

The bands are pure memorisation, so drill them. The scale numbers are the ones examiners ask for verbatim, so they reward the tightest retrieval practice. Cover the answers, recite each scale's structure and cut-off, and only then check against the scale topics. The instrument forms themselves are typeset centrally, so work from the accompanying scale plate rather than any pasted questionnaire.

SCALE	WHAT IT MEASURES	STRUCTURE AND THE NUMBER TO HOLD
Y-BOCS	**OCD *severity* (not diagnosis)**	10 items, each 0 to 4, total 0 to 40; bands subclinical 0 to 7, mild 8 to 15, moderate 16 to 23, severe 24 to 31, extreme 32 to 40; **16** is the trial-entry cut-off (floor of moderate); five parameters = TIDRC
GAD-7	GAD screen and severity	**7 items, each 0 to 3, total 0 to 21; bands 5/10/15; clinical cut-off 10; GAD-2 is the rapid screen**
HAM-A	Anxiety severity (clinician-rated)	14 items, each 0 to 4, max **56**; psychic and somatic factors; the GAD drug-trial outcome measure
PCL-5	PTSD screen and monitor	**20 items, each 0 to 4, total 0 to 80; provisional cut-off 31 to 33 for probable PTSD; not a diagnosis (CAPS-5/SCID is)**
LSAS	Social anxiety severity	24 items rating fear and avoidance, each 0 to 3; the social-anxiety trial outcome measure; Mini-SPIN is the rapid screen

The five chapter scales and the verified numbers to recall cold; the Y-BOCS bands and the PCL-5 cut-off are the two most-asked, and each instrument's form is set out on the accompanying scale plate (verified against the individual scale topics).

0 to 40 Y-BOCS TOTAL; MODERATE BAND FLOOR AT 16	**10** GAD-7 CLINICAL CUT-OFF (BANDS 5/10/15)	**31 to 33** PCL-5 PROVISIONAL CUT-OFF FOR PROBABLE PTSD	**10 to 12 weeks** ADEQUATE HIGH-DOSE SSRI TRIAL IN OCD

GOOD TO REMEMBER

- **The five scales:** Y-BOCS (10 items, 0 to 40, cut-off 16, bands 0-7/8-15/16-23/24-31/32-40); GAD-7 (7 items, 0 to 21, cut-off 10); HAM-A (14 items, max 56, clinician-rated); PCL-5 (20 items, 0 to 80, cut-off 31 to 33); LSAS (24 items, fear and avoidance) are the block's instruments; the defining fact each time is that a scale *grades severity or screens*, it never makes the diagnosis.

30.5 Active-recall prompt list: the PTSD algorithm and the two hard rules

State the ladder as one ordered line. PTSD management is one of the cleanest algorithms in the syllabus, and it hangs off two rules that should be the first sentence of any answer: *trauma-focused psychotherapy is first-line, and a benzodiazepine is never used*. Retrieve the sequence before checking it against the PTSD treatment topic.

- **First-line.** Prompt: which treatment, and which therapies qualify? (A manualised **trauma-focused psychotherapy**, either TF-CBT (cognitive processing therapy, cognitive therapy for PTSD, narrative exposure, prolonged exposure) or EMDR, over about 8 to 12 sessions, ahead of any drug.)
- **First-line drug.** Prompt: when a drug is used, which agents? (The two licensed SSRIs sertraline and paroxetine, or the SNRI venlafaxine; allow up to **12 weeks** for a trial.)
- **The symptom-targeted add-on.** Prompt: for nightmares and disturbed sleep? (Prazosin (Minipress, Prazopress), an alpha-1 blocker, started at **1 mg nocte** and titrated to 2 to 15 mg, as an add-on, never monotherapy.)
- **Non-response.** Prompt: the sequence? (Raise the dose, then switch, then augment with an antipsychotic (risperidone, olanzapine) or combine drug plus psychotherapy and refer.)
- **The exclusion.** Prompt: the one drug class ruled out? (The *benzodiazepine*, at every step, ineffective for the core clusters and possibly raising PTSD risk if given acutely.)

TRAP **A benzodiazepine in PTSD, or as monotherapy for any anxiety disorder.** Benzodiazepines touch none of the PTSD clusters and blunt the emotional engagement trauma-focused therapy needs; the exam-fatal error is to offer one for PTSD, or to write one up as the long-term treatment for GAD, panic or phobia.

GOOD TO REMEMBER

- **The PTSD algorithm:** trauma-focused psychotherapy (TF-CBT or EMDR) first everywhere; if a drug is used, a licensed SSRI (sertraline, paroxetine) or venlafaxine over a trial of up to 12 weeks; prazosin (Minipress, Prazopress) added for nightmares; on non-response raise, switch, then augment with an antipsychotic; continue a responder at least 12 months; and never a benzodiazepine at any step.
- **EMDR / trauma-focused CBT (the psychotherapies):** both process the traumatic memory directly and are the co-equal first-line for PTSD and complex PTSD over about 8 to 12 sessions; the principle is that generic supportive counselling does *not* qualify, and complex PTSD often needs a phased approach (stabilisation before trauma processing).

30.6 Active-recall prompt list: the trauma-disorder discriminators

The trauma cluster is discriminated by time and by structure. The stressor-related disorders are separated mainly by *duration* and by the *shape* of the reaction, and examiners test the boundaries, not the lists. Retrieve each discriminator before checking it against the relevant topic.

BOUNDARY	THE DISCRIMINATOR TO STATE
Acute stress reaction vs acute stress disorder	**ICD-11 acute stress reaction is *not a disorder* (QE84, a health-status factor, transient, hours to 1 to 3 days); DSM-5-TR acute stress disorder *is* a diagnosis (9 of 14 symptoms, 3 days to 1 month)**
Acute stress disorder vs PTSD	Purely the time window: acute stress disorder under a month; PTSD over a month
PTSD vs complex PTSD	**Complex PTSD = the full PTSD triad *plus* the three disturbances in self-organisation (affect dysregulation, negative self-concept, relationship difficulty)**
Complex PTSD vs personality disorder	**Trauma-reminder avoidance and current threat (absent in PD); a *stable* negative self-view (vs unstable); disconnection (vs abandonment-driven instability); less frequent but higher-lethality suicidality**
Prolonged grief disorder	Persistent yearning exceeding the cultural norm; at least 6 months (ICD-11) or at least 12 months in adults (DSM-5-TR); do not pathologise normal grief too early
Adjustment disorder	Maladaptive reaction to an identifiable stressor (ICD-11 core: preoccupation plus failure to adapt); onset within 1 month (ICD-11) or 3 months (DSM-5-TR); resolves within 6 months of the stressor ending; trumped by any full disorder

The trauma-disorder discriminator grid: the block is separated mainly by duration and by whether the reaction is a normal response, a diagnosable disorder, or a personality pattern (verified against the acute-stress, PTSD, complex-PTSD, prolonged-grief and adjustment-disorder topics).

GOOD TO REMEMBER

- **Complex PTSD versus personality disorder (the discrimination that unlocks treatment):** both share affective dysregulation, but complex PTSD carries the trauma fingerprint, reminder avoidance and a persistent sense of current threat, a *stable* negative self-view, relationships marked by disconnection (not fear of abandonment), and higher-lethality suicidality; getting the label right is what preserves a survivor's access to trauma-focused therapy.

30.7 The whole-chapter synthesis map, framed cover-the-branches

Build the tree, then redraw it blind. The strongest single revision act for this block is to **redraw from memory** a **synthesis map** that hangs every disorder off its trunk. The map has three trunks: the *anxiety disorders* (carved by the object of the fear), *OCD and the related disorders* (the obsessive-compulsive spectrum), and the *stressor-related disorders* (carved by time and structure). From each trunk hang the disorders, and from each disorder hang its one discriminator, its scale

and its first-line treatment. The accompanying figure draws this map; use it as a retrieval test by covering all the branches and regenerating them, then uncovering to score yourself, exactly the cover-the-branches method that makes **retrieval practice** work.

How to use it. First pass: cover everything but the three trunks and name the disorders under each. Second pass: for each disorder, cover the discriminator and pull it. Third pass: cover the treatment column and recite the first-line agent and the one twist. A branch you cannot regenerate is a branch to re-read in its own topic; a branch you can is one you can leave. Repeated over spaced sittings, the map converts the chapter from something you recognise into something you can produce.

PEARL

The chapter collapses to three trunks and one template. Trunk one, the *anxiety disorders*, are carved by the object of the fear (diffuse worry, unexpected attacks, escape impossible, negative evaluation, a cued object, separation) and all answer to SSRI/SNRI plus CBT. Trunk two, *OCD and its spectrum*, run the high-dose-long-trial ladder governed by the Y-BOCS. Trunk three, the *stressor-related disorders*, are carved by time (reaction, acute stress disorder, PTSD) and by structure (complex PTSD, prolonged grief, adjustment), with trauma-focused psychotherapy first for PTSD. Cover the branches, redraw the tree, and you own the block.

INDIA

The Indian thread runs through every trunk and is worth carrying as one line at consolidation: a very wide **anxiety, OCD and PTSD treatment gap** (most sufferers never reach formal care, distress is somatised and under-recognised), into which has flowed the entrenched **benzodiazepine over-prescription problem** (typically long-term alprazolam or clonazepam given first-line against every guideline). The corrective is the same across the block and is exactly what the **Indian Psychiatric Society CPGs** say: an SSRI or SNRI first-line with CBT or exposure, the high-dose-long-trial rule enforced in OCD, trauma-focused psychotherapy first in PTSD, and the benzodiazepine reserved and time-limited, never the maintenance treatment. The first-line agents are cheap and familiar as Indian brands, escitalopram (Nexito, Rexipra), sertraline, fluoxetine and fluvoxamine, with clomipramine (Anafranil), propranolol (Ciplar, Inderal) for performance anxiety, and prazosin (Minipress, Prazopress) for trauma nightmares.

HOLD THIS

Redraw the three-trunk synthesis map from memory: anxiety disorders (carved by the object of the fear, all SSRI/SNRI plus CBT), OCD and its spectrum (high-dose SSRI for a long trial with ERP, then clomipramine, then antipsychotic augmentation, governed by the Y-BOCS), and the stressor-related disorders (carved by time and structure, trauma-focused psychotherapy first for PTSD, prazosin for nightmares), with the benzodiazepine excluded from long-term use across the whole block.

Previously asked

This territory is examined at two levels at once: the syndrome (its clinical features, its differential diagnosis and its course) and the treatment (which first-line agent, the obsessive-compulsive-disorder ladder, the trauma-focused algorithm). The reliable pattern is that obsessive-compulsive disorder and panic disorder carry the most weight in the anxiety and related section, that post-traumatic stress disorder is the dominant trauma essay, and that a single disorder or a single treatment can be asked as a standalone note. Every long essay ends in a guideline-anchored management plan, so the first-line recommendation and the reason for it must be exam-ready. The genuine questions on record are grouped by band below. The anxiolytic and antidepressant pharmacology these disorders are treated with is developed in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes and the Mood disorders: pharmacotherapy notes; the fear-circuit anatomy is developed in the Neurochemistry, neuroendocrinology, neuroimaging and basic psychopharmacology notes; and the wider cognitive behaviour therapy technique is cross-referenced to the Psychotherapies, clinical assessment, MSE and nosology notes, while exposure and response prevention, trauma-focused therapy and Clark's model are owned here.

HOW THIS TERRITORY IS ACTUALLY TESTED

- **The anxiety disorders, with panic and generalised anxiety leading.** "Describe various anxiety disorders. Discuss the clinical features and management of generalized anxiety disorder" has come as a full 25-mark essay, and panic disorder recurs at every length: "Discuss etiopathology, clinical features, differential diagnosis and management of panic disorder" as a 25-mark essay, "Differential diagnosis, clinical features and course of Panic disorders" as a 10-mark note, and "Panic disorder" and "Panic disorders" as standalone notes across several sittings. Prepare the anxiety-disorders differential (generalised anxiety versus panic versus social anxiety versus the phobias), the medical mimics that must be excluded, and the guideline-anchored first-line management for each. essay and short note, recurring

- **Obsessive-compulsive disorder, its management and its recent advances.** This is the most heavily examined disorder in the band: "Discuss etiopathogenesis, clinical features and management of obsessive compulsive disorders", "Discuss the etiology, clinical features and management of obsessive compulsive disorder", "Discuss the recent advances in the treatment of obsessive compulsive disorder" and "Discuss the nosological shift of OCD in DSM-5 and its spectrum" have all come as 25-mark essays, and "Management of OCD" recurs as a 10-mark note. Prepare the full management ladder (the high-dose serotonin reuptake inhibitor for a long trial, clomipramine, exposure and response prevention, antipsychotic augmentation and the refractory options), the cortico-striato-thalamo-cortical model and the obsessive-compulsive related spectrum. essay and short note, recurring

- **The obsessive-compulsive related disorders.** "Trichotillomania" has come as a standalone 10-mark note, and the obsessive-compulsive related disorders are drawn into the wider "impulse control disorders" essay. Prepare body dysmorphic disorder, hoarding, trichotillomania and excoriation as a compact spectrum, each recognised by its defining repetitive behaviour or preoccupation. short note, recurring

- **Post-traumatic stress disorder, its features and its evidence-based treatment.** "Describe the core symptoms and risk factors in PTSD. Discuss management strategies of PTSD" and "Discuss the etiopathogenesis, clinical features and management of post-traumatic stress disorder" have both come as 25-mark essays, and "Post traumatic stress disorder" recurs as a 10-mark note. Prepare the symptom clusters (the DSM-5 four and the ICD-11 three), the trauma-focused-psychotherapy-first algorithm with

the pharmacotherapy and prazosin behind it, and the rule that a benzodiazepine is not used. essay and short note, recurring

Q **Acute stress, grief and the other trauma and stressor disorders.** "Acute Stress Disorder" (paired with chronic fatigue syndrome in one sitting), "Complicated grief" and "Grief" have each come as 10-mark notes across several years, and eye movement desensitisation and reprocessing ("EMDR") as a standalone note. Prepare the acute-stress-reaction-versus-disorder distinction, complex post-traumatic stress disorder and its separation from a personality disorder, prolonged grief disorder against normal grief, and EMDR as a trauma-focused therapy. short note, recurring

Prepare this material to be diagnosed and treated, not just recited: the anxiety-disorders and medical-mimic differentials, the scale cut-offs (the GAD-7, HAM-A, Y-BOCS and PCL-5 bands), the dose-anchored good-to-remember boxes, the obsessive-compulsive-disorder ladder and the trauma-focused algorithm in these notes are built to the way the block is examined. The anxiolytic and hypnotic pharmacology lives in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes; the deep antidepressant pharmacology in the Mood disorders: pharmacotherapy notes; the fear-circuit anatomy in the Neurochemistry, neuroendocrinology, neuroimaging and basic psychopharmacology notes; deep brain stimulation and neurosurgery for refractory obsessive-compulsive disorder in the ECT and neurostimulation notes; and the somatic-symptom and illness-anxiety boundary in the Somatic-symptom, sexual, impulse-control disorders and suicide notes.

Quick review

THE ANXIETY DISORDERS: THE FOCUS OF THE FEAR, THE FIRST-LINE, AND THE SCALES	
THE DISCRIMINATOR	The anxiety symptoms are shared; the disorders separate by the **focus of the fear**. GAD = free-floating worry about everything; panic = the next attack; social anxiety = negative evaluation; specific phobia = one circumscribed object; agoraphobia = no escape or help.
GENERALISED ANXIETY DISORDER	Chronic uncontrollable worry across domains. First-line an **SSRI or SNRI**; also **pregabalin** and **buspirone**; a benzodiazepine is **not** first-line and not for long-term use.
PANIC DISORDER AND CLARK'S MODEL	Recurrent unexpected panic; the vicious cycle is the **catastrophic misinterpretation** of benign body sensations, maintained by safety behaviours. First-line SSRI (start low, warn about early activation) and CBT.
SOCIAL ANXIETY, PHOBIAS, AGORAPHOBIA	Social anxiety: SSRI and CBT, with **propranolol** for discrete performance anxiety. Specific phobia: graded exposure and systematic desensitisation (blood-injection-injury is diphasic vasovagal, use applied tension). Agoraphobia: exposure, now diagnosable independent of panic.
THE SCALES	**GAD-7**: 7 items 0 to 3, total **0 to 21**; 5, 10 and 15 mark mild, moderate and severe, and **10 or more** is the clinical cut-off. **HAM-A**: 14 clinician-rated items 0 to 4, total **0 to 56**.
EXCLUDE THE BODY FIRST	Before naming an anxiety disorder, exclude the mimics by tempo: **sustained** thyrotoxicosis (TSH) mimics GAD; **episodic** phaeochromocytoma (metanephrines) and hypoglycaemia mimic panic; the sign-first arrhythmia (ECG) and asthma; **worst on waking** is alcohol or benzodiazepine withdrawal; caffeine over **250 mg**. Missing a mimic is the exam-fatal error.
OBSESSIVE-COMPULSIVE AND RELATED DISORDERS: FEATURES, THE CIRCUIT, THE LADDER	
OCD FEATURES	Obsessions (intrusive, unwanted, ego-dystonic) and compulsions (neutralising acts); symptom dimensions (contamination/washing, symmetry/ordering, forbidden thoughts, harm/checking); the **insight specifier** (good or fair, poor, absent or delusional) and the tic-related specifier.
Y-BOCS	10 clinician-rated items (5 obsession, 5 compulsion), each 0 to 4, total **0 to 40**. Bands: **0 to 7 subclinical, 8 to 15 mild, 16 to 23 moderate, 24 to 31 severe, 32 to 40 extreme**.

OBSESSIVE-COMPULSIVE AND RELATED DISORDERS: FEATURES, THE CIRCUIT, THE LADDER	
THE CSTC CIRCUIT	Orbitofrontal cortex and anterior cingulate to caudate to pallidum interna and substantia nigra reticulata to thalamus and back to cortex; the direct pathway disinhibits the thalamus, the indirect pathway brakes it. In OCD the direct loop is **overactive**, so the loop is hyperactive and self-sustaining.
THE MANAGEMENT LADDER	First-line a **high-dose SSRI** (fluoxetine 60, up to 80; sertraline 150 to 200; paroxetine 40 to 60; fluvoxamine to 300; escitalopram 20 to 30 mg) for a **long 10 to 12 week trial** plus CBT with ERP; then **clomipramine 150 to 225 mg** (ECG); then augment with **risperidone 1 to 3 mg** or aripiprazole for at least 8 weeks; then refractory options (DBS, neurosurgery). Continue a responder **1 to 2 years**.
CLOMIPRAMINE VERSUS SSRI, AND ERP	Clomipramine is marginally more efficacious on meta-analysis but less tolerable (cardiotoxicity, seizures), so an SSRI is first-line and clomipramine the switch. **Exposure and response prevention** (the exposure hierarchy plus prevention of the ritual, so anxiety habituates) is the core psychological treatment.
THE OCRD SPECTRUM	Body dysmorphic disorder (a perceived defect), hoarding, trichotillomania (hair-pulling) and excoriation (skin-picking); illness anxiety sits at the boundary with the somatic-symptom disorders. Each shares a repetitive act or a fixed preoccupation and responds in part to an SSRI and to behavioural therapy.

TRAUMA AND STRESSOR-RELATED DISORDERS: PTSD, ITS TREATMENT, AND THE REST	
PTSD CLUSTERS AND THE SCALE	DSM-5-TR requires four clusters (intrusion, avoidance, negative alterations in cognition and mood, arousal and reactivity); ICD-11 keeps three (re-experiencing in the here and now, avoidance, a persistent sense of current threat) and drops the negative-cognitions cluster. DSM-5 adds a dissociative subtype. **PCL-5**: 20 items 0 to 4, total **0 to 80**; provisional cut-off about **31 to 33**.
THE PTSD ALGORITHM	Two hard rules: **trauma-focused psychotherapy is first-line** (trauma-focused CBT or EMDR, 8 to 12 sessions), and a **benzodiazepine is never used**. If a drug is used: a licensed SSRI (**sertraline or paroxetine**) or **venlafaxine 37.5 to 300 mg**, trialled up to 12 weeks; add **prazosin 1 to 15 mg nocte** for nightmares; augment with risperidone or olanzapine; continue a responder at least **12 months**.

TRAUMA AND STRESSOR-RELATED DISORDERS: PTSD, ITS TREATMENT, AND THE REST	
COMPLEX PTSD	ICD-11 6B41 = the PTSD triad **plus** three disturbances in self-organisation (affect dysregulation, a persistent negative self-concept, interpersonal difficulty). Versus borderline personality disorder: complex PTSD shows trauma-reminder avoidance and current threat (absent in the PD), a **stable** negative self-view (not unstable identity), relationships of avoidance and disconnection (not abandonment), and suicidality that is less impulsive but of higher lethality.
ACUTE STRESS AND ADJUSTMENT	ICD-11 **acute stress reaction** is a transient normal response, classified outside the disorders; the DSM-5 **acute stress disorder** is a diagnosable disorder in the first month. Adjustment disorder is a maladaptive reaction to an identifiable stressor (ICD-11: preoccupation with the stressor plus failure to adapt); do not over-diagnose a normal reaction.
PROLONGED GRIEF; THE ATTACHMENT DISORDERS	Prolonged grief disorder (ICD-11 and DSM-5-TR): persistent, pervasive grief and yearning beyond the expected social norm and time; not normal grief. Reactive attachment and disinhibited social engagement disorders are the trauma disorders of early severe neglect (child home).
THE GUIDELINE SPINE AND THE HARD RULES	
THE GUIDELINE ORDER	Guidelines-first on the where-to-treat, target-by-phase, modes-of-treatment spine: **BAP leads**, then the **IPS CPG** (the 2025 guideline for OCD), NICE, CANMAT and WFSBP; state the BAP position first, then what the others recommend.
ANXIETY	**SSRI or SNRI first-line** for the anxiety disorders; the benzodiazepine is not first-line and not for long-term use; pregabalin and buspirone for GAD, propranolol for performance anxiety.
OCD	The anchoring rule is **high dose, long trial**: OCD needs a higher SSRI dose and a longer (10 to 12 week) trial than depression before it is called a failure; then clomipramine, then augmentation. A wrong first-line or an under-dose is critical.
PTSD	**Trauma-focused psychotherapy first**; then a licensed SSRI or venlafaxine with prazosin for nightmares; and **never a benzodiazepine**, which is not a treatment and may increase PTSD risk given early.
THE FIVE TRAPS	Missing a medical mimic of anxiety; under-dosing or stopping the OCD SSRI trial early; a benzodiazepine for PTSD; complex PTSD mislabelled as a personality disorder; and treating normal grief as prolonged grief disorder too soon.

References

The anxiety, obsessive-compulsive and trauma content is grounded in the standard psychiatry and psychopharmacology sources (the source hierarchy below), with Kaplan and Sadock and the Maudsley Prescribing Guidelines as the depth bar for the phenomenology, the neurobiology, the scale cut-offs and the doses, and Gelder's Shorter Oxford Textbook for the medical mimics of anxiety. The management is guideline-first, led by the British Association for Psychopharmacology, with the Indian Psychiatric Society (the 2025 clinical practice guideline for obsessive-compulsive disorder), NICE, CANMAT, the WFSBP, the United States VA/DoD and WHO mhGAP. Every scale cut-off, criterion, dose and first-line recommendation was checked against these sources and the adversarial content pass; anything that could not be confirmed was omitted and flagged rather than guessed. Each journal PMID below was verified against PubMed this build and matched on title, first author and year; identifiers that resolved to the wrong paper were corrected or dropped. Books and guideline documents are cited by author, title and year without a PMID.

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PART VIII

VIII

Dissociative, Conversion and Anxiolytic-Hypnotic Pharmacology

The dissociative and conversion disorders, and the pharmacology of the anxiolytics and hypnotics.

01 Dissociative and conversion disorders

02 Anxiolytic and hypnotic pharmacology

03 Apply and consolidate

PAPER II

Dissociative, conversion and anxiolytic-hypnotic pharmacology

Two sections . one complete notes document

This material gathers the dissociative and conversion disorders and the anxiolytic and hypnotic drugs into one document, by syndrome and by mechanism. The first band is **the dissociative and conversion disorders**: the concept and classification of dissociation, the pathogenesis across the psychodynamic, trauma and neurobiological models, dissociative identity disorder, conversion or dissociative neurological symptom disorder with its positive rule-in signs, depersonalisation-derealisation, dissociative amnesia and fugue, and the possession and trance states. The second band is **the anxiolytic and hypnotic pharmacology**: the benzodiazepines in full, buspirone and the azapirones, the z-drugs, the dual orexin receptor antagonists, melatonin and ramelteon, etifoxine and the other non-benzodiazepine anxiolytics, and the beta-blockers, antihistamines and gabapentinoids used for anxiety. The examinable skill is twofold: the safe discrimination of the dissociative presentations from one another and, above all, of a conversion disorder from an organic disease by its positive signs; and the guideline-anchored selection of an anxiolytic or hypnotic, with the benzodiazepine mechanism, its half-life classes, its dependence and taper, and the short-course rule at the centre.

HOW TO USE THESE NOTES

Read the two bands as one account of a shared theme: the boundary between a functional and an organic disturbance, and the drugs that act on the same GABA-A receptor. The **dissociative and conversion** band builds the frame: the classification of the dissociative disorders, the models of how dissociation arises, each named syndrome discriminated from the others, and conversion or functional neurological disorder taught in full as a diagnosis made on POSITIVE signs (Hoover's sign, the give-way weakness, tremor entrainment, the tubular field) rather than by exclusion. The **anxiolytic and hypnotic** band teaches the drugs by mechanism: the benzodiazepines as positive allosteric modulators at the GABA-A receptor, their half-life-based classes, their dependence and the withdrawal-and-taper, and flumazenil as the antagonist, then buspirone, the z-drugs, the orexin and melatonergic hypnotics and the adjunctive anxiolytics. Every management recommendation is guideline-anchored, led by the BAP guidelines with the NICE, Maudsley and Indian Psychiatric Society positions stated, on the where-to-treat, target-by-phase, modes-of-treatment spine, and the benzodiazepine-sparing short-course rule is the anchor. Every named syndrome ends with a **Good to remember** box giving the criterion, the discriminator and the first step, and every named drug ends with one giving the mechanism or class, the signature caution and the one dose or half-life. Figures declare one axis and code it in colour: **petrol** marks structure and the neutral case, **coral** marks the trap or the danger, and **marigold** highlights the number to hold; the dissociation rating scales are reproduced as the actual instruments where the licence permits, credited to their sources, or typeset from their structure where it does not. Several boundaries are stated up front and cross-referenced, not re-taught: the GABA-A receptor and the wider receptor systems in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the sedative and benzodiazepine use disorder as an addiction in the Substance use disorders notes; the lorazepam management of catatonia in the Other psychotic disorders, delusional syndromes and catatonia notes; the anxiety disorders where these anxiolytics are used in the Anxiety, OCD and trauma-related disorders notes; the SSRI and SNRI first-line anxiolytics in the Mood disorders: pharmacotherapy notes; clinical insomnia and CBT for insomnia in the Eating and sleep-wake disorders notes; the video-EEG work-up of dissociative convulsions in the Epilepsy and psychiatry notes; and the possession-trance states in the transcultural frame in the Consultation-liaison, geriatric and transcultural psychiatry notes. Conversion or dissociative neurological symptom disorder and the whole anxiolytic and hypnotic pharmacology are owned and fully taught here. This is doctor-facing revision, so the full technical vocabulary is used, brand names lead with the Indian brand, and every dose, half-life, scale cut-off, positive sign and first-line recommendation is verified against a source or omitted and flagged.

Dissociative and conversion disorders

1 . Dissociative disorders: classification and clinical types

Why this leads the chapter. This topic is the orienting map for everything that follows. Dissociation is the **disruption of the normal integration** of consciousness, memory, identity, emotion, perception, body representation, motor control and behaviour (DSM-5-TR; ICD-11). Once you can name the components that can come apart, the whole family of **dissociative disorders** falls into place as a small number of **clinical types**, each defined by *which* integrative

function has failed. The examiner reward here is a clean **disorder-class map**: the ICD-11 grouping, the DSM-5-TR grouping, and the single organising split that separates the disorders of mind from the disorder of body. Get the map right and every individual criterion set hangs off it; get it wrong and you will confuse a depersonalisation state for psychosis, a functional seizure for epilepsy, or a possession trance for delusional identification.

This fragment first defines dissociation and its positive and negative symptoms, then draws the **classification of dissociative disorders** as a decision-tree, then walks each named clinical type with its defining criterion, and closes on how dissociation is measured. The accompanying figure sets the same content out as a classification tree (a decision-tree, or criteria map) to be memorised as one image. The wider anxiety context and the dissociative subtype of PTSD live in the Anxiety, OCD & trauma-related disorders notes; the video-EEG work-up of dissociative (non-epileptic) convulsions is developed in the Epilepsy & psychiatry notes; the transcultural reading of possession and trance is expanded in the Consultation-liaison, geriatric & transcultural psychiatry notes; and the somatic-symptom, functional and factitious boundary sits in the Somatic-symptom, sexual, impulse-control disorders & suicide notes.

Fig 15.1 The classification of dissociative disorders as a decision tree: dissociation splits into disorders of mind and a single disorder of body, with ICD-11 keeping conversion inside the family and DSM-5 filing it elsewhere.

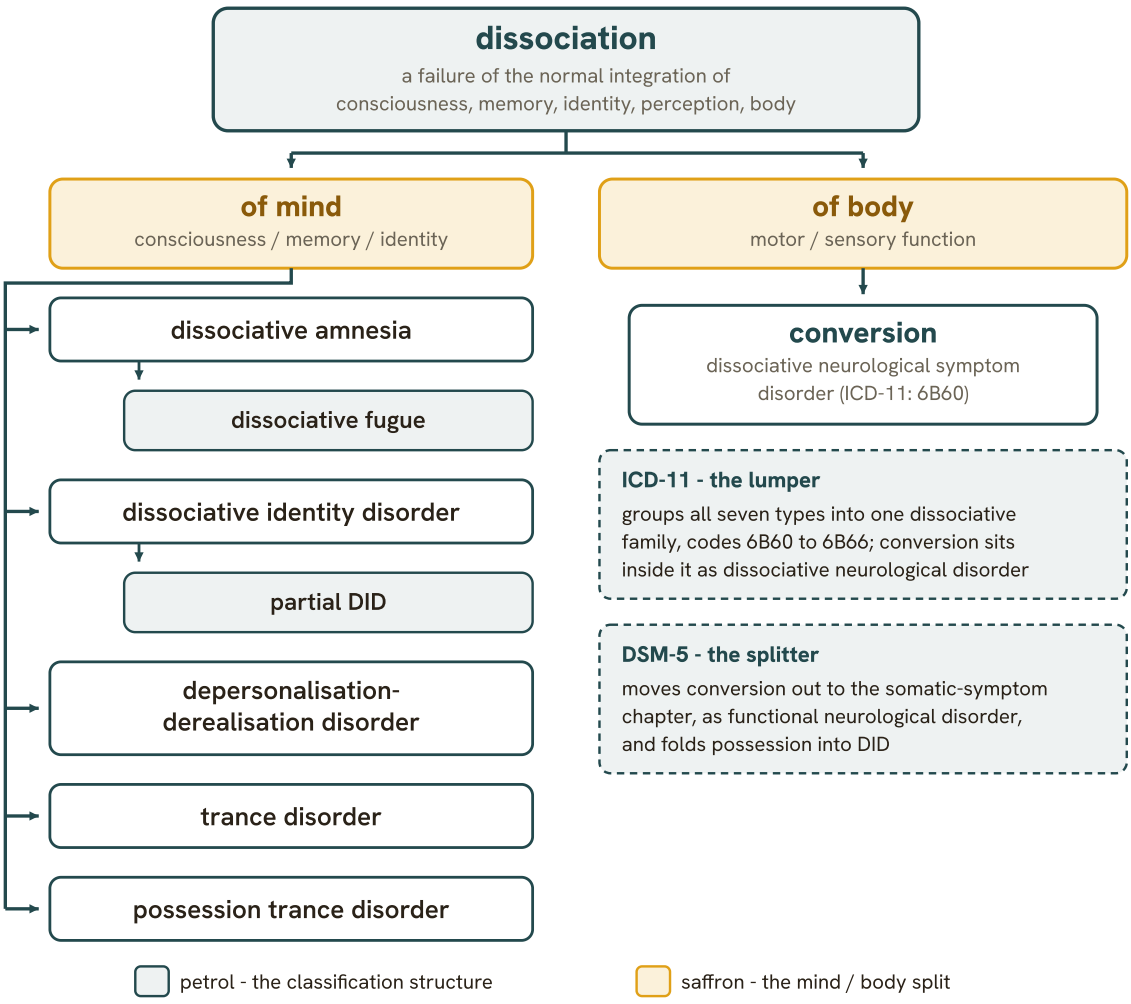


Fig 15.2 The Dissociative Experiences Scale (DES-II) reproduced in full: the 28-item self-report screen for dissociative experiences, scored as the mean of all items.

Dissociative Experiences Scale (DES-II)

Instructions. This questionnaire asks about experiences that you may have in your daily life. We are interested in how often you have these experiences. It is important that your answers show how often these experiences happen to you when you are not under the influence of alcohol or drugs. For each item, mark the percentage of the time the experience applies to you.

0% (never) · 10 · 20 · 30 · 40 · 50 · 60 · 70 · 80 · 90 · 100% (always)

1. Some people have the experience of driving or riding in a car or bus or subway and suddenly realizing that they don't remember what has happened during all or part of the trip.
2. Some people find that sometimes they are listening to someone talk and they suddenly realize that they did not hear part or all of what was said.
3. Some people have the experience of finding themselves in a place and have no idea how they got there.
4. Some people have the experience of finding themselves dressed in clothes that they don't remember putting on.
5. Some people have the experience of finding new things among their belongings that they do not remember buying.
6. Some people sometimes find that they are approached by people that they do not know, who call them by another name or insist that they have met them before.
7. Some people sometimes have the experience of feeling as though they are standing next to themselves or watching themselves do something and they actually see themselves as if they were looking at another person.
8. Some people are told that they sometimes do not recognize friends or family members.
9. Some people find that they have no memory for some important events in their lives (for example, a wedding or graduation).
10. Some people have the experience of being accused of lying when they do not think that they have lied.
11. Some people have the experience of looking in a mirror and not recognizing themselves.
12. Some people have the experience of feeling that other people, objects, and the world around them are not real.
13. Some people have the experience of feeling that their body does not seem to belong to them.
14. Some people have the experience of sometimes remembering a past event so vividly that they feel as if they were reliving that event.
15. Some people have the experience of not being sure whether things that they remember happening really did happen or whether they just dreamed them.
16. Some people have the experience of being in a familiar place but finding it strange and unfamiliar.
17. Some people find that when they are watching television or a movie they become so absorbed in the story that they are unaware of other events happening around them.
18. Some people find that they become so involved in a fantasy or daydream that it feels as though it were really happening to them.
19. Some people find that they sometimes are able to ignore pain.
20. Some people find that they sometimes sit staring off into space, thinking of nothing, and are not aware of the passage of time.
21. Some people sometimes find that when they are alone they talk out loud to themselves.
22. Some people find that in one situation they may act so differently compared with another situation that they feel almost as if they were two different people.
23. Some people sometimes find that in certain situations they are able to do things with amazing ease and spontaneity that would usually be difficult for them (for example, sports, work, social situations, etc.).
24. Some people sometimes find that they cannot remember whether they have done something or have just thought about doing that thing (for example, not knowing whether they have just mailed a letter or have just thought about mailing it).
25. Some people find evidence that they have done things that they do not remember doing.
26. Some people sometimes find writings, drawings, or notes among their belongings that they must have done but cannot remember doing.
27. Some people sometimes find that they hear voices inside their head that tell them to do things or comment on things that they are doing.

28. Some people sometimes feel as if they are looking at the world through a fog, so that people and objects appear far away or unclear.

Scoring and interpretation. Score each item 0 to 100. The DES-II score is the **mean** of all 28 items (range 0 to 100). A mean of about **30 or more** is a positive screen that warrants a full clinical interview for a dissociative disorder (a threshold of 20 to 30 is used across studies; only about 1 percent of people with dissociative identity disorder score below 30). The 8-item **DES-Taxon** (items 3, 5, 7, 8, 12, 13, 22, 27) estimates the probability of pathological dissociation. The DES is a screen, not a diagnosis.

Dissociative Experiences Scale (DES-II). Bernstein EM, Putnam FW (1986); Carlson EB, Putnam FW (1993), Dissociation 6(1):16-27. The copyright belongs to the authors, who have given permission for the scale to be copied, distributed or reproduced for clinical, research and educational use. Reproduced here for free, non-commercial educational use with acknowledgement.

Fig 15.3 The Somatoform Dissociation Questionnaire (SDQ-20): structure and cut-offs, typeset from the published instrument (not reproduced verbatim).

Somatoform Dissociation Questionnaire (SDQ-20)

A 20-item self-report measure of **somatoform (bodily) dissociation**: the disruption of the normal integration of sensory, motor and pain functions. It complements the DES, which measures the psychological forms of dissociation. Each item is rated on a five-point scale from 1 (this applies to me not at all) to 5 (this applies to me extremely).

Negative somatoform symptoms (losses)

Analgesia and kinaesthetic anaesthesia, blurred or tunnel vision, difficulty swallowing or passing urine, motor inhibition or functional paralysis, and loss of taste or smell.

Positive somatoform symptoms

Localised bodily pain and unusual, hard-to-explain bodily sensations.

Scoring and interpretation. Sum the 20 items (range **20 to 100**); a higher score indicates more somatoform dissociation. A total above about **30** is suggestive of a somatoform dissociative disorder. A derived five-item screener, the **SDQ-5**, uses a cut-off of **8 or more** to flag a probable dissociative disorder. The questionnaire is a screen, not a diagnosis.

Somatoform Dissociation Questionnaire (SDQ-20). Nijenhuis ERS, Spinhoven P, Van Dyck R, Van der Hart O, Vanderlinden J (1996), J Nerv Ment Dis. Structure and cut-offs typeset here in our own words with acknowledgement; the full item set is not reproduced.

1.1 What dissociation actually is

An integration failure, not a content abnormality. Normal mental life binds perception, memory, affect, identity and the sense of a body-in-control into one continuous stream owned by one self. In **dissociation** that binding fails, so functions that are normally seamless become detached, inaccessible or intrusive (DSM-5-TR; Kaplan 2024). DSM-5-TR frames the symptoms in two directions worth reproducing verbatim: **positive** dissociative symptoms are unbidden intrusions with loss of continuity in subjective experience (division of identity, depersonalisation, derealisation), while **negative** dissociative symptoms are an inability to access information or control mental functions that are normally available (amnesia). The historical spine runs from Pierre Janet, who described *desagregation*, the disaggregation of functions that should be integrated (Tasman 2024). Crucially, dissociation is best understood as a *transdiagnostic* process: a large meta-analysis of 219 studies across 19 diagnostic categories found dissociation cutting across most disorders and predicting poorer treatment response, which is why it should be assessed routinely rather than only when a dissociative disorder is suspected (Kaplan 2024).

RULE **Ask which function came apart.** Every dissociative disorder is named by the integrative function that has failed: memory (amnesia), identity (identity disorder), self and surroundings (depersonalisation-derealisation), awareness (trance), or motor and sensory control (conversion). Localise the failure and the diagnosis names itself.

1.2 The organising split: mind versus body

Psychoform against somatoform dissociation. The single most useful cut across the family is between dissociation of the *mind* (consciousness, memory and identity) and dissociation of the *body* (voluntary motor and sensory function). The first branch holds dissociative amnesia, dissociative identity disorder and its partial form, depersonalisation-derealisation disorder, and the trance and possession-trance disorders. The second branch is a single entity, conversion, which ICD-11 places *inside* the dissociative disorders as dissociative neurological symptom disorder, whereas DSM-5-TR keeps it under the somatic symptom disorders as functional neurological symptom disorder (Kaplan 2024). This is the heart of the **conversion versus dissociation** question: they are the same underlying process expressed in different currencies, one in the medium of consciousness and memory, the other in the medium of the body. Holding this split is what lets you place any new presentation on the **disorder-class map** in one step.

MNEMONIC

MIND SPLITS, BODY SPEAKS, GABA SLEEPS

The master hook for the whole chapter. **MIND SPLITS** is the psychoform half, the dissociative disorders of consciousness, memory and identity (amnesia, dissociative identity disorder and partial dissociative identity disorder, depersonalisation-derealisation, trance and possession trance). **BODY SPEAKS** is the somatoform half, conversion or dissociative neurological symptom disorder, the mind speaking through the body in motor and sensory symptoms. **GABA SLEEPS** hands over to the second half of the chapter, the anxiolytic and hypnotic pharmacology that acts on the GABA-A receptor. Carry these three beats and the whole chapter reassembles at consolidation from one line.

1.3 The ICD-11 dissociative grouping

The seven named types, in code order. ICD-11 defines dissociative disorders by "involuntary disruption or discontinuity in the normal integration of one or more of the following: identity, sensations, perceptions, affects, thoughts, memories, control over bodily movements, or behaviour" (ICD-11 CDDR). It then lists seven specified entities plus two residual codes. Reproduce the block as one table; the ICD-11 dissociative grouping is the version most examiners now expect first because it keeps conversion within the family.

ICD-11 CODE	DISORDER	INTEGRATIVE FUNCTION DISRUPTED
6B60	**Dissociative neurological symptom disorder**	Motor and sensory control (conversion)

ICD-11 CODE	DISORDER	INTEGRATIVE FUNCTION DISRUPTED
6B61	Dissociative amnesia (specify with or without dissociative fugue)	Autobiographical memory
6B62	Trance disorder	Awareness of surroundings, narrowed consciousness
6B63	Possession trance disorder	Identity replaced by an external agent
6B64	Dissociative identity disorder	Identity split into distinct personality states
6B65	Partial dissociative identity disorder	Identity intruded on, without executive takeover
6B66	Depersonalisation-derealisation disorder	Sense of self and of reality (with intact reality testing)
6B6Y / 6B6Z	Other specified / unspecified dissociative disorder	Residual

The ICD-11 dissociative-disorders grouping, ordered by code; conversion (6B60) sits inside the family.

1.4 The DSM-5-TR grouping and where conversion sits

The one deliberate difference to memorise. The DSM-5-TR dissociative disorders are dissociative identity disorder, dissociative amnesia (with dissociative fugue as a specifier), depersonalisation-derealisation disorder, other specified and unspecified dissociative disorder (Kaplan 2024). The load-bearing contrast is placement of conversion: ICD-11 keeps it as a dissociative disorder, DSM-5-TR classifies it under the somatic symptom disorders as functional neurological symptom disorder. DSM-5-TR also folds pathologic possession *into* dissociative identity disorder rather than giving it a separate code, and has no standalone trance or partial dissociative identity disorder categories, handling those subtler presentations under other specified dissociative disorder. The comparison, read side by side, is the examinable core of the **classification of dissociative disorders**.

ENTITY	ICD-11	DSM-5-TR
Amnesia	Dissociative amnesia (6B61)	Dissociative amnesia (fugue = specifier)
Identity fragmentation	Dissociative identity disorder (6B64)	**Dissociative identity disorder**
Sub-threshold identity intrusion	Partial dissociative identity disorder (6B65)	Other specified dissociative disorder
Detachment from self / world	Depersonalisation-derealisation (6B66)	Depersonalisation-derealisation disorder
Narrowed awareness	Trance disorder (6B62)	Other specified (dissociative trance)

ENTITY	ICD-11	DSM-5-TR
Possession	Possession trance disorder (6B63)	Folded into dissociative identity disorder
Conversion	**Dissociative neurological symptom disorder (6B60)**	Functional neurological symptom disorder (under somatic symptom disorders)

ICD-11 versus DSM-5-TR: same clinical types, two different filing decisions, conversion the pivotal one.

PEARL

The two manuals disagree in exactly one direction. ICD-11 is the "lumper" that keeps conversion, trance, possession and partial identity states inside the dissociative family; DSM-5-TR is the "splitter" that exports conversion to the somatic disorders and absorbs possession into dissociative identity disorder. Learn the ICD-11 list of seven, then learn what DSM-5-TR *moves*.

1.5 Dissociative amnesia (and dissociative fugue)

Retrograde loss of autobiographical memory. Dissociative amnesia is an inability to recall important autobiographical information, usually of a traumatic or stressful nature, that is inconsistent with ordinary forgetting (DSM-5-TR). The deficit is predominantly *retrograde* and the new-learning (anterograde) capacity is preserved, which is the discriminator from organic amnesia. It takes recognised patterns: **localised** (a circumscribed event or period), **selective** (some aspects of an event), **generalised** (whole life history and identity, and rare), and the older descriptors **continuous** and **systematised** (Kaplan 2024). Dissociative fugue, purposeful travel or bewildered wandering with amnesia for identity, is a specifier of dissociative amnesia rather than a free-standing disorder. Most patients are initially unaware of the gap, noticing it only when confronted with evidence of events they cannot recall.

TRAP **Calling organic amnesia dissociative.** Dissociative amnesia is retrograde and autobiographical with intact new learning; a dense *anterograde* deficit, clouding, or a focal neurological picture points to delirium, a seizure, transient global amnesia, Wernicke-Korsakoff or a head injury. Exclude the organic cause before you reach for a dissociative label.

GOOD TO REMEMBER

- **Dissociative amnesia:** defining criterion is an inability to recall important autobiographical information (usually stressful) inconsistent with normal forgetting; deficit is *retrograde*, new learning intact; subtypes localised / selective / generalised (continuous, systematised); fugue is a *specifier*, not a separate disorder. First step: rule out an organic amnestic cause.

1.6 Dissociative identity disorder and partial dissociative identity disorder

Two or more identity states, plus amnesia. Dissociative identity disorder is defined by (a) two or more distinct personality states, or an experience of possession, producing marked discontinuity in the sense of self and agency, and (b) recurrent episodes of *dissociative amnesia* (DSM-5-TR). The amnesia criterion is not optional: it is what separates dissociative identity disorder from non-pathological possession or from a purely intrusive picture. DSM-5 deliberately dropped the older requirement that states visibly "take control", because phenomenological studies showed most

cases are subtle, with overlapping and interfering states rather than dramatic switching; amnesia was endorsed by essentially all such patients. ICD-11 adds partial dissociative identity disorder for the common presentation in which one dominant state runs daily life but is intruded on by non-dominant states that take executive control only briefly; in DSM-5-TR most of these fall under other specified dissociative disorder because they lack the full amnesia picture.

The trauma model against the sociocognitive model. The dominant *trauma (posttraumatic) model*, formalised as structural dissociation theory, holds that the personality fails to integrate under severe, repeated early-childhood trauma, and cites consistently high verified trauma rates across cultures. The competing *sociocognitive (fantasy) model* argues the disorder is shaped by suggestion, media exposure and inadvertent therapist cueing in highly hypnotisable, fantasy-prone individuals. The examinable position is that the evidence robustly links dissociation to early trauma, while structural dissociation theory itself remains contested even among dissociation experts (Kaplan 2024).

GOOD TO REMEMBER

- **Dissociative identity disorder:** defining criteria are two or more distinct personality states (or possession) *plus* recurrent dissociative amnesia; DSM-5 removed the "takes control" requirement. Discriminator: the *amnesia* criterion. Debate: trauma / structural-dissociation model versus sociocognitive (fantasy) model.
- **Partial dissociative identity disorder (ICD-11):** one dominant state that functions in daily life, intruded on by non-dominant states that seize executive control only transiently; sits under other specified dissociative disorder in DSM-5-TR.

1.7 Depersonalisation-derealisation disorder

Detachment with the reality check intact. Depersonalisation-derealisation disorder is persistent or recurrent depersonalisation (unreality or detachment from one's own mind, self or body) and/or derealisation (unreality or detachment from surroundings), during which *reality testing remains intact* (DSM-5-TR criterion B). That intact reality testing, and the "as if" quality of the experience without any delusional or dereistic explanation, is the defining differential-diagnostic point separating the disorder from a psychotic disorder (Kaplan 2024). The symptoms must cause distress or impairment, not be attributable to a substance or medical condition (notably seizures), and not be better explained by another disorder. Transient depersonalisation is extremely common in the general population and after cannabis, ketamine or hallucinogens; it becomes a disorder only when persistent and impairing.

TRAP **Reading detachment as psychosis.** The patient who says the world feels unreal, "as if behind glass", but *knows* it is not truly unreal has intact reality testing and depersonalisation-derealisation, not schizophrenia. A delusional, ideas-of-reference or Schneiderian colouring, or belief that the unreality is literal, moves you toward the psychotic spectrum.

GOOD TO REMEMBER

- **Depersonalisation-derealisation disorder:** defining criterion is persistent/recurrent depersonalisation and/or derealisation with *intact reality testing* and an "as if" quality; the intact reality check is the discriminator from psychosis. Scale anchor: a Cambridge Depersonalisation Scale score of **70 or more** is the conventional diagnostic threshold (Kaplan 2024).

1.8 Trance disorder and possession trance disorder

Narrowed awareness, or replaced identity. Trance disorder is an acute narrowing or complete loss of awareness of immediate surroundings, with profound unresponsiveness or insensitivity to stimuli, and often stereotyped movements experienced as outside one's control. Possession trance disorder adds the replacement of the usual sense of personal identity by an external "possessing" identity, typically attributed to a spirit, deity or other agent, with amnesia for the episode. ICD-11 gives these two their own rubric, distinct from dissociative identity disorder; DSM-5-TR instead folds pathological possession into dissociative identity disorder and leaves non-possession trance under other specified dissociative disorder. The decisive criterion for both is the cultural exclusion: the state must be *involuntary, unwanted and outside accepted collective cultural or religious practice*. A trance willingly entered by a healer within an accepted ritual, causing no distress, is not a disorder (Kaplan 2024).

INDIA

Trance and possession presentations are among the most frequent dissociative presentations in Indian practice; the Indian texts describe them directly as "trance and possession disorders (possession hysteria)" and list conversion and dissociative signs such as pseudo-seizures and possession states together. This is the genuine culture-bound edge of the topic: possession and mediumship are woven into accepted ritual across many Indian communities, so the same phenomenology may be normative in one setting and pathological in another. The reading turns entirely on the ICD-11 and DSM-5-TR cultural-exclusion criterion and a proper cultural formulation, not on the surface picture. The transcultural frame is expanded in the Consultation-liaison, geriatric & transcultural psychiatry notes.

GOOD TO REMEMBER

- **Trance disorder:** defining criterion is acute narrowing/loss of awareness of surroundings with unresponsiveness; identity is *not* replaced.
- **Possession trance disorder:** defining criterion is replacement of identity by an external possessing agent with amnesia; both require the state to be involuntary, distressing and *outside accepted cultural or religious practice*. First step: apply the cultural-exclusion criterion.

1.9 Conversion: dissociative neurological symptom disorder

Diagnosed by positive signs, not by exclusion. Dissociative neurological symptom disorder (ICD-11), the functional neurological symptom disorder of DSM-5-TR, is motor, sensory or seizure-like symptoms that are genuinely experienced but incompatible with recognised neurological disease. The modern rule, from Stone and Carson, is that this is *not* a diagnosis of exclusion: it requires **positive signs of internal inconsistency** demonstrating that the nervous

system can work normally when attention is diverted (New Oxford 2024). The cardinal example is Hoover's sign: hip-extension weakness that returns to normal strength during contralateral hip flexion against resistance. The tremor entrainment test shows a functional tremor changing frequency to, or stopping with, a copied rhythm in the other hand. A "give-way" or collapsing weakness, a tubular visual field of the same width at 1 m and 2 m, and astasia-abasia are further positive findings. DSM-5-TR also *removed* the old requirement for an identifiable psychological stressor, and la belle indifference and the mere presence of a stressor are unreliable and are not diagnostic. Because it can coexist with true neurological disease, the positive sign is what rules it in.

POSITIVE SIGN	POSITIVE FINDING THAT RULES IN A FUNCTIONAL CAUSE
Hoover's sign	**Hip-extension weakness that normalises with contralateral hip flexion against resistance**
Tremor entrainment test	Unilateral tremor entrains to, stops with, or cannot copy a rhythm set by the other hand
Give-way (collapsing) weakness	Ratchety, inconsistent power that gives way rather than a fixed pyramidal pattern
Tubular visual field	A field defect of the same width at 1 m as at 2 m (physiologically it should widen)
Astasia-abasia / dragging gait	Bizarre, non-physiological gait, or a leg dragged with the forefoot kept on the floor

Positive rule-in signs of functional (conversion) neurological symptoms (Stone and Carson, New Oxford 2024).

RULE **Rule in, do not rule out.** Conversion is diagnosed on a positive sign of internal inconsistency (Hoover's, entrainment, tubular field), not on the absence of a lesion or the presence of a stressor. The sign shows the system works when attention is elsewhere.

WORKED EXAMPLE

A patient reports a dense right-leg weakness after an argument. Direct right hip extension is flaccid. You then ask her to flex the *left* hip against your hand; as she does, involuntary right hip extension presses firmly into your other palm. That is a positive Hoover's sign: the "paralysed" extensors fire automatically when attention shifts to the good leg. You have ruled the diagnosis *in* at the bedside, without imaging and without invoking the stressor.

COMMON TRAP

The mirror error: an early multiple sclerosis, a spinal cord lesion, a stroke or a focal seizure labelled "conversion" because the presentation seemed emotional or a stressor was present. A positive functional sign coexists with real disease more often than expected, so a rule-in sign never removes the duty to screen for an organic lesion when the picture is atypical, progressive or accompanied by hard neurological findings.

GOOD TO REMEMBER

- **Dissociative / functional neurological symptom disorder:** defining criterion is a neurological symptom with a *positive* sign of internal inconsistency (Hoover's sign, tremor entrainment, tubular field); it is *not* a diagnosis of exclusion, no stressor is required (DSM-5-TR), and la belle indifference is unreliable. First step: elicit a positive sign.

1.10 Measuring dissociation: the DES and the two-tier screen

Screen, then interview. The Dissociative Experiences Scale (DES) is the workhorse self-report measure: subjects rate the percentage of time, from 0 to 100, that each dissociative experience occurs. Most epidemiology uses a two-tier approach, screening with the DES and then applying a structured interview (the SCID-D or the DDIS) to everyone above a cut-off "generally **20 to 30**", with **30** the conventional screening threshold (Kaplan 2024). Mean DES scores rank the family in a way worth memorising: dissociative identity disorder **48.7**, all dissociative disorders combined 38.9, PTSD 28.6, borderline personality disorder 27.9, functional neurological (conversion) disorder 25.6, against a non-clinical mean near 8. The eight-item *DES-Taxon* (DES-T) subscale isolates pathological dissociation and identifies a distinct high-scoring group; the population point-prevalence of this dissociative taxon is about **3.4%**. Somatoform (bodily) dissociation is captured separately by the Somatoform Dissociation Questionnaire (SDQ-20). The instrument forms themselves are reproduced on the accompanying scale plate; a high DES is a flag for further interview, never a diagnosis on its own.

30	8	48.7	3.4%
USUAL DES SCREENING CUT-OFF	ITEMS IN THE DES-T TAXON SUBSCALE	MEAN DES IN IDENTITY DISORDER	POPULATION DISSOCIATIVE TAXON

HOLD THIS

The whole family divides once: dissociation of the mind (amnesia, identity, depersonalisation-derealisation, trance and possession) against dissociation of the body (conversion), with ICD-11 keeping conversion inside the dissociative disorders and DSM-5-TR exporting it to the somatic symptom disorders.

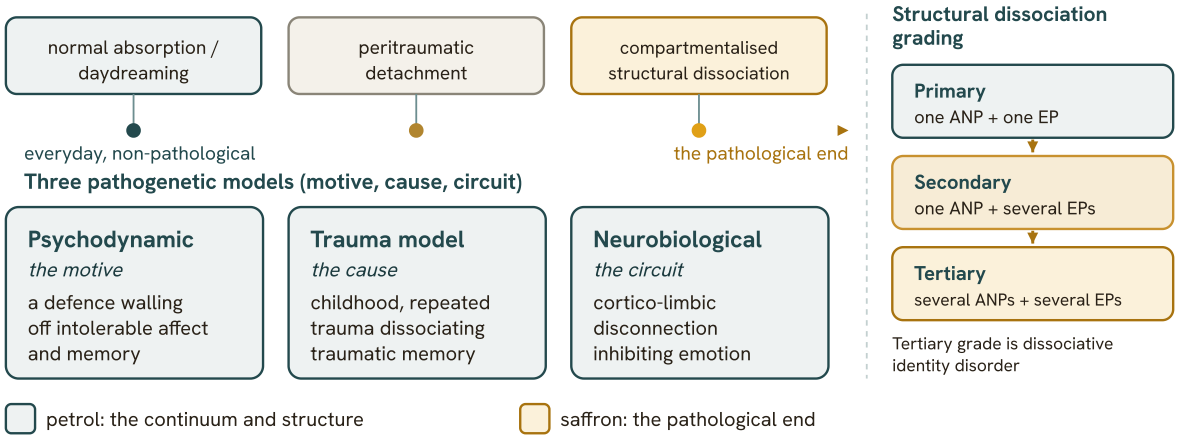
2 · The pathogenesis of dissociation

The **pathogenesis of dissociative disorders** is a favourite viva topic precisely because there is no single mechanism to recite; the examiner wants to hear that you can hold three complementary explanations at once and say what each adds. **The frame to open with.** Dissociation is a disruption of the normally integrated stream of consciousness, memory, identity, emotion, perception and body-sense; the question of pathogenesis asks how that integration comes to fail. The classical answer runs across a **psychodynamic model** (dissociation as a defence that walls off intolerable affect and memory), a **trauma model** (childhood and repeated trauma driving the dissociation of traumatic memory, formalised as the theory of structural dissociation of the personality), and a **neurobiological model** (a fronto-limbic, or cortico-limbic, disconnection with cortico-limbic inhibition visible on imaging). These are not

rival hypotheses to be scored against one another so much as three levels of the same process, and the candidate who names all three, and links them, has the marks.

Why it matters clinically. The three models are not academic; each tells you something the others cannot. The trauma model tells you to take a developmental and abuse history and to expect comorbid post-traumatic disorder. The psychodynamic model tells you why the patient cannot simply "remember" on command and why phased, safety-first therapy, not forced abreaction, is the treatment grammar. The neurobiological model tells you that reality testing stays intact (so this is not psychosis) and explains the numbing and detachment as emotional over-regulation rather than absence of feeling. Teach the **aetiology of dissociation** as one concept model with three faces; the accompanying figure sets it out as a dissociation continuum, from everyday absorption through peritraumatic detachment to the compartmentalised structural dissociation of the severe disorders. The wider dissociative subtype of post-traumatic stress disorder is developed in the Anxiety, OCD & trauma-related disorders notes; here we own the pathogenesis.

Fig 15.4 Dissociation as one continuum with three complementary pathogenetic models, and the primary-to-tertiary grading of structural dissociation (ANP the apparently-normal part, EP the emotional part).



2.1 The three-model scaffold and the dissociation continuum

The concept to fix first. Dissociation runs along a continuum. At one end are normal, non-pathological experiences (absorption in a book, highway hypnosis, momentary "spacing out"); at the other are the compartmentalised amnesias and identity alterations of the severe disorders. Overlaid on that continuum is a genuine debate about whether pathological dissociation is merely the high end of a smooth dimension or a discontinuous *type*; taxonometric work (see the scale section) argues for a distinct pathological taxon rather than a pure continuum. Either way, the pathogenetic question is the same: what pushes a person from normative, transient dissociation into the persistent, involuntary, compartmentalising kind?

Three answers, three levels. The psychodynamic model answers at the level of *meaning and motive* (a defence against unbearable experience); the trauma model answers at the level of *developmental cause* (early, repeated, relationship-based trauma); and the neurobiological model

answers at the level of *mechanism and circuit* (a cortico-limbic disconnection that inhibits emotion). Read them as motive, cause and circuit and they stop competing and start cooperating. The accompanying figure draws this as the concept model to carry through the whole answer.

RULE **Dissociation is a failure to integrate, not a loss of contact with reality.** The three models describe one process at three levels, a psychodynamic defence that walls off intolerable affect and memory, a developmental response to early repeated trauma, and a cortico-limbic disconnection that inhibits emotion; reality testing stays intact throughout, which is what separates dissociation from psychosis.

MNEMONIC

Three D's: Defence, Developmental trauma, Disconnection

Run the pathogenesis in three beats. **Defence** is the psychodynamic model (dissociation walls off intolerable affect and memory). **Developmental trauma** is the trauma model (childhood and repeated trauma, formalised as structural dissociation into an apparently-normal and an emotional part). **Disconnection** is the neurobiological model (cortico-limbic disconnection with prefrontal inhibition of the limbic system). Name the three D's, then link them, and the "aetiology of dissociation" answer writes itself.

2.2 The psychodynamic model: dissociation as a defence

The founding schism. The **psychodynamic model** descends from the late-nineteenth-century split between Pierre Janet and Sigmund Freud. Janet described *désagrégation*, a passive splitting-off of "fixed ideas" and traumatic memory from the integrated personality under the impact of overwhelming events; Freud, by contrast, moved toward *repression* and, later, "splitting" as the governing defences, and psychoanalysis broadened the word trauma to mean almost any developmental stressor. The consequence, as Kaplan & Sadock note, is that psychoanalytic theory has long had difficulty treating dissociation as a *specific* intrapsychic defence against awareness of trauma, tending instead to fold it into "splitting"; David Rapaport's Menninger group in the 1940s, and the older notion of "hypnoid states," were among the few attempts to reconcile the Freudian and Janetian lines.

The defensive core, and the autohypnosis variant. Stripped to its clinical claim, the psychodynamic model says dissociation protects the person by keeping intolerable affect, memory and self-knowledge out of integrated awareness. The most exam-relevant developmental version is the autohypnosis model (associated with Bliss and with Richard Kluft): a traumatised child recruits an innate hypnotic capacity to induce a self-protective dissociative state during overwhelming or repetitive abuse, and with continuous use that autohypnotic state becomes personified into self-states. It is supported by the observation that dissociative patients, especially those with dissociative identity disorder, are the most highly hypnotisable clinical group, though the model is criticised for reasoning backward from adults and for the fact that more systematic research has not confirmed that childhood trauma reliably raises hypnotisability. The grounding of grounding and hypnosis as psychotherapy technique sits in the Psychotherapies, clinical assessment, MSE & nosology notes.

2.3 The trauma model: childhood and repeated trauma

Trauma as the necessary antecedent. The **trauma model** is the dominant contemporary account of the **aetiology of dissociation**. Since the 1980s, several hundred studies across many cultures have found significantly higher dissociation, measured on the Dissociative Experiences Scale and comparable instruments, in traumatised groups than in non-traumatised clinical and general-population samples. **Childhood trauma** is the strongest correlate: childhood sexual and physical abuse, emotional abuse and neglect, and non-maltreatment traumas such as repeated painful medical procedures or wartime displacement, are all over-represented, and survivors of severe, chronic adult trauma (prisoners of war, torture survivors, trafficked and prostituted women, victims of intimate-partner violence) carry high dissociation scores. A meta-analysis by Vonderlin and colleagues of 65 DES studies (7,532 participants) found that a childhood history of abuse or neglect predicted significantly higher DES scores, with combined physical and sexual abuse, earlier onset, longer duration and parental (intrafamilial) abuse driving the highest scores.

Two mechanisms the model adds. First, *peritraumatic dissociation*, dissociation measured at or right after the event (depersonalisation, derealisation, time distortion, trance-like automatism, amnesia), predicts later post-traumatic stress disorder, and dissociation statistically *mediates* the relationship between trauma and subsequent psychopathology. Second, betrayal trauma theory (Jennifer Freyd) explains why abuse by a trusted, depended-upon caregiver is especially likely to be walled off: amnesia here is protective of the attachment the child cannot afford to lose, which is why intrafamilial childhood abuse produces more amnesia than, say, a natural disaster. This is the model that makes dissociation a target for early intervention after trauma.

2.4 Structural dissociation of the personality

The formal trauma theory to name. The trauma model's most cited theoretical elaboration is the theory of structural dissociation of the personality (Onno van der Hart, Ellert Nijenhuis and Kathy Steele), especially influential in Europe and the guiding force behind the ICD-11 criteria for dissociative identity disorder and partial dissociative identity disorder. It proposes that severe traumatic experience produces a "split" between an apparently normal personality (ANP), which is constricted and avoidant, focused on daily functioning, unaware of and phobic toward the traumatic material, and an emotional personality (EP), which carries the unintegrated, unprocessed traumatic memory and its raw affect. The degree of splitting is graded, which is the examinable part.

LEVEL OF STRUCTURAL DISSOCIATION	CONFIGURATION	PROTOTYPICAL DISORDER
Primary	one ANP + one EP	**Post-traumatic stress disorder (and simple conversion presentations)**
Secondary	**one ANP + several EPs**	Complex / "less complex" dissociative disorders, complex PTSD
Tertiary	several ANPs + several EPs	**Dissociative identity disorder**

Structural dissociation graded from primary to tertiary; the accompanying figure renders it as the compartmentalised end of the dissociation continuum. Grounded in Kaplan & Sadock CTP 2024 (van der Hart, Nijenhuis & Steele).

Hold the critique too. Examiners reward a candidate who can also say why the theory is contested: it over-reifies the mind as a "structure" made of "parts," it reasons backward from adult dissociative identity disorder rather than forward from child development, it posits adult-style psychological "structures" in infants (mapping the ANP/EP alternation onto Type-D attachment), and meta-analytic data fit dissociation better as a subtype or component of post-traumatic stress disorder than as the substrate of all of it. A cleaner contemporary framing treats these conditions as disorders of self-organisation, complex dynamic self-state systems, rather than a lesioned "personality."

2.5 The neurobiological model: cortico-limbic disconnection

The core hypothesis. The **neurobiological model** reframes dissociation as a hard-wired inhibitory response of the psychobiological survival system, one that damps anxiety and physiological hyperarousal under extreme threat and becomes pathological when it persists outside danger. Its anatomical statement is the corticolimbic disconnection hypothesis of Mauricio Sierra and German Berrios: in depersonalisation and derealisation there is a bilateral cortico-limbic disconnection with *prefrontal activation and limbic inhibition*, yielding hypoemotionality (the flat, detached, "unreal" quality) together with attentional difficulty. This is the fronto-limbic / cortico-limbic disconnection the question is pointing at.

The imaging and the PTSD bridge. The signature is captured on functional imaging: a positron-emission study using intravenous tetrahydrocannabinol found that cerebral blood-flow *increases* in right frontal and anterior cingulate cortex tracked depersonalisation/derealisation severity, while subcortical blood flow *fell* in the amygdala, hippocampus, basal ganglia and thalamus, exactly the "cortex up, limbic down" pattern. Ruth Lanius and colleagues extended this model to trauma: the dissociative subtype of post-traumatic stress disorder is a state of emotional *over*-modulation (prefrontal over-activation inhibiting the limbic system, producing hypoarousal, numbing and detachment), the mirror image of the emotional *under*-modulation (weak prefrontal restraint over a hyperaroused amygdala) seen in ordinary re-experiencing PTSD. The receptor systems and the wider fear circuitry are developed in the Neurochemistry, Neuroendocrinology, Neuroimaging & Basic Psychopharmacology notes and in the Anxiety, OCD & trauma-related disorders notes; that transcranial magnetic stimulation of the dorsolateral and ventrolateral prefrontal cortex and the temporoparietal junction can *reduce* depersonalisation symptoms, while deep stimulation over medial prefrontal cortex can *induce* depersonalisation in healthy volunteers, is direct causal support for the circuit.

> **PEARL**
>
> One circuit, two directions. Non-dissociative, re-experiencing PTSD is emotional *under*-modulation, a weak prefrontal brake over a hyperaroused amygdala. The dissociative subtype, and depersonalisation-derealisation disorder, is the mirror image, emotional *over*-modulation, prefrontal over-activation that inhibits the limbic system and produces numbing, detachment and hypoarousal. Same cortico-limbic axis, opposite setting; that one sentence answers "what is the neurobiology of dissociation?"

GOOD TO REMEMBER

- **Depersonalisation-derealisation disorder (the criterion anchor):** persistent or recurrent depersonalisation (detachment from one's own mind or body, an "as-if-in-a-dream" unreality) and/or derealisation (unreality of surroundings) with *reality testing kept intact throughout*; the intact reality testing is the discriminator from psychosis, and the cortico-limbic disconnection signature (prefrontal over-activation inhibiting the limbic system) is its putative mechanism, so the first step when it is mislabelled "psychotic" is to confirm that the patient knows the experience is not real.

2.6 The trauma model versus the sociocognitive challenge

The debate to state. The pathogenesis of dissociative identity disorder is where the models are fought over hardest, and this trauma-model-versus-sociocognitive debate is the single most examinable controversy in the chapter. The trauma model holds that severe, early, repeated (often betrayal-laden) trauma drives the disorder (tertiary structural dissociation, or a developmental failure to consolidate one self across states). Against it stand a family of sceptical accounts, the iatrogenic model (states cued and shaped by suggestible therapy, including hypnosis and "recovered-memory" work), the sociocognitive model (a socially learned role reinforced by media and culture), and the fantasy model (dissociation as a trait of fantasy-proneness and suggestibility, with the trauma link an artefact of confabulation).

Where the evidence sits. A systematic comparison by Dalenberg and colleagues (2012) tested the trauma and fantasy models against multiple predictions and found the trauma model confirmed on the great majority, including the point that neurobiological research supports dissociation as a regulatory response to fear with measurable biological correlates. The sociocognitive and iatrogenic accounts, by contrast, rest largely on old, small, analogue studies and cannot account for the large, cross-cultural epidemiological samples ascertained with validated instruments in ordinary clinical settings. The honest examination answer is that trauma is the principal driver, while sociocognitive and cultural factors shape the *secondary structuring* (the number, form and content of self-states) rather than manufacturing the disorder wholesale.

TRAP **Diagnosing dissociative identity disorder without the dissociative-amnesia criterion.** Distinct "states" or role enactments are not enough; the diagnosis requires a disruption of identity with two or more distinct personality states *plus* recurrent dissociative amnesia (gaps in recall for everyday events, personal information or trauma). If the amnesia is absent, or the picture is florid and suggestion-shaped, go back to the sociocognitive and iatrogenic differentials before you commit.

GOOD TO REMEMBER

- **Dissociative identity disorder (the criterion anchor):** on the trauma model it is the tertiary structural dissociation of a child overwhelmed by early, repeated, betrayal-laden **childhood trauma**; the defining criterion is a disruption of identity with two or more distinct personality states *and* recurrent dissociative amnesia, with the presentation not a normal part of a broadly accepted cultural or religious practice; never diagnose it without the amnesia criterion, and weigh the sociocognitive and iatrogenic challenge before accepting a suggestion-shaped presentation.

2.7 Measuring the process: the DES and the dissociative taxon

The instrument to name. Pathogenesis research runs on measurement, and the workhorse is the Dissociative Experiences Scale (DES; Bernstein & Putnam 1986, with the DES-II by Carlson & Putnam 1993), a self-report screen for the frequency of dissociative experiences. It is used in a two-tier way: the DES screens a population, and those above a cut-off are taken to a structured diagnostic interview (the SCID-D-R or the DDIS). The commonly cited screen cut-off is a DES mean of the order of 20 to 30, with a score above 30 indicating severe dissociative psychopathology; the meta-analytic mean DES climbs with severity, from around 25 in conversion disorder and 28 in post-traumatic stress disorder to about 39 across the dissociative disorders and 49 in dissociative identity disorder. The actual instrument is shown in the accompanying scale plate rather than pasted here.

Continuum or taxon. The DES also feeds the continuum-versus-type debate: a taxonometric analysis (Waller, Putnam & Carlson) isolated a DES-Taxon (the DES-T), a subset of items that identifies a discrete subgroup of genuinely pathological dissociators rather than simply high scorers on a smooth dimension. A large Finnish general-population study put the point prevalence of that pathological taxon at about 3.4%. The taxon reading implies a different developmental trajectory (and different treatment) from the merely-high end of normal, and dovetails with the trauma and neurobiological models by pointing to a distinct, trauma-linked pathological process.

2.8 The culture-bound lens and the Indian setting

Culture shapes the presentation. Sociocognitive and cultural factors do not create dissociation, but they strongly shape how it is expressed. Conversion-like dissociative presentations are, on cross-cultural data, more common in India than in certain affluent Western settings, and possession and trance phenomena are a major idiom of dissociative distress in the Indian clinic. The nosologies diverge here: DSM-5 folds pathological possession into dissociative identity disorder, whereas ICD-11 keeps trance disorder and possession trance disorder as categories distinct from dissociative identity disorder. The transcultural framing of possession, trance and the culture-bound syndromes is developed in the Consultation-liaison, geriatric & transcultural psychiatry notes.

The prescribing distortion. Onto this genuinely trauma-and-culture-driven presentation the Indian system too often lays a pharmacological reflex. Benzodiazepines are well documented to be over-prescribed for long-term anxiety, and alprazolam in particular is the widely used, default anxiolytic, dispensed freely for the "tension," insomnia and dissociative or possession-flavoured distress that actually call for a trauma-informed, phased psychotherapy. This is the wrong tool on every one of the three models: it addresses neither the defence, nor the developmental trauma, nor the cortico-limbic circuit, and it breeds dependence. The sedative and benzodiazepine use disorder, intoxication and dependence in the addiction sense are taught in the Substance use disorders notes.

TRAP **Reading a possession or trance state as a dissociative disorder without the cultural formulation.** Possession trance that is a sanctioned, time-limited part of a collective religious or cultural practice is normative, not pathological; the diagnosis requires that the state be unwanted, involuntary, distressing or impairing and occur outside an accepted cultural or religious practice.

INDIA

Dissociation is arguably *more* visible in Indian practice than in the Western textbook: conversion-like and possession/trance presentations are common, culturally embedded and frequently the first idiom in which trauma is spoken. The pathogenesis lens gives two correctives. First, formulate possession and trance culturally before pathologising them (ICD-11's possession trance disorder is defined by the involuntary, distressing, out-of-context state, not by belief in possession itself). Second, resist the country's **benzodiazepine over-prescription** pattern: alprazolam (Alprax, Restyl) is the default anxiolytic and is handed out long-term for exactly these presentations, which suits neither the defence, the developmental trauma, nor the cortico-limbic circuit, and courts dependence. The trauma-informed answer is a phased psychotherapy that builds safety and grounding first, with any anxiolytic kept to a genuine short course.

GOOD TO REMEMBER

- **Alprazolam (Alprax or Restyl), the dose anchor and the anti-pattern:** a high-potency, short-to-intermediate-acting benzodiazepine and India's default anxiolytic, a positive allosteric modulator at the GABA-A receptor (the mechanism is developed in the Neurochemistry, Neuroendocrinology, Neuroimaging & Basic Psychopharmacology notes); the licensed anxiolytic range is 1 to 4 mg per day (about 5 to 6 mg per day for panic), yet it does *not* treat dissociation. Its short action causes interdose rebound anxiety and its seizure risk is greatest in the first three days after abrupt discontinuation, so if used at all it is kept to the lowest effective dose for the shortest time (a course of the order of 4 weeks) with a slow taper; it is not a substitute for trauma-focused psychotherapy.

2.9 Putting the three models together

One process, three faces. The pathogenesis answer is strongest when the three models are stitched into a single developmental story: early, repeated, relationship-based **childhood trauma** (the trauma model) recruits a defensive walling-off of intolerable affect and memory (the psychodynamic model), and that defence is instantiated as a cortico-limbic disconnection in which the prefrontal cortex over-inhibits the limbic system (the neurobiological model), so the person is protected from unbearable feeling at the cost of an integrated, continuous sense of self. Structural dissociation names the endpoint of that process; the DES and its taxon measure it; culture shapes how it is expressed. Every effective treatment targets one of these levels, and none of them is a benzodiazepine.

MODEL	CORE CLAIM / MECHANISM	KEY FIGURES	SIGNATURE EVIDENCE	TREATMENT IMPLICATION
Psychodynamic	**Dissociation is a defence walling off intolerable affect and memory**	Janet, Freud; Bliss, Kluft (autohypnosis)	High hypnotisability of dissociative patients; clinical case material	Phased, safety-first therapy; not forced abreaction
Trauma (incl. structural dissociation)	Early, repeated trauma drives dissociation of traumatic memory; ANP / EP split	**van der Hart, Nijenhuis, Steele; Freyd (betrayal); Putnam**	Raised DES in traumatised groups; Vonderlin & Dalenberg meta-analyses; peritraumatic dissociation predicts PTSD	Trauma history mandatory; trauma-focused, integration-oriented therapy
Neurobiological	Cortico-limbic disconnection: prefrontal overactivation inhibits the limbic system	Sierra & Berrios; Lanius	**PET (cortex up, amygdala/limbic down); over- vs under-modulation in PTSD; rTMS reverses/induces symptoms**	Reality testing intact (not psychosis); circuit-targeted and psychotherapeutic approaches

The three complementary models of the pathogenesis of dissociative disorders, read as motive, cause and circuit; the accompanying figure carries the same three-model concept as a dissociation continuum. Grounded in Kaplan & Sadock CTP 2024.

Dissociation

A disruption of the normally integrated functions of consciousness, memory, identity, emotion, perception and body-sense, with reality testing preserved.

Structural dissociation

A trauma-driven "split" of the personality into an apparently-normal part and one or more emotional parts; graded primary, secondary and tertiary.

Apparently normal personality (ANP)

The constricted, avoidant part focused on daily life, unaware of and phobic toward the traumatic material.

Emotional personality (EP)

The part that holds the unintegrated, unprocessed traumatic memory and its raw affect.

Peritraumatic dissociation

Dissociation occurring at or immediately after the traumatic event; a predictor of subsequent post-traumatic stress disorder.

Cortico-limbic disconnection

The neurobiological model of dissociation: prefrontal (cortical) over-activation inhibiting limbic structures, producing hypoemotionality and detachment.

WORKED EXAMPLE

A woman with a history of chronic intrafamilial childhood sexual abuse presents with hours she cannot account for, a persistent sense that she is watching herself from outside her body, and two coworkers who describe her as "a different person" on some days. Read her through the three models at once. The *trauma model*: early, repeated, betrayal-laden abuse is the necessary antecedent, and her amnesia is the attachment-protective forgetting betrayal-trauma theory predicts. The *psychodynamic model*: the amnesia and the self-states are a defence that keeps unbearable memory and affect out of integrated awareness (an over-learned autohypnotic protection). The *neurobiological model*: her depersonalisation is the cortico-limbic disconnection, prefrontal over-modulation inhibiting the limbic system, which also tells you her reality testing is intact and this is not psychosis. No single model is complete; together they give the formulation, and the management is a phased trauma-focused psychotherapy, not a benzodiazepine.

30	48.7	3.4%	3
DES SCREEN CUT-OFF ABOVE WHICH SEVERE DISSOCIATIVE PSYCHOPATHOLOGY IS LIKELY (TWO-TIER THRESHOLD 20 TO 30)	MEAN DES IN DISSOCIATIVE IDENTITY DISORDER (META-ANALYSIS)	GENERAL-POPULATION PREVALENCE OF THE PATHOLOGICAL DISSOCIATIVE TAXON	LEVELS OF STRUCTURAL DISSOCIATION (PRIMARY, SECONDARY, TERTIARY)

HOLD THIS

The pathogenesis of dissociation is one process told at three levels: early, repeated **childhood trauma** (the trauma model) recruits a defence that walls off intolerable affect and memory (the psychodynamic model), instantiated as a cortico-limbic disconnection in which the prefrontal cortex over-inhibits the limbic system (the neurobiological model); structural dissociation into an apparently-normal and an emotional part names the endpoint, reality testing stays intact (so it is not psychosis), and the treatment is a phased trauma-focused psychotherapy, never a long-term benzodiazepine.

3 · Dissociative identity disorder

The examiner's whole target is one criterion. **Dissociative identity disorder** is a low-volume topic that punches above its weight because it is decided by a single discriminating fact. The disorder is defined by two or more distinct personality (identity) states with a marked discontinuity in the sense of self and agency, layered on *recurrent gaps in autobiographical memory*. That memory criterion is the pivot: the **dissociative-amnesia criterion is required**, and its absence is the classic trap that turns a confident answer into a wrong one.

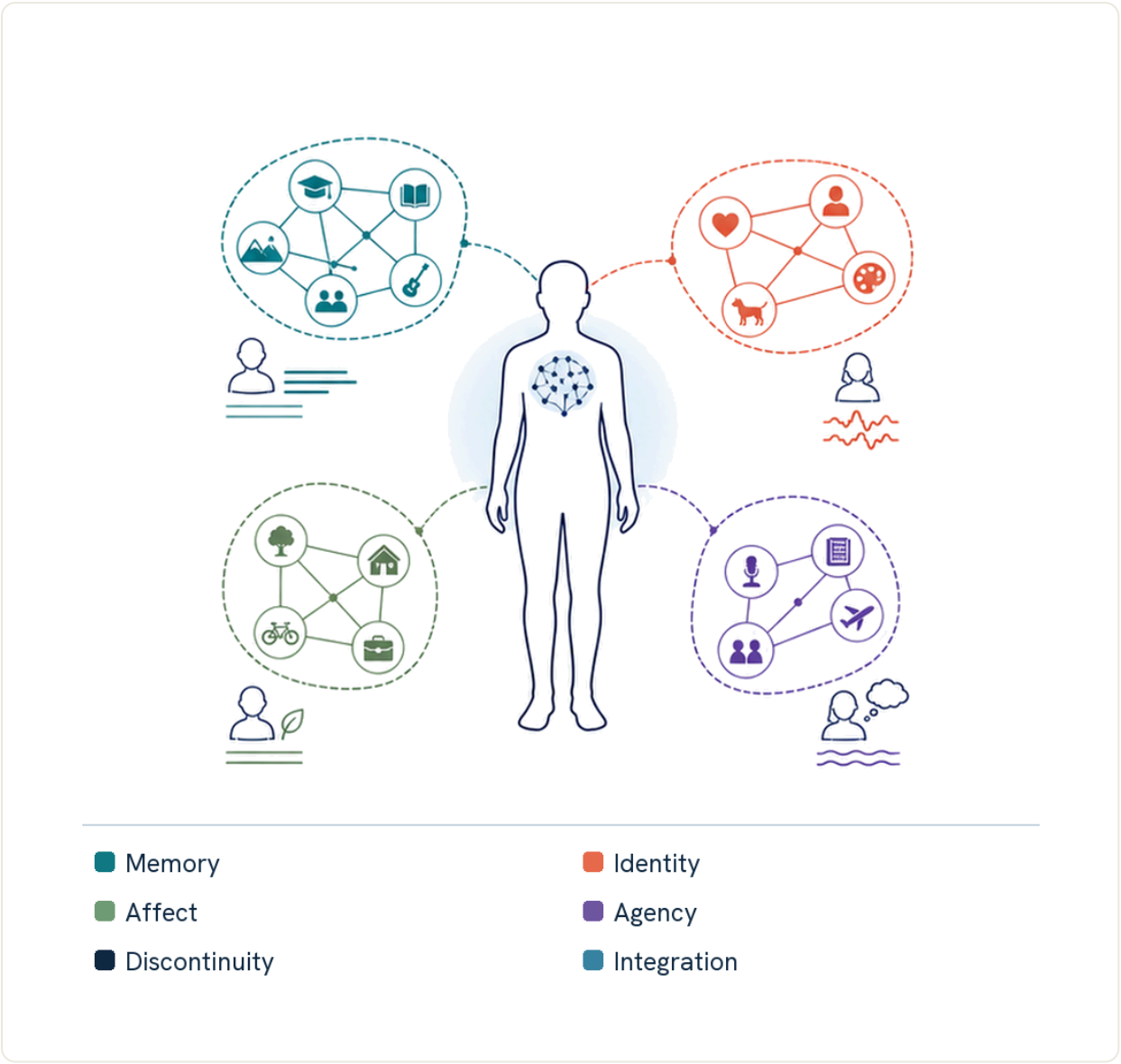


Fig 15.5 Dissociative identity disturbance is represented as discontinuity in the integration of autobiographical memory, identity, affect and agency rather than as separate literal people.

Two things must travel together in every answer. First, the criterion set, because DID without recurrent amnesia is a different (residual) diagnosis. Second, the **controversy**, because the viva examiner reliably asks whether the disorder is a genuine post-traumatic condition or an artefact of therapy and culture, the **trauma model versus sociocognitive model** debate. The older name multiple personality disorder is worth knowing, as is the fact that the flamboyant, fully personified **alter identities** of popular culture are the exception, not the diagnostic rule.

3.1 Criterion A: the disruption of identity

Two or more distinct states, discontinuity of self and agency. DSM-5-TR Criterion A requires a disruption of identity characterised by two or more distinct personality states (which may be described in some cultures as an experience of possession), involving marked discontinuity in the sense of self and sense of agency, with related alterations in affect, behaviour, consciousness, memory, perception, cognition or sensory-motor functioning. Crucially, the elaboration of states with different names, wardrobes, handwriting and accents occurs in only a *minority* of cases and

is *not* essential to diagnosis; in most people the switching is subtle and inferred from sudden discontinuities in the sense of self, not from theatrical alter identities.

3.2 Criterion B: recurrent dissociative amnesia (the anchor)

The required, most-tested criterion. DSM-5-TR Criterion B demands **recurrent gaps** in the recall of everyday events, important personal information and/or traumatic events that are inconsistent with ordinary forgetting. This dissociative amnesia shows up as lost autobiographical memory (a wedding, all schooling before a certain age), lapses for well-learned skills (how to drive or cook), and the discovery of possessions or writings the person has no memory of acquiring. The remaining criteria fence the diagnosis: distress or impairment (C); the disturbance is *not* a normal part of a broadly accepted cultural or religious practice, and in children is not better explained by imaginary playmates or fantasy play (D); and it is not due to a substance (alcohol blackouts) or another medical condition such as complex partial seizures (E).

RULE **Identity disruption plus recurrent amnesia.** DID = two or more distinct identity states with discontinuity of self and agency AND recurrent dissociative amnesia; the amnesia is a required criterion, never an optional associated feature.

TRAP **Diagnosing DID without the amnesia.** An identity disturbance or an episode of possession with *no history of recurrent dissociative amnesia* is other specified dissociative disorder (OSDD, DSM-5-TR example 1), not DID. Do not upgrade it.

3.3 The ICD-11 framing and partial DID

Executive control is the ICD-11 hinge. ICD-11 codes DID at 6B64: two or more distinct personality states (dissociative identities) with marked discontinuities in the sense of self and agency, where at least two *recurrently take executive control* of consciousness and functioning. Its innovation is partial dissociative identity disorder (6B65): a single dominant personality state runs day-to-day life and is *intruded upon* by non-dominant states (intruding thoughts, affects, actions) that do *not* recurrently take executive control. The clean split to memorise is control (full DID: states seize control; partial DID: they only intrude).

3.4 Associated features, screening and the trauma load

Intrusions that mimic psychosis, on a heavy trauma base. People with DID report recurrent, ego-dystonic intrusions: voices (a child's voice, commenting or command voices), thoughts and impulses experienced as not their own, and made actions, phenomena that superficially resemble Schneiderian first-rank symptoms and drive the frequent misdiagnosis as schizophrenia. The overwhelming majority describe severe, chronic, early childhood trauma (abuse and neglect), and most meet criteria for comorbid PTSD (Kaplan and Sadock, CTP 2024). Screening and diagnosis use the Dissociative Experiences Scale (DES) as a self-report screen, with the structured SCID-D-R interview and the MID for diagnosis; a DES mean around **30** is the commonly cited screen threshold for a dissociative disorder (Carlson and Putnam 1993). The instrument itself is set out in the accompanying scale plate.

3.5 The discriminations that get tested

Four fast separations. Against *bipolar II with mixed features* (the commonest misdiagnosis): DID state shifts happen within minutes to hours, far too fast for even rapid-cycling bipolar disorder, and lack the classic reduced need for sleep. Against *schizophrenia*: the voices and passive-influence are dissociative intrusions in a person with intact reality testing and a trauma narrative, not a primary psychosis. Against *traumatic brain injury amnesia*: TBI carries loss of consciousness, disorientation and neurological signs, whereas dissociative amnesia sits with a discontinuity of self and agency. Against *conversion (functional neurological symptom) disorder*: conversion lacks the two-or-more distinct personality states. The factitious, imitative and malingered presentations (states built around a diagnosis, sometimes to evade responsibility) round out the differential.

3.6 The controversy: trauma model versus sociocognitive model

The one debate to be able to argue both ways. The *trauma (post-traumatic) model* holds that DID arises when severe, repeated, inescapable early-childhood trauma prevents the integration of a unified self, so identity develops in fragments. The rival *iatrogenic / sociocognitive / fantasy model* holds that DID is a socially constructed role, shaped by therapist suggestion (leading questions, hypnosis), cultural and media scripts, and high fantasy-proneness, rather than a naturally occurring post-traumatic disorder (Kaplan and Sadock, CTP 2024). This is the **trauma model versus sociocognitive model** question in one line. The examinable rejoinder in favour of the trauma model is that controlled neuroimaging and psychophysiology (the Reinders studies) distinguish genuine DID identity states from high-fantasy-prone individuals asked to simulate them, which a purely role-play account struggles to explain.

WORKED EXAMPLE

A woman in her late twenties is referred as "treatment-resistant bipolar II". She describes hearing a young child's voice narrating her actions, finds clothes and written notes she has no memory of buying or writing, and loses blocks of time at work. Her mood and behaviour shift within an hour, not over days, and she has a documented history of chronic childhood sexual abuse. The rapid within-hour switching, the recurrent amnesia (the notes and lost time), the discontinuity of self and agency, and the trauma history make this dissociative identity disorder, not bipolar II and not schizophrenia. Confirming recurrent dissociative amnesia is what secures the diagnosis; had it been absent, the correct label would be other specified dissociative disorder.

INDIA

The genuine India device here is culture, not pharmacology. Possession and trance presentations, in which an external spirit, deity or ancestor is felt to take over, are a common idiom of distress in Indian settings and can look like the possession form of DID. DSM-5-TR Criterion D and the cultural formulation are the safeguard: a possession or trance that is a *sanctioned, non-distressing part of a broadly accepted religious or cultural practice is not a disorder at all*. It becomes DID only when it is involuntary, unwanted, recurrent outside accepted ritual, and paired with recurrent amnesia and impairment. In practice such presentations are too often sedated (the reflex reach for a benzodiazepine such as alprazolam) or routed to faith healers rather than assessed with a proper cultural formulation and a trauma history. The transcultural framing of possession and trance is developed in the Consultation-liaison, geriatric & transcultural psychiatry notes.

2 or more	**1.5%**	**30**
DISTINCT IDENTITY STATES, DSM-5-TR CRITERION A	12-MONTH PREVALENCE (DSM-5-TR, SMALL US COMMUNITY SAMPLE)	DES SCREEN CUT-OFF FOR A DISSOCIATIVE DISORDER (CARLSON AND PUTNAM 1993)

PEARL

The showy, fully named alter identities are the minority presentation. Most DID is quiet: subtle switching, chronic amnesia and passive-influence intrusions, which is exactly why it is missed or mislabelled as bipolar disorder or psychosis for years.

GOOD TO REMEMBER

- **Dissociative identity disorder (the syndrome):** the defining criteria are two or more distinct personality (identity) states with a marked discontinuity in the sense of self and agency (Criterion A) PLUS recurrent dissociative amnesia inconsistent with ordinary forgetting (Criterion B, required), causing impairment, not accounted for by an accepted cultural or religious practice, a substance or another medical condition; the discriminator from other specified dissociative disorder is the presence of the recurrent amnesia, and the first step is to confirm that amnesia criterion before ever applying the DID label.

HOLD THIS

DID needs BOTH halves: two or more distinct identity states with discontinuity of self and agency AND recurrent dissociative amnesia; drop the amnesia and it is other specified dissociative disorder, and the whole examinable debate is the trauma model versus sociocognitive model, with controlled neuroimaging that separates patients from simulators tilting the evidence toward trauma.

For the broader dissociative-disorders classification, the pathogenesis models and the conversion boundary, see the neighbouring topics; for the dissociative subtype of PTSD, the Anxiety, OCD & trauma-related disorders notes; for the somatic-symptom, functional and factitious boundary, the Somatic-symptom, sexual, impulse-control disorders & suicide notes; and for grounding and the place of hypnosis in dissociative work, the Psychotherapies, clinical assessment, MSE & nosology notes.

4 · Conversion (dissociative neurological symptom) disorder

One idea rewrites this whole topic. **Conversion disorder** is no longer a diagnosis of exclusion. The modern rule, from Stone and Carson, is that it is ruled *in* at the bedside by **positive signs** of internal inconsistency, findings that demonstrate the nervous system working normally when attention is diverted, and only secondarily by the absence of a lesion. Learn the signs and this becomes one of the most answerable clinical topics in the paper; miss the principle and you will either over-call a real neurological disease or, worse, sedate a functional presentation and never treat it.

Dissociative neurological symptom disorder is the ICD-11 name (code 6B60), which keeps the condition *inside* the dissociative family; DSM-5-TR files the same entity under the somatic symptom disorders as **functional neurological symptom disorder (conversion disorder)**, and the umbrella clinical term is **functional neurological disorder** (FND). Whatever the label, the examinable core is a small set of **rule-in signs** across four presentations: functional weakness and paralysis, functional movement and tremor, functional gait, and the sensory or special-sense forms, plus the **dissociative convulsions** that must be separated from true **epilepsy**. The two figures for this topic set the signs out as a positive-signs plate and a conversion-versus-**organic** discriminator grid to be memorised as images. The video-EEG work-up of the seizure form is developed in the Epilepsy & psychiatry notes; the wider somatic-symptom and factitious boundary in the Somatic-symptom, sexual, impulse-control disorders & suicide notes.

Fig 15.6 The positive rule-in signs of a functional neurological disorder, grouped by domain - each one demonstrating internal inconsistency at the bedside.

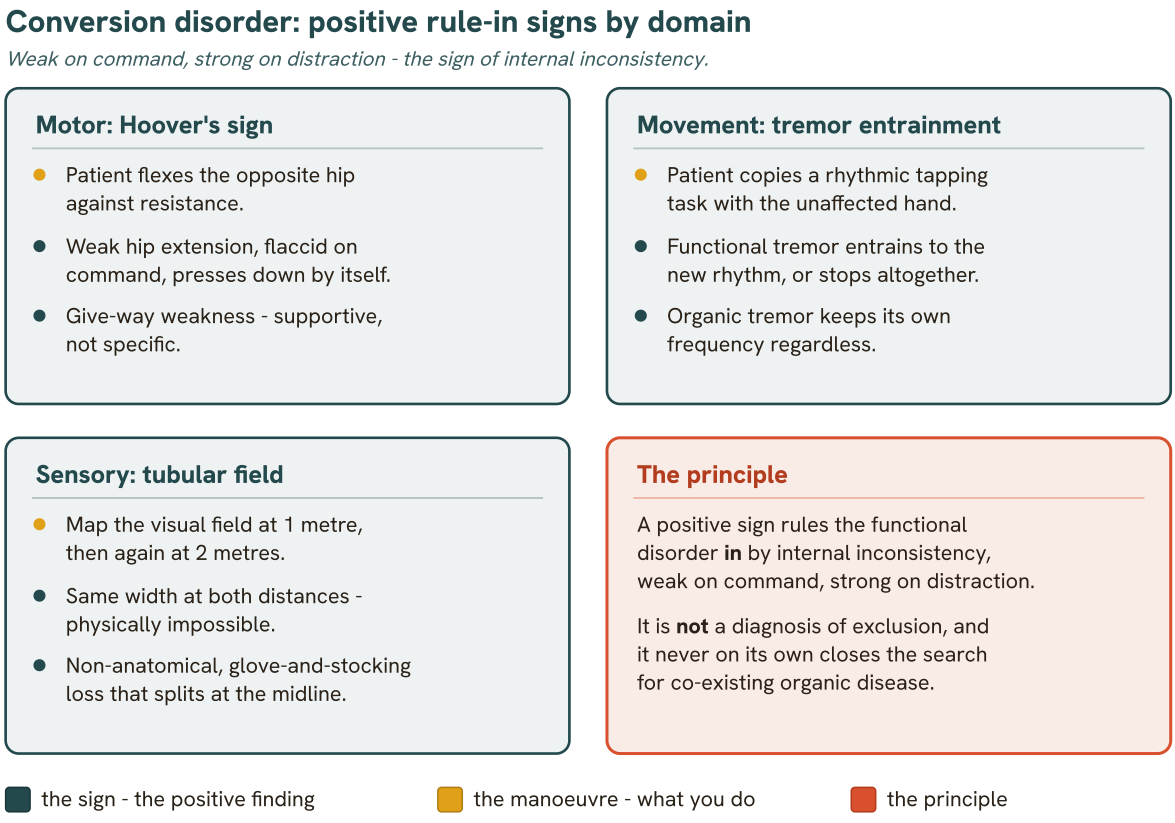


Fig 15.7 How to tell a functional (conversion) presentation from organic disease across five features, and why a positive sign never closes the organic work-up.

feature	functional (conversion)	organic disease
diagnostic basis	ruled in on a positive sign of internal inconsistency	a fixed anatomical or structural lesion
consistency	internally inconsistent, variable, distractible	consistent and reproducible on testing
signs	positive rule-in signs present: Hoover, entrainment, tubular field	hard neurological signs (reflexes, wasting, sensory level)
course and onset	often abrupt, may be linked to stress	progressive, vascular, or stepwise
imaging and investigations	investigations and imaging typically normal	structural or electrical abnormality (MRI, EEG)

Both can coexist.
A positive functional sign never ends the organic work-up.

functional (conversion) organic disease

Fig 15.8 Reading a convulsion: the reliable signs that separate a dissociative (non-epileptic) attack from an epileptic seizure, and the classic signs that do not.

reliable discriminator	dissociative (non-epileptic) convulsion	epileptic seizure
awareness during bilateral shaking	often preserved; can recall or interrupt it	lost in a bilateral tonic-clonic seizure
duration and pattern	long and fluctuating, over 2 to 3 minutes	short and stereotyped, under 2 minutes
the eyes	closed, with active resistance to opening	typically open
head movement	side-to-side	not side-to-side
post-ictal prolactin (at 10 to 20 min)	no rise	rises to over twice baseline (generalised)
ictal video-EEG (gold standard)	normal during an apparent attack	epileptiform discharge

unreliable on their own

occur in both and do not decide either way:
tongue-biting, urinary incontinence, injury, pelvic thrusting

dissociative convulsion · epileptic seizure · unreliable (occurs in both)

4.1 What conversion disorder is, and what it is not

Genuine symptoms, incompatible with disease, ruled in by a sign. Conversion disorder is one or more symptoms of altered voluntary motor or sensory function that are *genuinely experienced* (not feigned) yet demonstrably incompatible with recognised neurological or medical disease (DSM-5-TR Criterion B; ICD-11 6B60). DSM-5-TR deliberately *removed* the old requirement for an identifiable psychological stressor, so a stressor is neither necessary nor sufficient, and la belle indifference (bland unconcern) is unreliable and is *not* a diagnostic criterion. DSM-5-TR specifies the symptom type, which is the clinically useful map: with weakness or paralysis, with abnormal movement, with swallowing or speech symptoms, with attacks or seizures, with anaesthesia or sensory loss, with special-sensory symptoms, or mixed. The whole diagnosis now turns on Criterion B, the demonstration of internal inconsistency, not on Criterion D absence of disease.

RULE **Rule in, do not rule out.** Conversion disorder is a positive diagnosis made on a sign of internal inconsistency (Hoover, tremor entrainment, tubular field), never on the mere absence of a lesion or the presence of a stressor.

4.2 The positive-signs principle: internal inconsistency

The system works when attention is elsewhere. The unifying mechanism behind every rule-in sign is that the symptom depends on abnormally focused attention: divert attention and the "lost" function returns, revealing the pathways to be intact (Stone and Carson; New Oxford 2024). This is *internal inconsistency*, an incompatibility between the deficit shown on formal testing and the function that appears automatically or when the patient is distracted. It is a different logic from anatomical implausibility: a glove-and-stocking sensory loss is suggestive because it defies dermatomes, but a positive Hoover's sign is far stronger because it demonstrates the extensors *firing* a moment after they were "paralysed". The accompanying figure lays the signs out by domain as a single positive-signs plate. A skilled neurologist can make the positive diagnosis; the psychiatric assessment then secures a complete history and addresses the comorbid anxiety, panic, depression and PTSD that often travel with it (New Oxford 2024).

4.3 Functional weakness and paralysis: Hoover's sign

The single most testable sign in psychiatry. Hoover's sign exploits the automatic synergy of hip extension. With the patient supine, direct hip extension of the "weak" leg is flaccid; but when the patient flexes the *opposite* hip against resistance, the weak leg's extensors fire automatically and press down into the examiner's hand (Kaplan 2024). Weak on command, strong on distraction: that is a positive Hoover's sign, and it rules the diagnosis in at the bedside without imaging. Its sibling, the hip abductor sign, shows the same reversal in hip abduction. A give-way weakness (collapsing, ratchety power that builds then suddenly yields) and a global pattern of weakness affecting extensors and flexors equally are further pointers, but note the honest caveat: give-way weakness is *supportive, not specific*, because pain and poor effort in genuine organic disease can produce it too, whereas Hoover's sign is the discriminating one.

WORKED EXAMPLE

A woman develops a dense right-leg "paralysis" after a family argument. Direct right hip extension is flaccid. You cup your hand under the right heel and ask her to flex the *left* hip against your other hand; as she does, the right heel drives firmly down into your palm. The extensors she could not fire on command have fired automatically. That is a positive Hoover's sign, a rule-in for conversion disorder, elicited in seconds and without a scanner, and it doubles as the most persuasive thing you can later show her when you explain the diagnosis.

4.4 Functional movement disorder and tremor: the entrainment test

A tremor that copies the other hand is functional. The tremor entrainment test is the movement-domain equivalent of Hoover's sign. The patient with a unilateral tremor is asked to copy a rhythmical tapping movement with the *unaffected* limb; a functional tremor will *entrain* to the new rhythm (change its frequency to match), stop altogether, or the patient becomes unable to perform the simple copied rhythm at all (DSM-5-TR; New Oxford 2024). An organic tremor keeps its own frequency regardless. Other positive movement signs are a *fixed dystonic posture* (characteristically a flexed hand or a plantar-flexed, inverted ankle) and a typical functional facial overactivity (orbicularis or platysma over-contraction with jaw deviation) that masquerades as

facial weakness. The distractibility that defines these signs is the whole point: attention drives the symptom, so shifting attention exposes it.

4.5 Functional gait

Bizarre, effortful, and better when unwatched. The functional gaits are among the most recognisable presentations. A *dragging gait* keeps the forefoot in contact with the floor with the hip held externally or internally rotated, a pattern that fits no pyramidal or extrapyramidal disease. Astasia-abasia is a wide-based, staggering, dramatic and irregular gait with exaggerated near-falls yet a conspicuous absence of injury, the effort of not falling being greater than that of walking normally. The bedside rule-in is distraction: a patient with an apparently positive Romberg's test is asked to guess numbers written on the back or to carry out a complex task on a phone, and the balance improves markedly (New Oxford 2024). These motor and convulsive forms are especially common in Indian and other lower-income settings.

4.6 Sensory and special-sense presentations

Boundaries that disobey anatomy and physics. The classic sensory form is a glove-and-stocking anaesthesia: a loss of all modalities with a sharp boundary at the wrist or ankle that does not conform to any dermatome, and a splitting of vibration sense exactly at the midline, even though a tuning fork on the sternum or skull conducts through bone to both sides. In vision, the rule-in signs are the tubular field (also called tunnel vision): a visual-field defect of the *same* width at 1 metre as at 2 metres, which is physically impossible because a real field subtends a wider area with distance. The *fogging test* proves a claimed monocular blindness is functional, by progressively fogging the good eye with lenses while the patient reads an acuity chart; retained acuity at the end means the "blind" eye is doing the reading. Functional deafness and non-anatomical hemi-anaesthesia complete the group.

GOOD TO REMEMBER

- **Conversion / dissociative neurological symptom disorder (the syndrome):** defining criterion is a motor or sensory symptom, genuinely experienced, shown by a *positive* sign of internal inconsistency to be incompatible with neurological disease (Hoover's sign, tremor entrainment, tubular field); it is a *rule-in* diagnosis, *not* one of exclusion, no stressor is required (DSM-5-TR) and la belle indifference is non-diagnostic. First step: elicit a positive sign at the bedside.

4.7 Dissociative (non-epileptic) convulsions: the differentiation from epilepsy

The seizure form, and how it parts from true epilepsy. Dissociative convulsions (dissociative or psychogenic **non-epileptic** seizures, ICD-11 6B60.4 "with non-epileptic seizures") are paroxysmal episodes of altered movement, sensation or responsiveness that resemble an epileptic seizure but arise without epileptiform electrical discharge. The examinable skill is the **differentiation** from epilepsy on semiology (New Oxford 2024; Companion Box 13.12). Features that point to a dissociative convulsion are: preserved awareness during bilateral shaking, with the patient later able to recall being in the attack or even able to interrupt it; a long duration (often longer than 2 to 3 minutes, waxing and waning); closed eyes with active resistance to eye opening; side-to-side head movement and out-of-phase, asynchronous limb thrashing; and ictal or immediate post-ictal weeping. A post-ictal serum prolactin drawn 10 to 20 minutes after onset

that *rises to more than twice baseline* supports a true generalised or complex-partial seizure, so the *absence* of a prolactin rise is consistent with a dissociative convulsion, though the test has limited value (false positives and negatives) and a normal result never excludes epilepsy. The gold standard remains a normal *ictal* video-EEG captured during an apparently generalised attack (Companion), cross-referenced to the Epilepsy & psychiatry notes.

FEATURE	POINTS TO A DISSOCIATIVE CONVULSION	POINTS TO EPILEPSY (OR UNHELPFUL)
Awareness in bilateral shaking	**Preserved; can recall the attack or interrupt it**	Lost in a generalised tonic-clonic seizure
Duration	Often longer than 2 to 3 minutes, fluctuating	Usually under 2 minutes, stereotyped
Eyes	**Closed, with resistance to eye opening**	Typically open
Movements	Side-to-side head movement, out-of-phase asynchronous thrashing	Rhythmic, synchronous, evolving clonic jerks
Weeping	Ictal or immediate post-ictal crying	Rare
Post-ictal prolactin (10 to 20 min)	No rise (consistent with, not proof of)	Rise to more than twice baseline (limited value)
Ictal video-EEG	**Normal during an apparent generalised attack**	Epileptiform discharge (gold-standard test)
Tongue-biting, incontinence, pelvic thrust, injury	Unhelpful, occur in both; do not use to decide either way (Companion)	

Semiological differentiation of dissociative (non-epileptic) convulsions from epilepsy; the last row lists the classic unreliable discriminators.

GOOD TO REMEMBER

- **Dissociative convulsions (the seizure form):** defining criterion is a seizure-like attack with positive rule-in features (preserved awareness in bilateral shaking, duration over 2 to 3 minutes, closed and resisted eyes, no post-ictal prolactin rise) and a *normal ictal video-EEG*, the gold-standard confirmation; tongue-biting, incontinence and pelvic thrusting do NOT distinguish it from epilepsy. First step: capture the attack on video-EEG.

4.8 The conversion-versus-organic discrimination and its trap

A positive sign never cancels the duty to screen. The safe practice of this topic is a two-way **discrimination**: rule the functional disorder *in* on a positive sign, but keep screening for organic disease because the two coexist more often than expected. A sizable minority of patients with non-epileptic seizures *also* have epilepsy (Kaplan 2024), and functional signs are described alongside real disease. The accompanying discriminator grid contrasts the functional and organic pictures side by side. The classic misdiagnoses run in the mirror direction: early multiple sclerosis, a spinal cord lesion, frontal-lobe epilepsy (which can look bizarre and show a normal surface EEG), stiff-person syndrome, Wilson's disease and autoimmune encephalitis have all been

mislabelled conversion because the presentation seemed emotional or a stressor was present. So the positive sign rules the functional diagnosis in, but a progressive course, hard neurological findings, or an atypical picture reopens the organic search.

TRAP **Missing the organic cause behind a "conversion".** A stressor or a dramatic presentation is not evidence of a functional disorder; early MS, a cord lesion, frontal-lobe epilepsy or autoimmune encephalitis can all mimic it, and functional signs coexist with real disease, so never let a positive sign close the organic work-up in an atypical or progressive case.

4.9 Management: positive explanation, physiotherapy, CBT

The explanation is the first treatment. Management rests on three evidence-based pillars (New Oxford 2024). First, a clear *positive explanation* of the diagnosis: take the problem seriously, give it a positive diagnostic label rather than a list of what it is not, *show the patient their own positive sign* (the Hoover's sign, the tremor stopping on entrainment), use the software-versus-hardware metaphor to emphasise reversibility, and signpost written resources such as neurosymptoms.org. Second, *physiotherapy* is first-line for the functional motor forms (limb weakness and functional movement disorders), using distraction and retraining rather than generic stroke-style physiotherapy; a specific programme achieved a good outcome in about 72 percent despite years of symptoms. Third, *cognitive behavioural therapy*, generic tailored CBT for mixed functional symptoms and a dedicated CBT for dissociative seizures (number needed to treat around 5 for seizure remission). There is *no* specific drug for conversion disorder itself; medication is only for comorbid anxiety or depression, for which the SSRIs are the first-line agents taught in the Mood disorders: pharmacotherapy notes, and hypnosis and grounding sit in the Psychotherapies, clinical assessment, MSE & nosology notes.

2 min	10 to 20 min	2×
DURATION ABOVE WHICH A CONVULSION FAVOURS A DISSOCIATIVE ATTACK	POST-ICTAL PROLACTIN SAMPLING WINDOW AFTER SEIZURE ONSET	PROLACTIN RISE OVER BASELINE THAT SUPPORTS A TRUE SEIZURE

INDIA

Two genuine India devices meet here. First, the culture-bound one: dissociative motor and convulsive presentations, and the possession and trance states, are among the most frequent dissociative presentations in Indian practice, and the convulsive form is recorded as "very common" in India and other developing countries. Read through a cultural formulation, not the surface picture: a possession or trance sanctioned within an accepted religious practice is not a disorder, a boundary developed in the Consultation-liaison, geriatric & transcultural psychiatry notes. Second, the pharmacological one: the reflex Indian response to a dramatic dissociative or convulsive presentation is too often a sedative, and India has a well-recognised benzodiazepine over-prescription problem with alprazolam (Alprax, Restyl) as the default anxiolytic. A benzodiazepine treats nothing in conversion disorder, risks dependence, and is exactly the wrong move; the Indian Psychiatric Society and the wider benzodiazepine-sparing position favour a positive explanation, physiotherapy and CBT instead. The sedative and benzodiazepine use disorder as an addiction is covered in the Substance use disorders notes.

PEARL

The most powerful therapeutic tool is the diagnostic sign itself. Demonstrating a patient's own Hoover's sign or entrainment, and explaining that a leg that moves automatically is a leg that *can* move, converts the bedside examination into the opening move of treatment: it proves the diagnosis, shows reversibility, and replaces “there is nothing wrong” with “here is what is wrong and here is why it can get better”.

HOLD THIS

Conversion disorder is ruled *in* on positive signs of internal inconsistency, weak on command but strong on distraction (Hoover's sign, tremor entrainment, tubular field), never out by exclusion; and its seizure form is separated from epilepsy by preserved awareness, closed and resisted eyes, a long fluctuating attack, no post-ictal prolactin rise, and above all a normal ictal video-EEG.

For the wider dissociative-disorders map and the pathogenesis models see the neighbouring topics; the somatic-symptom, functional and factitious boundary sits in the Somatic-symptom, sexual, impulse-control disorders & suicide notes; the video-EEG work-up of dissociative convulsions in the Epilepsy & psychiatry notes; and the transcultural reading of possession and trance in the Consultation-liaison, geriatric & transcultural psychiatry notes.

5 · Depersonalisation-derealisation disorder

One discriminator carries this whole topic. **Depersonalisation-derealisation disorder** is a low-volume entity that is decided by a single question: is reality testing intact? The patient describes the world and the self as strange, flat and unreal, yet *knows* that this is only how things feel, not how they truly are. That preserved reality check is what separates the disorder from a psychotic illness, and forgetting it is the classic error that turns detachment into a mistaken diagnosis of schizophrenia.

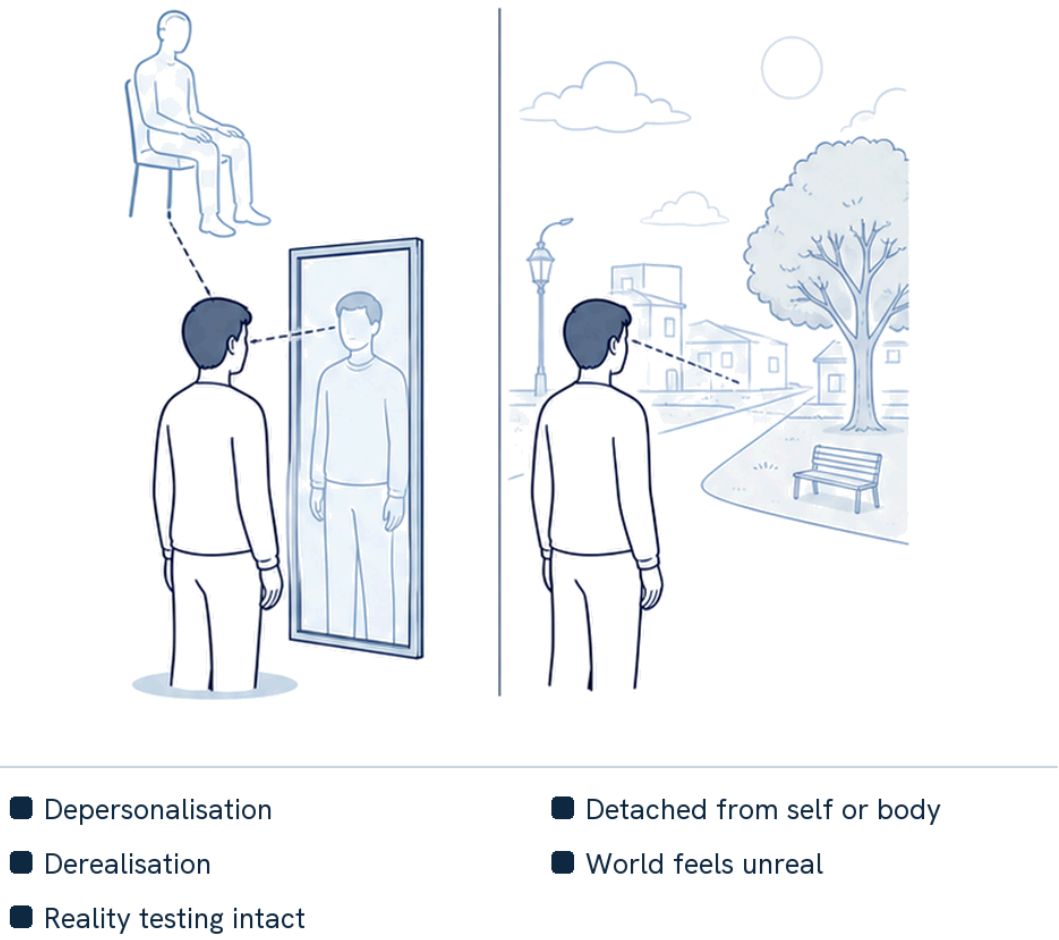


Fig 15.9 Depersonalisation is detachment from one's self, mental processes or body; derealisation is an altered sense of the external world as unreal. In both, reality testing remains intact.

Two experiences travel together in the name. **Depersonalisation** is a sense of **unreality** or **detachment from self**, one's own mind, feelings, actions or body. **Derealisation** is the same unreal, detached quality applied to the surroundings, the world seen as if behind glass or like a stage set. The examiner reward is small and precise: the definition, the intact-reality-testing anchor, the fact that transient forms are extremely common and benign, and the awkward truth that *no drug has an established place* in treatment.

5.1 The two halves: depersonalisation and derealisation

Detachment from the self, detachment from the world. The disorder is built from two symptom clusters that may occur singly or together (DSM-5-TR; ICD-11 6B66).

Depersonalisation

Unreality, detachment or being an outside observer of one's own thoughts, feelings, body or actions; emotional or physical numbing, a distorted sense of time, an unreal or absent self.

Derealisation

Unreality or detachment applied to surroundings; people or objects felt as unreal, dreamlike, foggy, lifeless or visually distorted (as if behind glass).

The "as if" quality

The experiences are described in the conditional, "as if" I were not real, "as if" the world were a painting; the person never asserts that it is *literally* so.

5.2 The DSM-5-TR criteria and the intact-reality-testing anchor

Persistent or recurrent, with the reality check preserved. DSM-5-TR requires persistent or recurrent experiences of depersonalisation, derealisation or both (Criterion A); crucially, *during these experiences reality testing remains intact* (Criterion B). The symptoms cause clinically significant distress or impairment (C); they are not attributable to a substance or another medical condition, notably seizures (D); and they are not better explained by another mental disorder such as schizophrenia, panic disorder, major depression or another dissociative disorder (E). Because transient depersonalisation is extremely common in the general population and after cannabis, ketamine or hallucinogens, the label is reserved for presentations that are persistent, recurrent and impairing.

RULE **Intact reality testing is the diagnosis.** Persistent unreality of self and/or world with an "as if" quality and a preserved reality check is depersonalisation-derealisation disorder; the moment the patient believes the unreality is literally true, you have left the diagnosis for the psychotic spectrum.

TRAP **Mislabelling depersonalisation-derealisation as psychosis.** "The world feels unreal, like a film" is not a delusion. Historically these patients were read as psychotic-spectrum and started on antipsychotics, for which there is no evidence and which can deepen the very emotional deadening they complain of (Kaplan and Sadock, CTP 2024).

5.3 Onset, course and the trauma signature

An adolescent onset with a heavy comorbidity load. The mean age of onset is **16 years**, and the disorder can begin in early or middle childhood; onset for the first time in later life is unusual and should prompt a search for an organic or substance cause (DSM-5-TR). The course splits into rough thirds: about one in three run an episodic, relapsing-remitting course, one in three a chronic course, and one in three an episodic course that becomes chronic (Kaplan and Sadock, CTP 2024). Comorbidity is the rule rather than the exception, with major depressive disorder in around **73%** and an anxiety disorder in around **64%**, which is why most patients are first treated for the secondary mood and anxiety symptoms. The trauma signature is distinctive: unlike the sexual-abuse loading of dissociative identity disorder, it is *emotional (verbal) abuse* that most specifically predicts depersonalisation-derealisation scores.

5.4 Screening: the Cambridge Depersonalization Scale

A dedicated instrument from the Maudsley unit. The standard screen is the Cambridge Depersonalization Scale (CDS), developed by Sierra and Berrios at the Depersonalization Research Unit (Maudsley Hospital, London); the same unit and Daphne Simeon's group in the United States generated most of the modern clinical picture. A depersonalisation-derealisation

subscale of the broader Dissociative Experiences Scale (the DES-D) is also used. The instrument forms are set out centrally in the accompanying scale plate; carry the CDS as the named screen and read its cut-off off the reproduced plate rather than committing an unverified threshold to memory.

5.5 Management: no drug cures it

Psychotherapy first, medication only for the comorbidity. The single most examinable management fact is a negative one: extensive treatment histories show *no* established pharmacotherapy for the core disorder, with benzodiazepines, serotonin reuptake inhibitors and stimulants only partially helpful in some patients, and no evidence at all for antipsychotics (Kaplan and Sadock, CTP 2024). Antipsychotics are reserved strictly for overwhelming associated anxiety or mood disturbance and may worsen the emotional numbing. The mainstays are a range of psychotherapies (psychodynamic, cognitive, cognitive-behavioural, hypnotherapeutic and supportive, with no comparative data favouring one) plus definitive treatment of the comorbid depression or anxiety. Where a short course of an anxiolytic is used for a crisis, the benzodiazepine-sparing short-course rule still holds: it is a brief measure, not a long-term treatment for the unreality itself. The grounding techniques and the place of hypnosis are developed in the Psychotherapies, clinical assessment, MSE & nosology notes; the SSRIs and SNRIs as first-line anxiolytics for the comorbid anxiety are in the Mood disorders: pharmacotherapy notes and the Anxiety, OCD & trauma-related disorders notes.

WORKED EXAMPLE

A man in his early twenties is referred with a query psychotic illness. Since his late teens he has felt "outside" himself, watching his own actions from a step to one side; his voice sounds tinny and far away, his emotions muffled, the street "like a painting". He is frightened and desperate to "get back to me", but when asked he is clear that the world is not *actually* unreal, it only feels that way. The persistence since adolescence, the detachment from self and surroundings, the distress, and above all the intact reality testing make this depersonalisation-derealisation disorder, not schizophrenia. Confirming the preserved reality check is what secures it; starting an antipsychotic would be both unsupported and likely to deepen the emotional deadening.

16 yrs	**73%**	**1 in 3**
MEAN AGE OF ONSET (DSM-5-TR)	CARRY COMORBID MAJOR DEPRESSION (KAPLAN 2024)	FOLLOW A CHRONIC COURSE (KAPLAN 2024)

INDIA

The genuine India device here is what *not* to prescribe. India carries a well-recognised benzodiazepine over-prescription problem, with alprazolam (Alprax or Restyl) functioning as the default anxiolytic reached for almost reflexively when a patient describes unreality, numbness or anxious detachment. Depersonalisation-derealisation disorder is precisely the presentation where that reflex fails: no benzodiazepine treats the core symptom, dependence and rebound follow long use, and the Indian Psychiatric Society position, like BAP and NICE, is benzodiazepine-sparing, a short course for crisis only. The safer move is to name the disorder, reassure about the intact reality check, treat the comorbid depression or anxiety, and refer for psychotherapy.

PEARL

Depersonalisation is best understood as a "hard-wired" protective response, an inhibitory dampening of overwhelming affect that is adaptive in acute terror or intoxication and pathological only when it persists. That is why transient unreality after trauma, a panic attack or cannabis is normal and self-limiting, and why the disorder sits at the anxious, not the psychotic, end of the spectrum.

GOOD TO REMEMBER

- **Depersonalisation-derealisation disorder (the syndrome):** the defining criterion is persistent or recurrent depersonalisation (unreality or detachment from self) and/or derealisation (unreality or detachment from the surroundings) during which *reality testing remains intact* (DSM-5-TR Criterion B), causing distress or impairment and not due to a substance, seizure or another disorder; the discriminator from psychosis is that intact reality check and the "as if" quality, and the first step is always to confirm reality testing is preserved before the label is applied.

HOLD THIS

Persistent unreality of self and world with an "as if" quality and INTACT reality testing is depersonalisation-derealisation disorder, onset around 16 years, screened with the Cambridge Depersonalization Scale, and it has no established drug treatment, so the answer is psychotherapy plus treating the comorbid mood or anxiety, never a reflex antipsychotic or a long-term benzodiazepine.

For the classification map and the pathogenesis models this disorder sits within, see the neighbouring dissociative-disorders topics; for the dissociative subtype of PTSD and the anxiolytics in anxiety, the Anxiety, OCD & trauma-related disorders notes; for possession and trance in the transcultural frame, the Consultation-liaison, geriatric & transcultural psychiatry notes; and for grounding and hypnosis, the Psychotherapies, clinical assessment, MSE & nosology notes.

6 · Dissociative amnesia and fugue

One discrimination decides this topic. **Dissociative amnesia** is an inability to recall important autobiographical information, usually of a traumatic or stressful nature, that is too extensive to be ordinary forgetting. The examiner is not really testing whether you can recite the criterion; he is

testing whether you can separate it from an *organic* amnesia at the bedside, because the two are worked up in opposite directions. The whole answer turns on one pattern: a retrograde loss of already-stored personal memory with an intact ability to lay down new memory, on a trauma trigger, and in the absence of a neurological or substance cause.

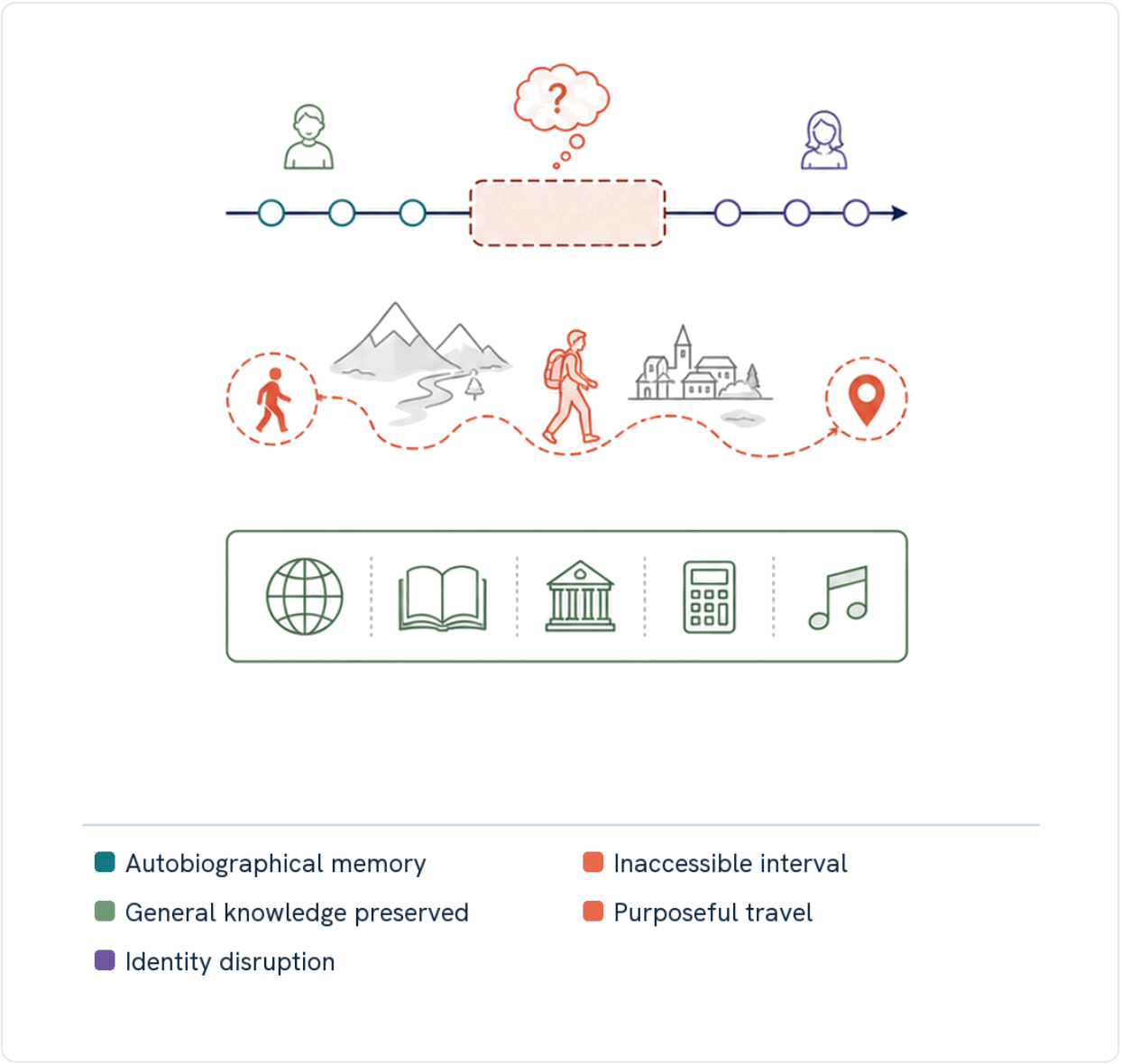


Fig 15.10 Dissociative amnesia produces an autobiographical memory gap that exceeds ordinary forgetting. Fugue adds apparently purposeful travel or wandering with disruption of autobiographical identity.

The disorder was long called psychogenic amnesia (the ICD-10 and older term), and dissociative fugue is now folded into it as a specifier rather than standing as a separate disorder. Keep two moves ready: name the *type* of amnesia (the commonest is a **localised amnesia**), and rule *in* the dissociative picture against the organic mimics, transient global amnesia, the amnestic (Korsakoff) syndrome and complex partial seizures, by the direction of the memory loss and the fate of personal identity.

6.1 What dissociative amnesia is

A reversible retrieval deficit for autobiographical memory. DSM-5-TR Criterion A is an inability to recall important autobiographical information, usually of a traumatic or stressful

nature, that is inconsistent with ordinary forgetting. The memory has been successfully stored and would ordinarily be freely recollected, so the deficit is one of *retrieval* and is potentially reversible; that is precisely how dissociative amnesia differs from the amnesias of neurobiological damage or toxicity, which impair storage. Criterion B requires distress or impairment; Criterion C excludes a substance and a neurological or other medical condition (complex partial seizures, transient global amnesia, a closed head injury); Criterion D excludes dissociative identity disorder, PTSD, acute stress disorder, somatic symptom disorder and a neurocognitive disorder. In DSM-5-TR the deficit is primarily *retrograde* and, except in the rare continuous type, there is no ongoing amnesia for contemporary life events.

6.2 The five types (name the shape of the gap)

Localised is the commonest. DSM-5-TR and ICD-11 define the recognised types by the shape of the memory gap, and the examiner expects you to label the pattern.

Localised
inability to recall all events in a circumscribed period, usually the period around the stressor (the commonest form)

Selective
recall of some but not all of the events within that circumscribed period

Generalised
failure to recall one's entire life, including personal identity (rare, acute, and it usually brings the person to the police or emergency services)

Continuous
failure to recall each new event as it occurs; this is the *anterograde* form of dissociative amnesia, and it is rare

Systematised
loss of a specific category of memory, for example all memories of one person or of the family

6.3 Dissociative fugue (now a specifier)

Purposeful travel plus amnesia for identity. DSM-5-TR codes fugue as the specifier "with dissociative fugue" (F44.1): apparently **purposeful travel** or bewildered wandering that is associated with amnesia for identity or for other important autobiographical information. It is commonly associated with generalised dissociative amnesia, has a sudden onset under severe stress, and terminates abruptly, with recovery of the earlier life and a residual amnesia for the episode itself. Both DSM-5-TR and ICD-11 judge that there are insufficient data to keep fugue as a disorder distinct from dissociative amnesia; ICD-11 makes it a presence specifier of 6B61 (6B61.0 with, 6B61.1 without). Note the nosological shift that gets tested: the older criterion of "assumption of a new identity" during the episode would now meet criteria for dissociative identity disorder, so the classic full identity-swap fugue has been reallocated.

6.4 The critical discrimination: dissociative versus organic amnesia

Direction of the loss, and the fate of identity. This is the single most examinable separation on the topic, and it is a positive comparison, not a hunch. Dissociative amnesia is a retrograde **loss**

of autobiographical memory with new learning intact and personal identity frequently lost; the organic amnestic syndrome is the mirror image.

FEATURE	DISSOCIATIVE AMNESIA	ORGANIC AMNESIA
Predominant deficit	**retrograde: loss of stored autobiographical memory**	anterograde: failure to form new memories, with a retrograde gradient
New learning (anterograde)	**intact**	impaired
Personal identity	**often lost (name, whole life history)**	preserved (the person knows who they are)
Trigger	acute psychological trauma or stress	a neurological insult or a substance
Onset and recovery	sudden onset, can recover suddenly and completely	tracks the lesion, recovery often incomplete
Consciousness and signs	clear sensorium, neurological examination normal	clouding or disorientation, focal signs may appear

The bedside separation of dissociative from organic amnesia rests on the direction of the deficit and on whether personal identity is lost.

RULE **Retrograde loss of identity with intact new learning is dissociative.** Dissociative amnesia loses the stored past and often the personal identity while new memories still form; the organic amnestic syndrome does the reverse, failing to lay down new memory while identity is preserved.

6.5 Ruling in against the organic mimics

Rule the picture in, do not just assume it. The same positive-versus-organic logic that governs conversion applies here: dissociative amnesia and fugue are rule-in diagnoses that still require the organic mimics to be excluded (Criterion C). Transient global amnesia gives an abrupt, isolated anterograde amnesia with repetitive questioning, preserved personal identity, typically in an older adult, and it resolves within 24 hours. Complex partial seizures and temporal lobe epilepsy can produce an epileptic wandering with no assumption of a new identity, with confusion or disorientation during the episode, episodes not tied to a psychological stressor, and an abnormal EEG. The amnestic (Korsakoff) syndrome gives a dense anterograde amnesia with confabulation on a thiamine-deficiency base. Head injury, post-ictal states and a substance blackout complete the exclusions. Screening for dissociation itself uses the Dissociative Experiences Scale (DES), where a mean around 30 flags a probable dissociative disorder; the instrument is set out in the accompanying scale plate.

TRAP **Labelling a wandering, amnesic patient "dissociative" too soon.** Purposeful travel with amnesia can be an epileptic automatism, transient global amnesia or a post-ictal fugue; missing the organic cause is the classic error. Get an EEG, imaging and a substance history before the label sticks. The video-EEG work-up that separates epileptic from dissociative events is set out in the Epilepsy & psychiatry notes.

6.6 Course and the one management principle

Recover the memory, do not sedate the patient. Onset is typically sudden and under stress, and the localised form often recovers abruptly and completely, so the prognosis is generally good. The management principle is a safe, contained environment, removal from or resolution of the precipitating stressor, and a phased, psychologically informed recovery of the memory; a drug-assisted (abreaction) interview has historically been used but is not first-line, and grounding and the place of hypnosis are developed in the Psychotherapies, clinical assessment, MSE & nosology notes. What the disorder does *not* need is a benzodiazepine: there is no anxiolytic indication for dissociative amnesia, and reflexive sedation both masks the picture and courts dependence.

WORKED EXAMPLE

A man in his thirties is brought in by railway police having been found several hundred kilometres from home, unable to give his name, address or occupation, and calm rather than distressed. On examination the sensorium is clear, there are no focal neurological signs, and he can learn and recall a new list of three objects without difficulty. A relative later reports that he left home the morning after being served with a large debt notice. The intact new learning, the clear sensorium, the loss of personal identity and the clear psychological precipitant point to a dissociative fugue with generalised dissociative amnesia, not an organic amnesia. The immediate job is still to exclude a seizure, transient global amnesia and a substance cause before the label is fixed, and the treatment is safety, contact with family and gentle memory recovery, not a sedative.

INDIA

Two genuine India devices meet here. First, culture: possession and trance states, in which a deity, spirit or ancestor is felt to take over, are a common idiom of distress in Indian settings and can present with amnesia and purposeful travel that mimic dissociative amnesia and fugue. ICD-11 keeps these as separate categories (trance disorder 6B62, possession trance disorder 6B63), and a sanctioned, non-distressing ritual state is not a disorder at all; the cultural formulation is the safeguard. Second, the treatment reflex: such presentations, and dissociative amnesia generally, are too often met with a reflexive benzodiazepine rather than an assessment. Alprazolam (Alprax, Restyl) is the default anxiolytic of Indian practice and the emblem of the country's benzodiazepine over-prescription problem; the standard rule is that a benzodiazepine should not ordinarily run beyond 2 to 4 weeks. Dissociative amnesia has no benzodiazepine indication. The transcultural reading of possession and trance is developed in the Consultation-liaison, geriatric & transcultural psychiatry notes.

30	6 to 20	2 to 4	0.5 to 6
DES SCREEN CUT-OFF FOR A DISSOCIATIVE DISORDER (CARLSON AND PUTNAM 1993)	ALPRAZOLAM HALF-LIFE IN HOURS	BENZODIAZEPINE SHORT-COURSE CEILING IN WEEKS	ALPRAZOLAM ANXIOLYTIC DOSE (MG PER DAY)

PEARL

A patient who cannot say who they are is far more likely to have a dissociative (or a malingered or factitious) amnesia than an organic one, because the organic amnestic syndromes leave personal identity intact. Loss of the name is a psychogenic flag until proven otherwise, and the feigned or factitious version is covered in the Somatic-symptom, sexual, impulse-control disorders & suicide notes.

GOOD TO REMEMBER

- **Dissociative amnesia and fugue (the syndrome):** DSM-5-TR Criterion A is an inability to recall important autobiographical information, usually traumatic or stressful, that is inconsistent with ordinary forgetting (localised is the commonest type); fugue is the specifier "with dissociative fugue", apparently purposeful travel or bewildered wandering with amnesia for identity; the deficit is retrograde and reversible, and the first step is to exclude an organic cause (Criterion C) and to check whether personal identity is lost, which points away from an organic amnesia.
- **Alprazolam (Alprax, Restyl):** a short-acting benzodiazepine and the default Indian anxiolytic, half-life about 12 to 15 hours with no clinically important active metabolite, usual anxiolytic range 1 to 4 mg per day; it has no role in dissociative amnesia and should not ordinarily run beyond 2 to 4 weeks, the short-course rule that guards against the Indian over-prescription pattern.

HOLD THIS

Dissociative amnesia is a retrograde, reversible loss of autobiographical memory (localised is commonest) on a trauma trigger, with personal identity often lost but new learning intact; the organic amnestic syndrome is the mirror image (anterograde, identity preserved), so exclude a neurological or substance cause before you commit, and never sedate it with a benzodiazepine.

For the wider dissociative-disorders classification and dissociative identity disorder, see the neighbouring topics; the benzodiazepine mechanism, the half-life classes and the taper are developed in the neighbouring benzodiazepine topic; for the dissociative subtype of PTSD and the trauma-related disorders, the Anxiety, OCD & trauma-related disorders notes; and for the somatic-symptom, functional and factitious boundary, the Somatic-symptom, sexual, impulse-control disorders & suicide notes.

7 · Possession and trance states

One question decides this whole topic: is this a disorder at all, or a sanctioned cultural act? **Possession** and **trance** presentations are a genuinely **culture-bound** corner of the dissociative disorders, and the examinable skill is not the phenomenology but the boundary. A narrowing of awareness with stereotyped, seemingly uncontrolled behaviour, or the sense of being replaced by an external identity, is a *disorder* only when it is involuntary, unwanted, distressing or impairing, and lies *outside* an accepted collective cultural or religious practice. Read as an accepted ritual, the very same behaviour is not pathology at all.

The two systems diverge here, so carry both. **ICD-11 keeps two separate categories**, trance disorder (6B62) and possession trance disorder (6B63); **DSM-5-TR keeps neither as a standalone**, folding possession-form presentations into dissociative identity disorder and listing

dissociative trance only as an example under Other Specified Dissociative Disorder. In the Indian setting this is high-yield because possession presentations are common, and the clinician's first move is a cultural formulation, decoding the local **idioms of distress** before any label is applied.

7.1 The two ICD-11 entities: trance versus possession trance

Narrowed awareness versus a replacing identity. Both are trance states with a marked alteration of consciousness or a loss of the normal sense of personal identity; what separates them is whether an *external identity takes over* (ICD-11 CDDR).

Trance disorder (6B62)

A trance state with narrowing of awareness of the immediate surroundings (or unusually narrow, selective focus) *and* restriction of movements, postures and speech to a small repertoire experienced as outside one's control; crucially, it is *not* experienced as being replaced by an alternate identity.

Possession trance disorder (6B63)

A trance state in which the normal sense of personal identity is *replaced by an external "possessing" identity*, with behaviours or movements experienced as controlled by the possessing agent (a spirit, deity, demon or the dead); full or partial amnesia for the episode is usual.

Shared thresholds

Episodes are recurrent, or, if the diagnosis rests on a single episode, that episode has lasted at least several days; the state is involuntary and unwanted, is not a sanctioned collective practice, is not organic or substance-related, and causes distress or impairment.

RULE **The sanctioned-practice line is the diagnosis.** An involuntary, unwanted, distressing or impairing trance or possession state that falls *outside* an accepted collective cultural or religious practice is a disorder; the identical experience embraced as ritual, without distress or impairment, is not.

7.2 The critical boundary: accepted cultural practice is not a disorder

Where possession is welcomed, it is not pathology. ICD-11 states the exclusion twice over: the diagnosis is *not* applied to experiences accepted in the person's context as collective cultural phenomena or religious practice, and *not* applied where there is no significant distress or impairment. Single, transitory experiences lasting minutes to hours, and states cultivated within religious or cultural groups where possession is normative, are explicitly excluded, and people who gradually gain control and acceptance of the experience within such a group carry no excess of mental disorder over the general population. DSM-5-TR draws the same line in its own words: dissociative trance "is not a normal part of a broadly accepted collective cultural or religious practice."

7.3 ICD-11 versus DSM-5-TR versus the old ICD-10 label

Same phenomenon, three homes. The classification map is itself the examiner's favourite question here.

SYSTEM	WHERE POSSESSION / TRANCE LIVES	KEY POINT
ICD-11	**Two categories: trance disorder (6B62), possession trance disorder (6B63)**	Possession trance = identity replaced by an *external* agent
DSM-5-TR	Possession folded into dissociative identity disorder; dissociative trance under Other Specified Dissociative Disorder	**No standalone possession/trance disorder**
ICD-10	F44.3 trance and possession disorder	A single combined rubric ("possession hysteria")

The one entity ICD-11 splits in two, DSM-5-TR scatters across DID and OSDD, and ICD-10 merged under F44.3.

7.4 Reading the differential: identity, psychosis, PTSD and the organic mimics

External agent, brief and stress-bound, normal EEG. Four boundaries decide the case. Against dissociative identity disorder and partial DID, the possession identity is attributed to an *external* agent, whereas DID identities are internal and not so attributed; someone describing both internally and externally attributed identities is diagnosed with DID, not possession trance. Against schizophrenia, the intrusive voices, inserted thoughts and controlled behaviours occur *primarily during* the brief possession state, with no other positive or negative psychotic symptoms. Against PTSD, if trance-like states are confined to flashback re-experiencing, no additional trance diagnosis is made. Against the organic mimics, possession trance can resemble focal unaware (complex partial) seizures of temporal lobe epilepsy or delirium, but trance disorder shows a *normal EEG even during episodes* and lacks the global confusion of delirium.

TRAP **Reading a possession state without the cultural formulation, or missing an organic cause.** Two errors sink this presentation: labelling a sanctioned ritual possession as a disorder because the culture was never assessed, and stamping "possession trance" on what is actually temporal lobe epilepsy, delirium or a substance effect. Take the cultural formulation and clear the organic differential before the label.

7.5 The Indian frame: a common presentation, decoded through culture

Common here, and best understood as an idiom of distress. Possession trance presentations are very commonly seen in India and certain African countries, where the possessing agent characteristically matches a figure from the local religious tradition and the episode is often precipitated by domestic disharmony, interpersonal conflict or acculturative stress. The clinical task is not to sedate the phenomenon but to read it: apply the cultural formulation, decode the **idioms of distress** the family is using, and separate a sanctioned, welcomed ritual possession from an involuntary, distressing state that meets criteria. The wider transcultural framing and the neighbouring culture-bound syndrome concept sit in the Consultation-liaison, geriatric & transcultural psychiatry notes; the dissociative subtype of PTSD and the trauma-linked trance in the Anxiety, OCD & trauma-related disorders notes; and the video-EEG work-up that excludes non-epileptic (dissociative) convulsions in the Epilepsy & psychiatry notes.

20 to 25	6B62 · 6B63	F44.3
MEAN AGE AT ONSET (YRS), ICD-11 CDDR	ICD-11 TRANCE AND POSSESSION TRANCE CODES	ICD-10 TRANCE AND POSSESSION DISORDER RUBRIC

INDIA

Possession is a mainstream idiom of distress across much of India, expressed through spirit intrusion, temple and dargah healing, mediumship and family-attended possession episodes, so the same behaviour can be devotional ritual in one setting and disorder in another. The examinable move is discipline: run the cultural formulation, ask whether the community accepts and welcomes the state, and reserve the diagnosis for the involuntary, unwanted, distressing or impairing form. The genuine local pitfall is the reflex to reach straight for a benzodiazepine, alprazolam (Alprax or Restyl) being the default anxiolytic in Indian practice, when the presentation calls first for cultural understanding and treatment of the underlying stress or comorbidity, not sedation of a culturally meaningful experience.

PEARL

The cleanest discriminator between the two ICD-11 entities is a single question: *who is acting?* If awareness narrows and behaviour shrinks to a small repertoire that feels outside control but the self is still the self, it is trance disorder; if the self is replaced by an external spirit, deity or demon that directs the behaviour, it is possession trance disorder. Replacement of identity by an external agent is the whole of the difference.

GOOD TO REMEMBER

- **Trance disorder (the syndrome):** the defining criterion is a trance state with a marked alteration of consciousness marked by *both* narrowing of awareness of the surroundings *and* restriction of movement, posture and speech to a small, seemingly uncontrolled repertoire, *without* replacement by an alternate identity; recurrent or a single episode of at least several days, involuntary and unwanted, outside sanctioned cultural practice, and distressing or impairing. The first step is always to check that it is not an accepted collective ritual and not organic (normal EEG even during the episode).
- **Possession trance disorder (the syndrome):** the defining criterion is a trance state in which the normal sense of identity is *replaced by an external "possessing" identity*, with behaviours experienced as controlled by that agent and usual full or partial amnesia; the discriminator from dissociative identity disorder is that the identity is attributed to an *external* agent, and the discriminator from all of them is that a sanctioned, non-distressing collective practice is not a disorder.

HOLD THIS

Trance disorder is narrowed awareness with a small uncontrolled behavioural repertoire and the self intact; possession trance disorder is the self replaced by an external agent; both are disorders ONLY when involuntary, unwanted, distressing or impairing and outside an accepted collective cultural or religious practice, which is why the cultural formulation, not sedation, is the first step in the Indian setting.

Anxiolytic and hypnotic pharmacology

8 · Benzodiazepines

This is the weightiest topic in the pharmacology block, and it rewards a single organising idea. A **benzodiazepine** is a **positive allosteric modulator** at the **GABA-A receptor**: it does nothing on its own, but where GABA is already present it turns the inhibitory signal up. Hold that mechanism and three examinable strands fall out of it in order, the *receptor* story (how it works), the *kinetic* story (how long it works, which sorts the agents into short-acting and long-acting classes), and the *clinical* story (that it is a powerful short-term drug and a dangerous long-term one). The paper tests the last strand hardest: the single most answerable management statement on this material is that a benzodiazepine is **not** a first-line long-term anxiolytic or hypnotic.

The guideline spine is fixed. For anxiety and insomnia the British Association for Psychopharmacology (BAP) leads, the National Institute for Health and Care Excellence (NICE) sets the short-course limit, the Maudsley Prescribing Guidelines carry the receptor detail, the doses, the half-lives and the diazepam-equivalence table, and the Indian Psychiatric Society carries the Indian layer. The receptor mechanism and the GABA-A detail here are the same ones cross-referenced to the Neurochemistry, Neuroendocrinology, Neuroimaging & Basic Psychopharmacology notes; the sedative and benzodiazepine *use* disorder as an addiction sits in the Substance use disorders notes; the lorazepam challenge in catatonia in the Other psychotic disorders, delusional syndromes & catatonia notes; and the SSRIs and SNRIs that outrank benzodiazepines as first-line anxiolytics in the Mood disorders: pharmacotherapy notes. The accompanying figures set out the receptor with its binding site, the half-life map, the withdrawal time-course, the class-and-mechanism map and the taper.

Fig 15.11 The anxiolytic and hypnotic class-and-mechanism map: five mechanism classes and the agents that sit under each, so the whole band recalls from the receptor action outward.

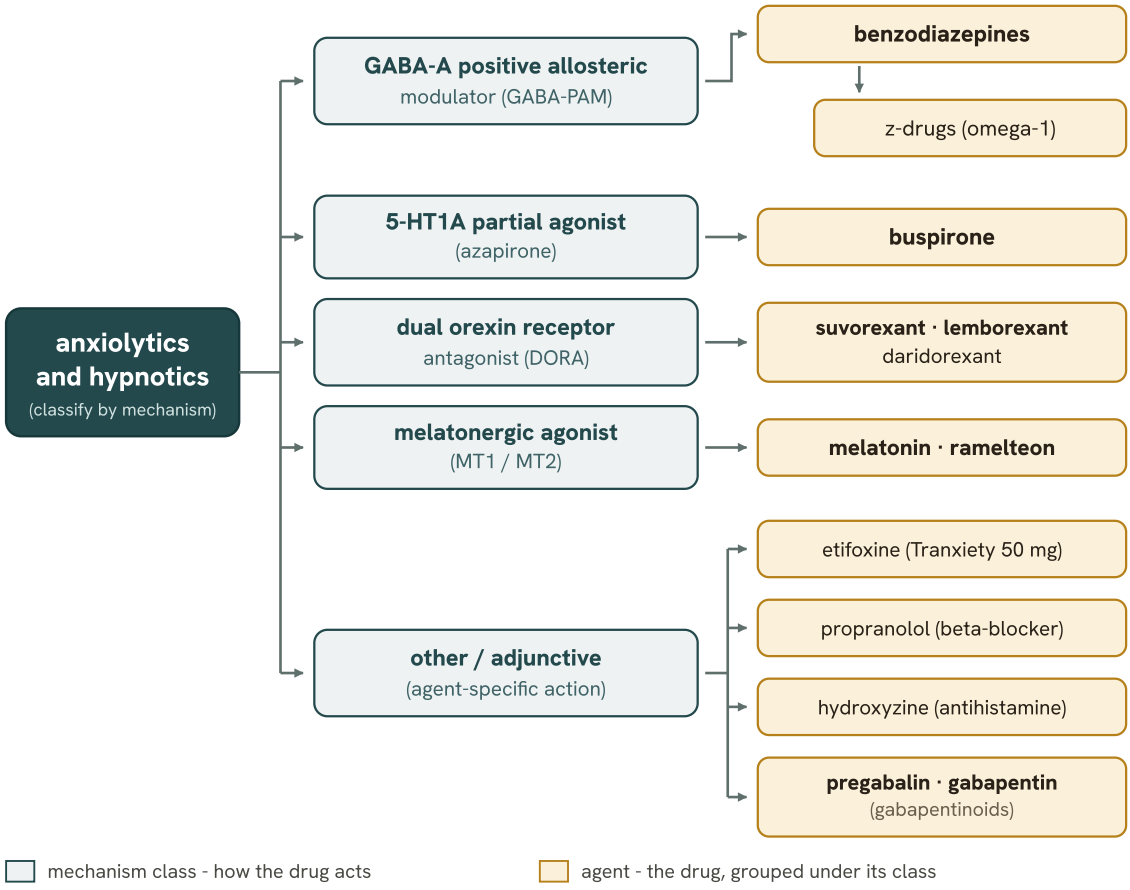


Fig 15.12 The GABA-A receptor is a pentameric chloride channel; the benzodiazepine binds the allosteric site at the alpha/gamma interface and, only with GABA present, raises the frequency of channel opening.

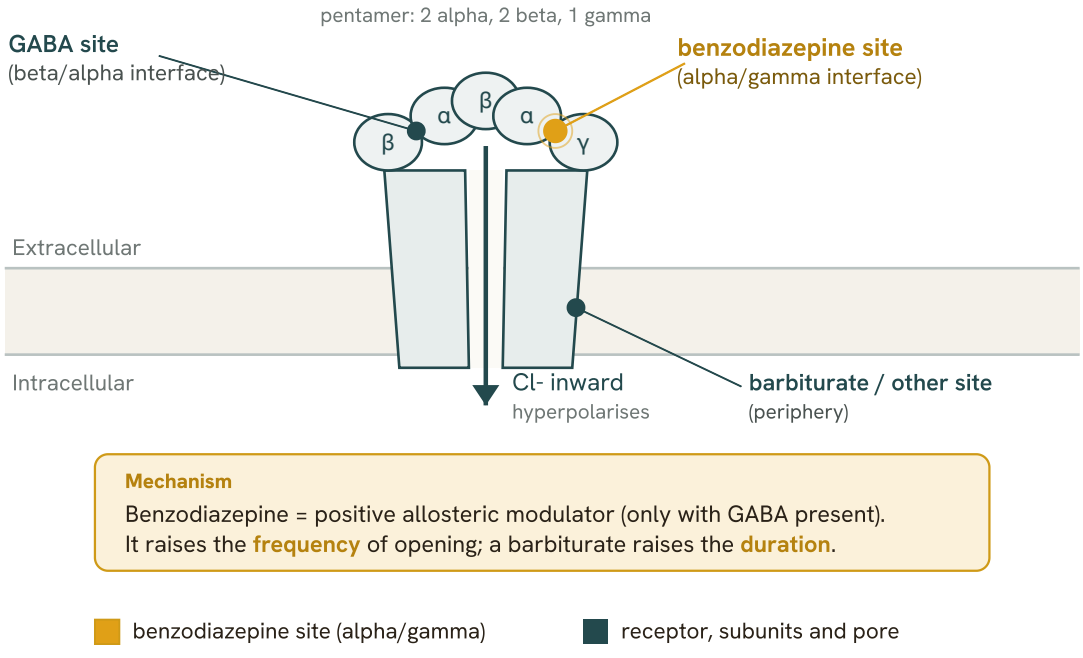


Fig 15.13 The benzodiazepines sorted by elimination half-life into short-, intermediate- and long-acting classes, with the shared long-acting metabolite and the duration-to-use rule.

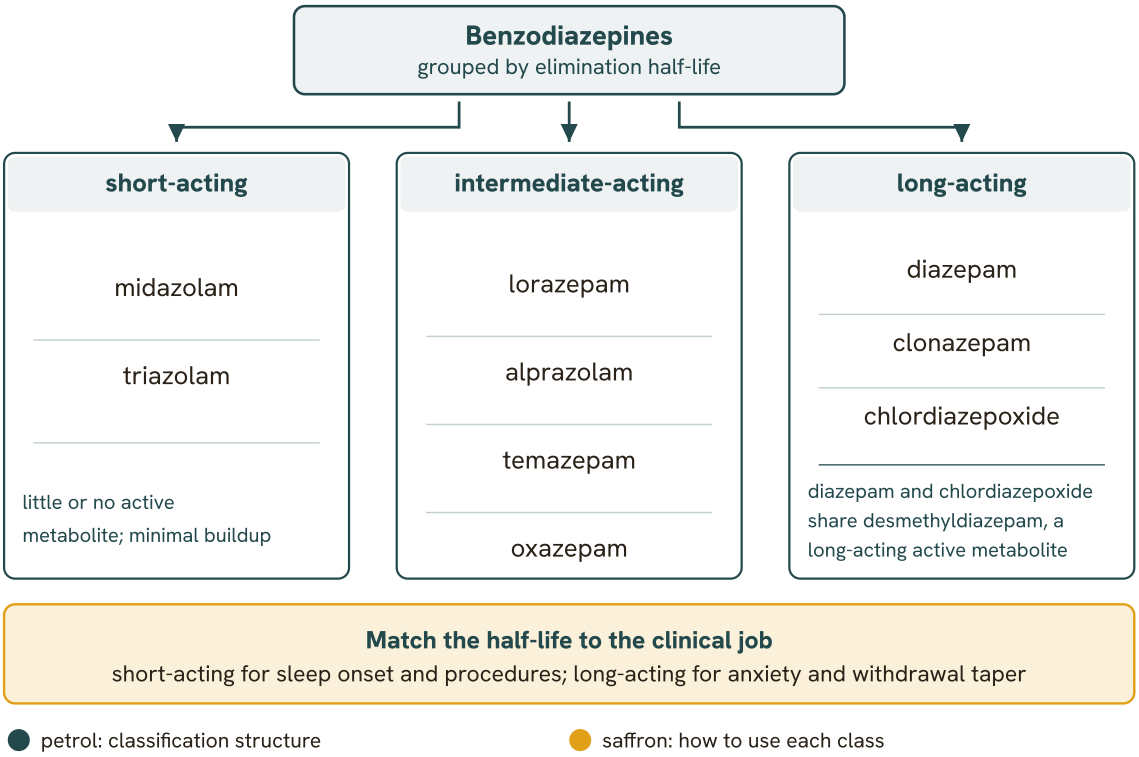
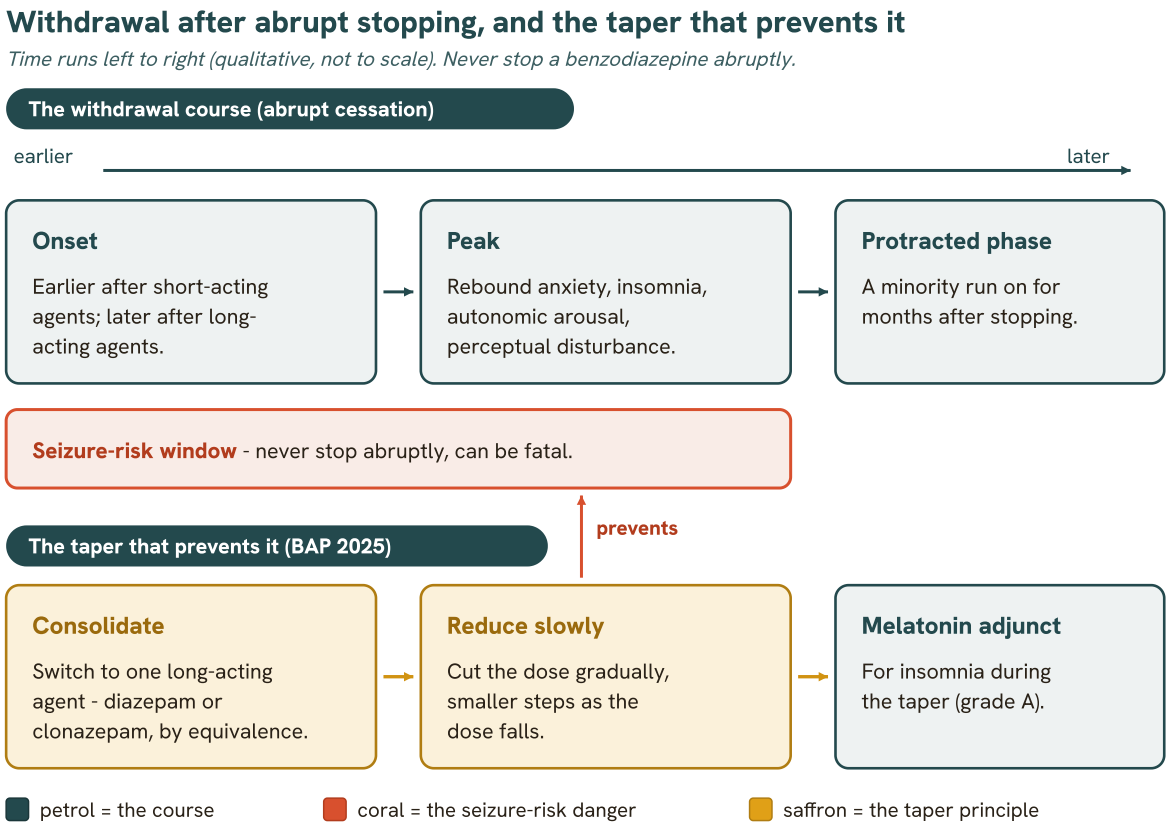


Fig 15.14 The benzodiazepine withdrawal course after abrupt cessation, and the long-acting taper that prevents it.



8.1 Mechanism: a positive allosteric modulator that raises the frequency of channel opening

Frequency, not duration, and only in the presence of GABA. A **benzodiazepine** binds the **benzodiazepine binding site** on the GABA-A receptor and, by **allosteric modulation**, increases the affinity of the receptor for its own transmitter GABA (Stahl; KDT). The functional result is an increase in the *frequency* of **chloride channel** opening when GABA is bound, more chloride enters, the neurone hyperpolarises, and inhibition deepens (KDT). Two properties define the class from this one fact. First, the drug is a *modulator*, not a direct agonist: with no GABA present it opens no channel, which is the pharmacological reason benzodiazepines have a ceiling on respiratory depression and are relatively safe in isolated overdose. Second, the contrast with barbiturates is a favourite: barbiturates increase the *duration* (lifetime) of each chloride channel opening, and at high concentration open the channel directly without GABA, which removes the ceiling and makes them lethal in overdose (KDT). In Stahl's neuroscience-based nomenclature the class is written literally as a GABA positive allosteric modulator (GABA-PAM).

RULE **Frequency up, GABA required.** A benzodiazepine is a positive allosteric modulator that raises the *frequency* of chloride-channel opening only when GABA is present (contrast the barbiturate, which raises channel-opening *duration* and can open the channel alone), and that GABA-dependence is why it has a ceiling effect and is relatively safe in a pure overdose.

8.2 The GABA-A receptor and the benzodiazepine binding site

GABA sits on the beta interface, the benzodiazepine between alpha and gamma. The **GABA-A receptor** is a pentameric ligand-gated chloride channel, most commonly two alpha, two beta and one gamma subunit. GABA itself, the orthosteric ligand, binds at the interface involving the beta subunit and gates the channel; the **benzodiazepine binding site** is a separate, allosteric site at the interface between the *alpha and gamma* subunits (KDT; Stahl). Because occupancy of that site only modulates a channel GABA is already working on, agonists such as diazepam facilitate inhibition while inverse agonists at the same site (the beta-carbolines) hinder it and are anxiogenic and convulsant, a clean demonstration that this is genuine allosteric modulation in both directions. The subtype detail is worth a line for the paper: benzodiazepine action at alpha-1-containing receptors mediates sedation and the amnestic and anticonvulsant effects, while alpha-2 (and alpha-3) receptors carry the anxiolytic and muscle-relaxant effects (Stahl). This receptor-and-site anatomy is the shared substrate developed further in the Neurochemistry, Neuroendocrinology, Neuroimaging & Basic Psychopharmacology notes, and the accompanying figure lays it out as the membrane-grammar plate.

GOOD TO REMEMBER

- **Benzodiazepine (the class):** a positive allosteric modulator at the GABA-A receptor, binding the benzodiazepine site at the *alpha-gamma* interface and increasing the *frequency* of chloride-channel opening in the presence of GABA; alpha-1 drives sedation, alpha-2 drives anxiolysis; the signature caution is dependence with long-term use and seizures on abrupt withdrawal.

8.3 The half-life classification and active metabolites

The clinically useful sort is by half-life, because that predicts accumulation, hangover and withdrawal. Agents split into **short-acting** or short-to-intermediate drugs, which clear quickly,

carry little or no active metabolite and so accumulate less, and **long-acting** drugs, which have long half-lives and long-lived active metabolites and therefore build up (a hazard in the elderly and in liver disease). The pivotal metabolite is desmethyldiazepam (nordiazepam), the long-lived active metabolite shared by diazepam and chlordiazepoxide, which is what makes those agents behave as long-acting even beyond their parent half-life (Stahl). The short-acting drugs with no clinically important active metabolite are the ones preferred when the liver is impaired, remembered as the LOT group. The half-lives below are the verified Stahl and Maudsley figures.

AGENT	ELIMINATION HALF-LIFE (HOURS)	ACTIVE METABOLITE	CLASS
lorazepam	**10 to 20**	none	short-to-intermediate
alprazolam	**12 to 15**	none of note	short-to-intermediate, high-potency
oxazepam / temazepam	short (not tabulated here)	none	short-acting (the LOT group, liver-safe)
chlordiazepoxide	24 to 48	nordiazepam (long-lived)	long-acting
clonazepam	**30 to 40**	none of clinical note	long-acting, high-potency
diazepam	**20 to 50 (parent)**	nordiazepam, oxazepam, temazepam	long-acting
zolpidem (z-drug, for contrast)	about 2.5	none	ultra-short

Half-life classification with verified Stahl elimination half-lives; the long-acting agents owe their duration to the shared active metabolite nordiazepam (desmethyldiazepam). Oxazepam and temazepam half-lives were not individually verified here.

MNEMONIC

LOT

Lorazepam, **O**xazepam, **T**emazepam: the short-acting benzodiazepines with *no* active metabolite. They do not accumulate, so they are the preferred choice in hepatic impairment (lorazepam is explicitly named for this in Stahl) and the safer choice in the elderly.

8.4 Clinical uses and the short-course rule

Powerful, fast, and reserved. Benzodiazepines are genuinely useful for a small set of jobs, acute and severe anxiety or agitation, alcohol withdrawal, status epilepticus and acute seizures, catatonia (the lorazepam challenge, developed in the Other psychotic disorders, delusional syndromes & catatonia notes), pre-medication, and very short-term insomnia. What the examiner wants is the **short-course** discipline around chronic anxiety and insomnia. For generalised anxiety disorder an SSRI is the **first-line** pharmacological treatment (BAP 2014; NICE CG113 2011 names sertraline first), with an SNRI or pregabalin as the alternative; buspirone and hydroxyzine cover acute anxiety only. A benzodiazepine is not first-line and not for maintenance: BAP reserves it only after non-response to an SSRI, an SNRI, pregabalin *and* buspirone, for

persistent, severe, distressing, impairing anxiety, and NICE says do not offer a benzodiazepine for generalised anxiety disorder except as a short-term measure of no more than 2 to 4 weeks during a crisis (NICE 2011). For chronic insomnia CBT for insomnia is first-line (BAP 2019), with a benzodiazepine or a z-drug only as a short-term option, matching the half-life to the pattern. If a benzodiazepine is genuinely effective and continued, it is continued for a defined period and then tapered, never open-endedly.

TRAP **Starting a benzodiazepine for chronic anxiety or insomnia.** The reflex prescription for persistent worry or poor sleep is exactly the error the guidelines forbid: the first-line agents are the SSRI (anxiety) and CBT for insomnia, and the benzodiazepine is a 2 to 4 week crisis measure at most (NICE 2011), because tolerance, dependence and a withdrawal seizure risk follow long-term use.

8.5 Agent selection and the benzodiazepine-sparing principle

Match the agent to the goal, and spare the benzodiazepine wherever a non-dependence option exists. The practical skill of **agent selection** is deciding **which agent** for which target, and the organising rule is **benzodiazepine-sparing**: reach past the benzodiazepine to a drug that does the job without dependence whenever the clinical goal allows it. The class-and-mechanism map below (also drawn as the accompanying figure) sets out the Band B options with their Indian brands. For sustained anxiety, prefer the SSRI or SNRI, pregabalin or buspirone; for the somatic and performance-anxiety picture, propranolol; for short-term insomnia, a z-drug, melatonin or very-low-dose doxepin; and keep the benzodiazepine for the acute crisis, the seizure, the alcohol withdrawal and catatonia.

CLASS	EXAMPLE AGENT (INDIAN BRAND)	MECHANISM	PLACE IN THERAPY
Benzodiazepine	diazepam (Valium, Calmpose)	GABA-A positive allosteric modulator, raises frequency of chloride-channel opening	**short-course / acute only**
Z-drug	zolpidem (Zolfresh, Nitrest)	GABA-A benzodiazepine-1 (omega-1) subtype selective	short-term hypnotic
Azapirone	buspirone (Buspin)	5-HT1A partial agonist	non-dependence anxiolytic, delayed onset
Gabapentinoid (alpha-2-delta ligand)	pregabalin (Pregeb, Pregastar)	voltage-gated calcium channel alpha-2-delta binding	GAD alternative first-line
Antihistamine	hydroxyzine (Atarax)	H1 antagonist	acute anxiolytic
Beta-blocker	propranolol (Ciplar, Inderal)	peripheral beta-adrenergic blockade	somatic / performance anxiety
Melatonergic	melatonin (Meloset, Zytonin)	MT1 / MT2 receptor agonist	circadian / insomnia over 55 years
Non-benzodiazepine GABA modulator	etifoxine (Tranxiety 50 mg)	GABA-A modulation (non-benzodiazepine site)	anxiolytic (brand unverified)
Orexin antagonist (DORA)	suvorexant	dual orexin / hypocretin receptor block	insomnia

The anxiolytic and hypnotic class-and-mechanism map; the SSRIs and SNRIs that outrank all of these as first-line anxiolytics are developed in the Mood disorders: pharmacotherapy notes.

8.6 Dependence, tolerance and the withdrawal syndrome

Three syndromes, and one of them can kill. Long-term use produces **tolerance** (a diminishing effect, so the dose is pushed up) and physical **dependence**. Kaplan separates three things that follow stopping. *Relapse* is the slow return of the original disorder over weeks to months. *Rebound* is a brief, more intense re-emergence of anxiety or insomnia, worse than baseline, lasting up to about 3 weeks; with a short-acting agent it appears as *interdose* rebound anxiety 3 to 4 hours after each dose (classically alprazolam, mistaken for craving). *Withdrawal* is the true discontinuation syndrome with new autonomic features. Its onset is kinetic: it begins within hours to a few days of stopping a **short-acting** benzodiazepine, but may not start for 1 to 2 weeks after abrupt cessation of a **long-acting** one (Kaplan). Minor symptoms are sweating, tachycardia, nausea, tremor, restlessness, and the characteristic *perceptual disturbance* (heightened sensitivity to light and sound, depersonalisation). The dangerous, major symptoms are *seizures*, psychosis and delirium, and seizures are the reason a benzodiazepine must never be stopped abruptly (Maudsley: abrupt cessation can cause seizures and can be fatal). Withdrawal is more severe with high-potency, short-half-life agents, typically lasts 2 to 4 weeks, and can occasionally become

protracted over many months. The accompanying figure lays this out as a withdrawal time-course timeline.

3 to 4 h	1 to 2 wk	2 to 4 wk
INTERVAL AT WHICH INTERDOSE REBOUND ANXIETY FOLLOWS A SHORT-ACTING AGENT	DELAY BEFORE WITHDRAWAL STARTS AFTER A LONG-ACTING AGENT IS STOPPED ABRUPTLY	USUAL DURATION OF THE WITHDRAWAL SYNDROME

GOOD TO REMEMBER

- **Benzodiazepine withdrawal syndrome (the syndrome):** the defining features are rebound anxiety and insomnia, perceptual disturbance and autonomic arousal, with the criterion-level dangers being *seizures*, psychosis and delirium; the discriminator from relapse is the timing (hours to days after a short-acting drug, up to 1 to 2 weeks after a long-acting one) and the new autonomic signs. First step: never stop abruptly, taper.

8.7 The taper: switch to a long-acting agent, then reduce slowly

Consolidate, convert, then come down in proportions. The evidence-based **taper** (BAP 2025; Maudsley) has a fixed shape. First *consolidate* the patient onto a single long-acting benzodiazepine, **diazepam** or **clonazepam**, chosen for their long half-life and dosing flexibility (use lorazepam or oxazepam instead where the liver is impaired). Converting to diazepam needs the diazepam-equivalence table, verified from the Maudsley Prescribing Guidelines below. Then *reduce gradually*: patients often tolerate reductions of about 10 percent of the last dose every 2 to 4 weeks, roughly 5 to 10 percent per month, with the steps becoming smaller as the dose falls (the dose-effect relationship is hyperbolic) and the final doses very small (often less than 1 mg of diazepam-equivalent). Melatonin is a useful adjunct for insomnia during the taper (BAP grade A). Two anchors for the paper: doses above 30 mg diazepam-equivalent daily may cause harm and are avoided (Maudsley), and the difficult final doses of alprazolam are often eased by substituting clonazepam (Kaplan).

BENZODIAZEPINE	DOSE EQUAL TO DIAZEPAM 10 MG (MG)
Diazepam	10
Chlordiazepoxide	25
Clonazepam	**0.5**
Lorazepam	**1**
Lormetazepam	1 to 2
Nitrazepam	10
Oxazepam	20
Temazepam	20

Approximate diazepam-equivalent doses, verified from the Maudsley Prescribing Guidelines (Table 3.29). Alprazolam is deliberately not tabulated there, so no alprazolam equivalence is asserted here (see gaps).

GOOD TO REMEMBER

- **Diazepam (Valium, Calmpose):** the long-acting anchor of the taper; oral 4 to 40 mg per day in divided doses; GABA-A positive allosteric modulator with the active metabolite nordiazepam; verified equivalence, diazepam 10 mg equals clonazepam 0.5 mg equals lorazepam 1 mg equals chlordiazepoxide 25 mg (Maudsley).
- **Clonazepam (Clonotril, Rivotril):** long-acting (half-life 30 to 40 hours), high-potency; panic 0.5 to 2 mg per day, seizures up to 20 mg per day; the other consolidation agent for the taper and the substitute that eases the final doses of alprazolam.
- **Alprazolam (Alprax, Restyl):** short-to-intermediate (half-life 12 to 15 hours), high-potency; anxiety 1 to 4 mg per day; the most toxic benzodiazepine in overdose (Maudsley) and the hardest to taper, manufacturer limit 2 to 4 weeks.
- **Lorazepam (Ativan, Loraz):** short-to-intermediate (half-life 10 to 20 hours), *no* active metabolite so liver-safe; oral 2 to 6 mg per day; the catatonia challenge agent at 1 to 2 mg.

8.8 Flumazenil: the antagonist and its seizure caution

The antidote that can precipitate the seizure it looks like it should treat. Flumazenil is the benzodiazepine-receptor *antagonist*, a competitive blocker at the benzodiazepine binding site used to reverse benzodiazepine sedation and respiratory depression (Stahl; Maudsley). Two facts matter clinically. Its half-life is short, only 41 to 79 minutes, much shorter than most benzodiazepines it reverses, so re-sedation follows a single dose and repeat dosing is often needed. And it carries a real *seizure* hazard: it can precipitate seizures in a patient who is tolerant to or dependent on benzodiazepines, in a mixed overdose (particularly with cyclic antidepressants), or where the benzodiazepine was suppressing seizures, so it is used cautiously and at the minimally effective dose, not reflexively in every benzodiazepine overdose. Because uncomplicated benzodiazepine overdose is usually benign with supportive care, the risk of flumazenil often outweighs the benefit.

GOOD TO REMEMBER

- **Flumazenil (the antagonist):** a competitive benzodiazepine-receptor antagonist with a short half-life of 41 to 79 minutes (so re-sedation and repeat dosing); the signature caution is that it can *precipitate seizures* in benzodiazepine dependence and in mixed or cyclic-antidepressant overdose, so it is used selectively at the lowest effective dose, not routinely.

8.9 Buspirone and the z-drugs: the non-benzodiazepine comparators

Two agents the paper contrasts against the benzodiazepine. **Buspirone** is an azapirone anxiolytic, a *5-HT1A partial agonist* (not a GABA drug at all), with a short half-life of 2 to 3 hours and a usual dose of 20 to 30 mg per day (up to 60 mg per day). Its defining contrast with the benzodiazepine is a *delayed* onset of 2 weeks or more and *no* dependence, sedation, anticonvulsant effect or interaction with alcohol, which is exactly why it is a benzodiazepine-sparing choice for sustained anxiety but useless for an acute crisis. The *z-drugs* (zolpidem, zopiclone, eszopiclone) act at the benzodiazepine-1 (omega-1) subtype of the GABA-A receptor, so they are hypnotic with less anxiolytic and muscle-relaxant effect; zolpidem is dosed 10 mg at bedtime for 7 to 10 days (short elimination half-life about 2.5 hours), and their signature warning is complex sleep behaviours (sleep-driving, sleep-eating with amnesia), plus dependence and

next-day impairment, so tolerance and rebound insomnia are real despite the earlier marketing that they were not.

GOOD TO REMEMBER

- **Buspirone (Buspin):** a 5-HT1A partial agonist, 20 to 30 mg per day; the mechanism-and-caution signature is a *delayed* onset (2 weeks or more) with *no* dependence, sedation or anticonvulsant effect, so it spares the benzodiazepine in sustained anxiety but is no use acutely.
- **Zolpidem (Zolfresh, Nitrest):** a z-drug at the benzodiazepine-1 (omega-1) GABA-A subtype, 10 mg at bedtime for 7 to 10 days; the signature caution is complex sleep behaviours (sleep-driving) with dependence and next-day impairment.

PEARL

Every hard fact on this topic is a corollary of one sentence: a benzodiazepine only turns up an inhibition that GABA is already producing. That is why it has a ceiling and is safe in a pure overdose (mechanism), why the receptor adapts and rebounds when it is removed (dependence and withdrawal), why the antidote flumazenil unmasks that rebound as a seizure, and why the long-term answer is a slow taper rather than an abrupt stop.

INDIA

India carries a genuine benzodiazepine over-prescription problem, and **alprazolam** (Alprax, Restyl) is the default anxiolytic reached for in general and psychiatric practice alike; benzodiazepines are among the most frequently prescribed drugs. Two consequences follow. First, alprazolam is the *most toxic* benzodiazepine in overdose (Maudsley) and, being short-acting and high-potency, the hardest to taper, so it is a poor default. Second, the Indian Psychiatric Society position and the wider benzodiazepine-sparing principle favour the SSRI or SNRI for sustained anxiety and CBT for insomnia, reserving the benzodiazepine for the genuine short course. The culture-bound relevance is real too: possession, trance and dissociative presentations are common in Indian settings and are frequently met with a reflex sedative, which treats nothing; read them through a cultural formulation (the Consultation-liaison, geriatric & transcultural psychiatry notes) rather than sedating them. The sedative and benzodiazepine use disorder as an addiction is developed in the Substance use disorders notes.

HOLD THIS

A benzodiazepine is a GABA-A positive allosteric modulator that raises the *frequency* of chloride-channel opening (barbiturates raise the *duration*); it is never a first-line long-term anxiolytic or hypnotic (NICE: a 2 to 4 week crisis course only); it is withdrawn by consolidating onto a long-acting agent (diazepam or clonazepam) and tapering slowly because *abrupt cessation can cause seizures*; and its antagonist flumazenil can itself precipitate seizures in dependence and mixed overdose.

For the receptor systems behind the GABA-A detail see the Neurochemistry, Neuroendocrinology, Neuroimaging & Basic Psychopharmacology notes; for the sedative use disorder as an addiction the Substance use disorders notes; for the lorazepam management of catatonia the Other psychotic disorders, delusional syndromes & catatonia notes; for the SSRIs

and SNRIs as first-line anxiolytics the Mood disorders: pharmacotherapy notes; and for clinical insomnia and CBT for insomnia the Eating & sleep-wake disorders notes.

9 · Buspirone and the azapirones

This is the anxiolytic the examiner uses to test whether you understand what a benzodiazepine is not. Buspirone is a non-benzodiazepine anxiolytic of the **azapirone** class (chemically an azaspiro-decanedione), and almost every mark on it comes from a single contrast: it is a **5-HT1A partial agonist** that works through slow serotonergic adaptation rather than fast GABAergic inhibition, so it carries a **delayed onset** of two weeks or more and, crucially, **no dependence**, no sedation, no anticonvulsant effect and no abuse potential (Stahl, Prescriber's Guide).

Hold two opposing lists in your head. The benzodiazepine works within minutes, sedates, is a good PRN rescue, and breeds tolerance, dependence and a withdrawal syndrome. Buspirone does the reverse on every count: useless as a PRN because the effect takes a fortnight to appear, but clean on dependence and sedation across long-term use. That is why the guidelines place it as an acute-GAD option sitting *after* an SSRI and *before* a benzodiazepine in the benzodiazepine-sparing ladder, and why the classic trap is to expect it to abort acute anxiety.

9.1 Mechanism: a 5-HT1A partial agonist

Serotonergic, not GABAergic. Buspirone binds the 5-HT1A receptor as a partial agonist. At the presynaptic somatodendritic autoreceptor its agonism damps 5-HT neuronal firing acutely, while its postsynaptic partial agonism modulates onward serotonergic tone; the therapeutic anxiolysis emerges only once these receptors down-regulate and adapt over weeks, which is precisely why the onset is delayed (Stahl). It *does not act on the benzodiazepine receptor or the GABA-A chloride channel at all*, so it confers none of the GABAergic effects, sedation, muscle relaxation, anticonvulsant cover or cross-tolerance with alcohol and barbiturates. It additionally shows weak dopamine autoreceptor antagonism. For the receptor biology of the 5-HT1A and GABA-A systems, see the Neurochemistry, Neuroendocrinology, Neuroimaging & Basic Psychopharmacology notes.

RULE **5-HT1A, weeks, no dependence.** Buspirone is a 5-HT1A partial agonist whose anxiolysis depends on slow receptor adaptation, so it has a delayed onset of two weeks or more and produces no dependence, sedation, anticonvulsant effect or abuse; it is an acute-GAD agent, never a PRN rescue.

9.2 The azapirone family

Buspirone is the only one in routine anxiolytic use. The **azapirones** are a small family of selective 5-HT1A partial agonists. Buspirone is the marketed anxiolytic; gepirone (extended-release) has since been approved as an *antidepressant* for major depression rather than as an anxiolytic; and ipsapirone, tandospirone and flesinoxan remained investigational 5-HT1A agonists that did not establish a first-line anxiety niche (New Oxford Textbook of Psychiatry;

Companion to Psychiatric Studies). The examinable point is the shared mechanism, not the minor agents.

AZAPIRONE	5-HT1A ACTION	ESTABLISHED ROLE
Buspirone	**Selective 5-HT1A partial agonist**	**Anxiolytic for GAD (acute)**
Gepirone (ER)	5-HT1A partial agonist	Antidepressant for major depression
Ipsapirone	5-HT1A partial agonist	Investigational / research agent
Tandospirone	5-HT1A partial agonist	Anxiolytic in some Asian markets
Flesinoxan	5-HT1A agonist	Investigational

The azapirone class shares one mechanism; only buspirone is a mainstream anxiolytic, and gepirone crossed over to depression.

9.3 The place in GAD: the guideline ladder

An acute-GAD option, not first-line, ahead of a benzodiazepine. BAP is explicit that buspirone (and hydroxyzine) are efficacious in the *acute* treatment of generalised anxiety disorder but that neither has published evidence for relapse prevention (BAP 2014, Baldwin et al.). The first-line pharmacological treatment for GAD is an SSRI, with an SNRI or pregabalin as alternatives; a benzodiazepine is reserved and, in the BAP sequence, considered only after non-response to an SSRI, an SNRI, pregabalin *and* buspirone. NICE CG113 (NICE 2011) builds its stepped care on the SSRI/SNRI/pregabalin sequence and restricts benzodiazepines to short-term crisis use; the Maudsley Prescribing Guidelines carry buspirone as a second-line/adjunctive anxiolytic option. The first-line SSRI position is developed in the Mood disorders: pharmacotherapy notes, and the wider anxiety-disorder pharmacology in the Anxiety, OCD & trauma-related disorders notes.

TRAP **Calling buspirone first-line, or using it as a PRN.** Buspirone is *not* first-line for GAD (an SSRI is) and is worthless taken as-needed for an acute surge; a delayed-onset drug given for immediate relief simply fails and gets abandoned.

9.4 Delayed onset: useless as a PRN anxiolytic

Two weeks to work is the whole clinical personality. Buspirone takes roughly **2 weeks** before its anxiolytic effect is evident, and if it has not worked within **6 to 8 weeks** it may not work at all (Stahl). Because relief is not tied to the plasma level of any single dose, it cannot be used to abort a panic surge or as an as-needed rescue, the exact niche where a benzodiazepine excels. This delayed onset also drives the higher discontinuation seen versus a benzodiazepine, and it means a patient must never be switched abruptly from a benzodiazepine to buspirone: buspirone does not suppress benzodiazepine withdrawal, so the patient takes a therapeutic buspirone dose for two to four weeks first, and only then is the benzodiazepine tapered (Kaplan and Sadock, CTP 2024).

FEATURE	BUSPIRONE (5-HT1A PARTIAL AGONIST)	A BENZODIAZEPINE (GABA-A PAM)
Onset of anxiolysis	**Delayed, 2 weeks or more**	**Minutes to hours**
PRN / as-needed rescue	**No, ineffective acutely**	Yes, effective
Sedation, psychomotor impairment	**None**	Yes
Anticonvulsant / muscle relaxant	**None**	Yes
Dependence, tolerance, withdrawal	**None; taper generally not needed**	Yes; seizure risk on abrupt stop
Respiratory depression	None	Yes (dose-related)
Abuse potential	**Low / none**	Present

The buspirone-versus-benzodiazepine contrast is the single most examinable content on this drug: fast-but-dependent against slow-but-clean.

9.5 The safety signature: no dependence, no sedation, no anticonvulsant, no abuse

Four clean "no"s. Buspirone does not appear to cause dependence and shows virtually no withdrawal symptoms; it is not habit-forming and a taper is generally not necessary on stopping (Stahl). It causes no sedation, psychomotor impairment, cognitive impairment or respiratory depression (Kaplan and Sadock, CTP 2024), and it is anxioselective with no anticonvulsant or muscle-relaxant properties. This profile makes it attractive where a benzodiazepine is hazardous, in respiratory disease, sleep apnoea, a history of substance misuse, or the older adult, though its efficacy may be diminished in patients previously maintained on a benzodiazepine. Its own side effects are limited and non-sedating: dizziness, headache, nausea and nervousness. The benzodiazepine dependence and withdrawal picture that buspirone deliberately avoids is covered in the Substance use disorders notes.

MNEMONIC

5-HT1A · TWO WEEKS · NO DEPENDENCE

The three anchors that answer any buspirone question: the mechanism (a selective 5-HT1A partial agonist azapirone), the delayed onset (two weeks or more, so never PRN), and the clean tail (no dependence, no sedation, no anticonvulsant, no abuse).

9.6 Dosing, half-life and pharmacokinetics

Short half-life, divided dosing, delayed clinical effect. Buspirone is given at **15 to 30 mg/day** in divided doses, typically a thrice-daily schedule because the elimination half-life is short at only about **2 to 3 hours** (Stahl). A common titration starts around 15 mg daily in divided doses and increases in 5 mg steps every two to three days; the usual effective range is 20 to 30 mg/day, and the maximum is generally 60 mg/day (Stahl; Kaplan and Sadock, CTP 2024). It is metabolised by CYP3A4 to an active metabolite, 1-(2-pyrimidinyl)piperazine (1-PP), so a 3A4 inhibitor (for example a CYP3A4-inhibiting antifungal or nefazodone) raises buspirone levels and a 3A4

inducer such as carbamazepine lowers them. The apparent paradox worth stating in a viva is that a very short-half-life drug still has a delayed clinical onset, because the effect depends on receptor adaptation, not on drug accumulation.

2 to 3	2 weeks+	20 to 30	60
ELIMINATION HALF-LIFE (HOURS)	ONSET BEFORE ANXIOLYTIC EFFECT APPEARS	USUAL EFFECTIVE DOSE (MG PER DAY)	MAXIMUM (MG PER DAY)

WORKED EXAMPLE

A woman in her fifties with chronic generalised anxiety and mild COPD asks for "something for the nerves" and has been buying alprazolam from a chemist for months. She wants immediate relief. Buspirone is a reasonable maintenance anxiolytic here precisely because it will not sedate or depress respiration and carries no dependence, but she must be told it will take about two weeks to help and is useless as a tablet-when-anxious. The correct plan is to start an SSRI as the first-line agent for her GAD, use buspirone as an add-on or alternative rather than a benzodiazepine, and, because she is already on alprazolam, keep the alprazolam running at a therapeutic buspirone dose for two to four weeks before tapering it slowly; buspirone will not cover benzodiazepine withdrawal.

INDIA

Buspirone (marketed in India as Buspin, verify locally) matters most in India as the answer to a real problem: benzodiazepine over-prescription, with alprazolam (alprazolam; Alprax or Restyl) as the default anxiolytic reached for reflexively and often continued long-term. The Indian Psychiatric Society position, in line with BAP and NICE, is that an SSRI or SNRI is first-line for GAD and that a benzodiazepine is a short-course measure only, not a maintenance anxiolytic. Buspirone is a genuinely useful non-dependence-forming alternative in the patient who would otherwise be parked on alprazolam, and the exam-safe line is that its delayed onset and lack of a "kick" are exactly why patients (and prescribers) drift back to the benzodiazepine, which is the behaviour the guidelines are trying to correct.

PEARL

A drug can have a very short half-life and still a long onset. Buspirone clears in two to three hours yet takes two weeks to work, because anxiolysis rides on 5-HT1A receptor adaptation, not on plasma concentration. State that dissociation and the mechanism mark is yours.

GOOD TO REMEMBER

- **Buspirone (the drug):** a selective 5-HT1A partial agonist of the azapirone class, dosed at 15 to 30 mg/day in divided doses (maximum 60 mg/day) with a short elimination half-life of about 2 to 3 hours but a delayed onset of two weeks or more, so it is never a PRN anxiolytic; it is efficacious in acute GAD (no relapse-prevention evidence) and its signature is no dependence, no sedation, no anticonvulsant effect and no abuse potential.

HOLD THIS

Buspirone is a 5-HT1A partial agonist azapirone with a short half-life (about 2 to 3 hours) but a delayed onset of two weeks or more, so it is useless as a PRN rescue; it has no dependence, sedation, anticonvulsant effect or abuse, and it sits in acute GAD after an SSRI and before a benzodiazepine.

10 · The z-drugs

The z-drugs are the examiner's test of whether you can separate a chemical class from a mechanism. The **z-drugs** (zolpidem, zopiclone, zaleplon and eszopiclone) are **non-benzodiazepine hypnotics**: they belong to different chemical families from the benzodiazepines, yet they act at the very same GABA-A benzodiazepine site, and specifically at its **benzodiazepine-1 (omega-1)** subtype. That single fact answers most questions on them, because it explains both why they work as hypnotics and why "non-benzodiazepine" does not mean non-addictive.

Almost every mark comes from four discriminators: the receptor (an omega-1-selective GABA-A positive allosteric modulator), the half-lives (short, and different from each other, which is how you choose one), the guideline place (a short-term hypnotic after CBT-I, never a long-term one), and the signature caution (**complex sleep behaviour**). Hold those four and the topic is yours.

10.1 The class: four non-benzodiazepine hypnotics

One shared site, three chemical families. The z-drugs are grouped by their shared action, not their structure. Zolpidem is an imidazopyridine, zaleplon a pyrazolopyrimidine, and zopiclone and its active S-enantiomer eszopiclone are cyclopyrrolones (Kaplan and Sadock, CTP 2024). None is a benzodiazepine, so the "z-drug" or "non-benzodiazepine hypnotic" label is a statement about chemistry; the pharmacology is benzodiazepine-like because the binding site is shared. Zopiclone is available across most of the world including India; eszopiclone (Lunesta) is chiefly a US agent, and zaleplon has been withdrawn in several markets. For the GABA-A receptor biology and the wider receptor systems, see the Neurochemistry, Neuroendocrinology, Neuroimaging & Basic Psychopharmacology notes.

10.2 Mechanism: the benzodiazepine-1 (omega-1) site

A GABA-A positive allosteric modulator, but selective for the alpha-1 subtype. Like a benzodiazepine, a z-drug is a **positive allosteric modulator** at the GABA-A receptor's benzodiazepine site, enhancing GABA-driven chloride-channel opening; it has no effect without GABA present (Stahl). The difference is selectivity. Whereas benzodiazepines bind fairly non-selectively across GABA-A receptors carrying the alpha-1, -2, -3 and -5 subunits, the z-drugs bind more selectively to receptors that contain the alpha-1 subunit, the population classically called the benzodiazepine-1 (BZ1, omega-1) receptor (Kaplan and Sadock, CTP 2024; Tasman). Because the alpha-1 subtype mediates sedation and hypnosis (and the amnestic effect), this selectivity gives a relatively cleaner hypnotic with comparatively less of the anxiolytic, myorelaxant and anticonvulsant action that the alpha-2, -3 and -5 subtypes carry. The examinable line is that the

z-drugs share the benzodiazepines' GABA-positive-allosteric-modulator mechanism but are a different chemical class acting preferentially at omega-1.

RULE **Same site, different molecule, same short-course rule.** A z-drug is a non-benzodiazepine hypnotic that still modulates the GABA-A benzodiazepine site, selectively at the omega-1 (alpha-1) subtype; it is a short-term hypnotic after CBT-I, not a long-term one.

10.3 Half-lives, and matching the drug to the insomnia pattern

The half-life is how you choose between them. All four are short-acting, but they differ enough to matter clinically. Elimination half-lives run from the ultrashort zaleplon at about **1 hour** (1 to 1.5 hours), through zolpidem at roughly **2.4 hours** and zopiclone at about **5.2 hours**, to eszopiclone as the longest at approximately **6 hours** (Tasman; Saunders, Addiction Medicine). The practical rule (which BAP states directly) is to match the half-life to the problem: a very short-acting agent (zaleplon, zolpidem) for sleep-onset insomnia, and a slightly longer-acting agent (zopiclone) for sleep-maintenance insomnia where the patient wakes in the second half of the night (BAP 2019). The trade-off is symmetrical: the shortest half-lives give the least next-morning hangover but the greatest rebound on stopping.

Z-DRUG	CHEMICAL CLASS	APPROX HALF-LIFE (HOURS)	BEST INSOMNIA MATCH
Zaleplon	Pyrazolopyrimidine	~1 (1 to 1.5)	Sleep-onset; middle-of-night dosing
Zolpidem	Imidazopyridine	~2.4	Sleep-onset
Zopiclone	Cyclopyrrolone	~5.2	Sleep-maintenance
Eszopiclone	Cyclopyrrolone (S-zopiclone)	~6	Sleep-maintenance (US agent)

Ascending half-life is the memorable spine: zaleplon < zolpidem < zopiclone < eszopiclone, and it drives the onset-versus-maintenance choice.

~1	2.4	5.2	5 to 10
ZALEPLON HALF-LIFE (HOURS)	ZOLPIDEM HALF-LIFE (HOURS)	ZOPICLONE HALF-LIFE (HOURS)	ZOLPIDEM DOSE (MG PER DAY)

MNEMONIC

zAleplon · zOlpidem · zOpiclone · Eszopiclone

Read left to right for ascending half-life (roughly 1, 2.4, 5.2 and 6 hours). The two at the short end (zaleplon, zolpidem) are your sleep-onset drugs; the two at the long end (zopiclone, eszopiclone) hold sleep through the night.

10.4 The guideline place: a short-term hypnotic after CBT-I

BAP leads: CBT-I first, then a short course of a GABA-positive hypnotic. BAP is explicit that CBT-I (with sleep restriction and stimulus control) is first-line for chronic insomnia, and that a pharmacological agent is offered where CBT-I fails, is unavailable, or the patient cannot engage with it (BAP 2019, Wilson et al.). When a drug is used, a GABA-positive-allosteric-modulator

hypnotic, meaning a benzodiazepine or a z-drug such as zolpidem or zopiclone, is the short-term option, with the half-life matched to the insomnia pattern (BAP 2019). NICE restricts the z-drugs (zaleplon, zolpidem and zopiclone) to the short-term management of insomnia at the lowest effective dose, and advises against switching from one z-drug to another if the first has not helped (NICE TA77 2004, reviewed 2010). The Maudsley Prescribing Guidelines carry the same short-course, lowest-dose framing, and the Indian Psychiatric Society (IPS_CPG 2017) mirrors the short-term hypnotic position for insomnia in the Indian setting. The wider treatment of clinical insomnia and CBT-I itself is developed in the Eating & sleep-wake disorders notes.

TRAP **Treating a z-drug as dependence-free because it is "non-benzodiazepine".** The z-drugs cause tolerance, dependence, rebound insomnia and complex sleep behaviours; prescribing one long-term for chronic insomnia contradicts BAP and NICE, which both restrict them to short-term use after CBT-I.

10.5 Doses and the diazepam equivalence

Low milligram doses at night; roughly a diazepam-5-mg equivalent each. Usual adult doses are zolpidem **5 to 10 mg** at night (immediate-release; prolonged-release 6.25 to 12.5 mg), zaleplon **5 to 10 mg**, zopiclone **3.75 to 7.5 mg**, and eszopiclone **1 to 3 mg** (Tasman; Geriatric Psychiatry Study Guide). In the older adult the dose is halved (zolpidem 5 mg, prolonged-release 6.25 mg; zopiclone 3.75 mg) because of falls, next-morning impairment and delirium risk. For the withdrawal-and-taper arithmetic that a benzodiazepine consolidation uses, the verified equivalences are that zolpidem 10 mg, zopiclone 7.5 mg and zaleplon 10 mg are each approximately equivalent to diazepam 5 mg (Saunders, Addiction Medicine, Table 3.4). The benzodiazepine-equivalence switch and the slow taper themselves belong to the Substance use disorders notes.

Z-DRUG	USUAL DOSE (MG PER DAY)	OLDER-ADULT DOSE (MG PER DAY)	APPROX DIAZEPAM-5-MG EQUIVALENT
Zolpidem	**5 to 10 (PR 6.25 to 12.5)**	5 (PR 6.25)	**10 mg**
Zaleplon	5 to 10	5	**10 mg**
Zopiclone	**3.75 to 7.5**	3.75	**7.5 mg**
Eszopiclone	1 to 3	1	Not established here

Doses are single-figure milligrams at night; the diazepam equivalence is the verified figure to quote when consolidating before a taper.

10.6 The z-drug-specific cautions: complex sleep behaviour, dependence, next-day impairment

Three cautions define the class. First, **complex sleep behaviour**: patients can carry out complex acts (sleep-walking, sleep-driving, sleep-eating, and even sleep-cooking or telephoning) while not fully awake and with no memory of the event afterwards. This prompted an FDA labelling change requiring warnings of complex sleep-related behaviours, and zolpidem in particular is associated with sleepwalking, sleep-driving and hallucinations (Dulcan; Maudsley Deprescribing Guidelines). Second, dependence: the z-drugs carry genuine abuse liability,

tolerance and a withdrawal syndrome, so "non-benzodiazepine" is not a safety guarantee (Lowinson and Ruiz). Third, next-day impairment: residual sedation, psychomotor and driving impairment, and, in the older adult, falls, fracture and delirium, which is why the 2019 Beers Criteria advise avoiding this class in older people (Kaplan and Sadock, CTP 2024). The sedative and z-drug use disorder as an addiction is covered in the Substance use disorders notes.

COMMON TRAP

A patient reports night-eating, an out-of-place car journey, or a partner's account of a full conversation, all with dense amnesia, and is worked up for a dissociative or nocturnal-seizure disorder. If they are on zolpidem or another z-drug, the first move is to stop the drug: this is a complex sleep behaviour until proven otherwise, and it is a reason to discontinue, not merely to reduce.

10.7 Choosing, dosing short, and stopping

Lowest dose, shortest course, taper alongside CBT-I. The management pattern that satisfies the guidelines is: reserve the z-drug for when CBT-I is not the route, pick the agent by half-life (onset versus maintenance), start at the lowest effective dose, and cap the intended duration to a short course rather than open-ended repeats. On stopping, taper slowly rather than ceasing abruptly, and deliver CBT-I concurrently during the taper to improve the outcome; melatonin is a useful adjunct for the insomnia that surfaces during withdrawal (BAP 2019). Abrupt cessation after regular use risks rebound insomnia and rebound anxiety, and where a z-drug has been co-prescribed with a benzodiazepine the seizure risk of the benzodiazepine dominates the taper plan.

WORKED EXAMPLE

A man in his forties with three weeks of sleep-onset insomnia after a job loss asks for "a sleeping tablet". CBT-I is offered first. Because he cannot access it quickly and the problem is falling asleep rather than staying asleep, a short course of zolpidem 10 mg at night (the short half-life suiting sleep-onset) is reasonable, explicitly time-limited and at the lowest effective dose. He is warned about next-morning driving and about complex sleep behaviours, told not to combine it with alcohol, and booked for CBT-I so the drug can be tapered rather than repeated indefinitely. Had he been waking at 4 a.m., zopiclone (longer half-life) would have been the better match.

INDIA

The z-drugs sit against a real Indian backdrop of benzodiazepine over-prescription, with alprazolam (Alprax or Restyl) as the default anxiolytic and hypnotic reached for reflexively and often continued long-term. Zolpidem (Indian brands Zolfresh or Nitrest) and zopiclone (Zopicon) are widely prescribed and easily obtained, and the same short-course discipline that the Indian Psychiatric Society applies to benzodiazepines applies to them: a hypnotic is a short-term measure after CBT-I, not a standing prescription. The exam-safe framing is that the z-drugs are marketed as the "safer, non-benzodiazepine" alternative, but they carry dependence, rebound and complex sleep behaviours of their own, so they do not solve the over-prescription problem, they simply relabel it.

PEARL

Selectivity, not chemistry, is the answer to "how do z-drugs differ from benzodiazepines". Both are GABA-A benzodiazepine-site positive allosteric modulators; the z-drugs are chemically distinct and bind preferentially at the omega-1 (alpha-1) subtype, which is why they are marketed as selective hypnotics yet still share the dependence and withdrawal liabilities.

GOOD TO REMEMBER

- **Zolpidem (imidazopyridine):** an omega-1-selective GABA-A positive allosteric modulator dosed 5 to 10 mg at night (prolonged-release 6.25 to 12.5 mg; 5 mg in the older adult), half-life about 2.4 hours, best for sleep-onset insomnia; the z-drug most linked to sleep-driving and sleepwalking; 10 mg approximately equals diazepam 5 mg. Indian brands Zolfresh, Nitrest.
- **Zopiclone (cyclopyrrolone):** the same omega-1-selective mechanism, dosed 3.75 to 7.5 mg at night (3.75 mg in the older adult), half-life about 5.2 hours, better for sleep-maintenance; 7.5 mg approximately equals diazepam 5 mg. Indian brand Zopicon.
- **Zaleplon (pyrazolopyrimidine):** the ultrashort z-drug, half-life about 1 hour, dosed 5 to 10 mg, useful for sleep-onset or middle-of-night dosing with the least next-morning hangover; 10 mg approximately equals diazepam 5 mg.
- **Eszopiclone (S-enantiomer of zopiclone):** the longest-acting z-drug, half-life about 6 hours, dosed 1 to 3 mg, chiefly a US agent (Lunesta) for sleep-maintenance insomnia.

HOLD THIS

The z-drugs (zolpidem, zopiclone, zaleplon, eszopiclone) are non-benzodiazepine hypnotics that bind selectively at the benzodiazepine-1 (omega-1, alpha-1) subtype of the GABA-A receptor; match half-life to the insomnia pattern (short-acting zolpidem or zaleplon for onset, longer zopiclone for maintenance), use them short-term after CBT-I, and watch for complex sleep behaviour, dependence and next-day impairment.

11 · Dual orexin receptor antagonists

This is the competitor-delta hypnotic: the newest way to make someone sleep without touching the GABA-A channel at all. The dual orexin receptor antagonist class (a **DORA**) contains suvorexant, lemborexant and daridorexant, and its entire examinable identity is one mechanistic pivot: instead of adding inhibitory GABAergic sedation the way a benzodiazepine or a Z-drug does, a DORA *subtracts the wake signal* by blocking the orexin (hypocretin) wake-promoting system, so the patient falls asleep because arousal is switched off rather than because the brain is chemically sedated.

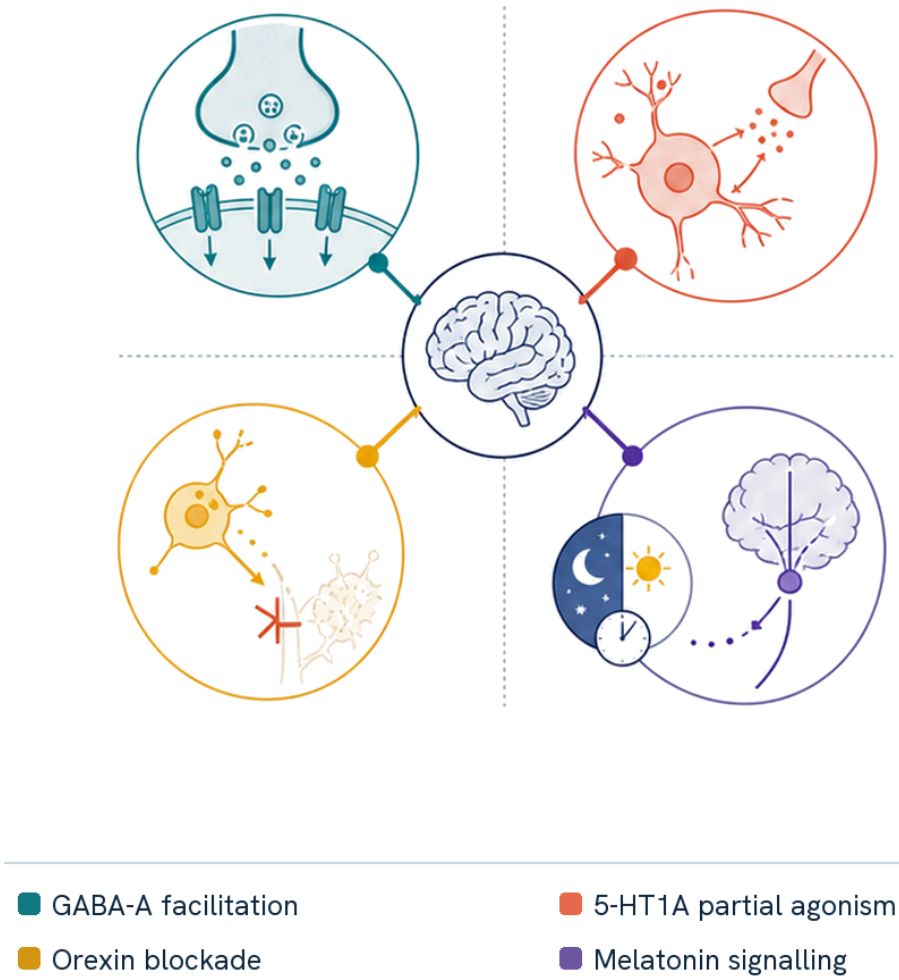


Fig 15.15 Four pharmacological systems used across anxiety and insomnia: GABA-A facilitation, serotonin 5-HT1A partial agonism, blockade of orexin-mediated wake drive and melatonin-linked circadian signalling.

For a low-yield, current-through-2026 class the mark is won by holding three things: the target (orexin, acting at the OX1 and OX2 receptors), the class action (dual antagonism of both, promoting sleep by removing wakefulness), and the fact that suvorexant is the agent named in the BAP 2019 insomnia evidence base among the pharmacological options when CBT-I is not the route. Everything else is dose detail. Where these agents sit relative to CBT-I and the GABAergic hypnotics belongs to the Eating & sleep-wake disorders notes.

11.1 The target: the orexin/hypocretin wake system

Orexin stabilises wakefulness; lose it and you get narcolepsy. **Orexin** A and orexin B (also called hypocretin, the same peptide under two names) are excitatory neuropeptides cleaved from a single precursor, released by a small cluster of neurons in the lateral hypothalamus that act as the master "wake-stabilising" switch (Stahl; KDT). They project to and drive the arousal nuclei, the noradrenergic locus coeruleus, the histaminergic tuberomammillary nucleus and the wider reticular activating system, and they signal through two G-protein-coupled receptors, the OX1 receptor and the OX2 receptor, whose stimulation raises arousal and wakefulness. The clinching

physiology, and a favourite viva mirror, is that selective loss of orexin neurons is the lesion in narcolepsy with cataplexy (hypocretin deficiency); a DORA therefore reproduces a slice of that orexin-deficient state on purpose, at night, to let sleep come. The receptor biology of the arousal systems is developed in the Neurochemistry, Neuroendocrinology, Neuroimaging & Basic Psychopharmacology notes.

11.2 The class action: block wakefulness, do not add sedation

Dual OX1 and OX2 antagonism, not a GABA-A modulator. A DORA is a competitive antagonist at *both* orexin receptors; by occupying OX1 and OX2 it removes the orexin drive onto the arousal network, so wakefulness is no longer actively maintained and the brain transitions into sleep (Stahl; KDT: "suvorexant blocks both OX1R and OX2R"). This is the whole point of the class: it initiates and maintains sleep without the positive allosteric modulation of the GABA-A chloride channel that a benzodiazepine or a Z-drug relies on, and it therefore lacks their signature of dependence, tolerance and a seizure-risk withdrawal to the same degree, while tending to preserve more of normal sleep architecture (Stahl notes the effect comes "without the side effects expected of a benzodiazepine or Z-drug hypnotic"). The GABAergic mechanism it deliberately avoids is the anchor of the Benzodiazepines topic and the wider Neurochemistry notes.

RULE **Subtract wakefulness, do not add sedation.** A DORA blocks OX1 and OX2 to switch off the orexin wake drive, so it promotes sleep without GABA-A modulation, and that non-GABAergic mechanism is the single fact every DORA question is testing.

PEARL

A DORA is pharmacologically induced, time-limited narcolepsy. Narcolepsy with cataplexy is the disease of orexin loss; a dual orexin receptor antagonist manufactures a brief orexin-blocked state at bedtime to produce sleep. State that mirror and the mechanism mark is yours, and it also explains the class cautions: next-morning somnolence and rare sleep paralysis, hypnagogic hallucinations or cataplexy-like phenomena.

11.3 The three agents and their doses

Suvorexant, lemborexant, daridorexant, each once nightly. All three are taken as a single dose shortly before bed. Suvorexant (international brand Belsomra) was the first, at **10 to 20 mg** nocte; lemborexant (Dayvigo) at **5 to 10 mg** nocte; and daridorexant (Quviviq), the most recently introduced agent, at **25 to 50 mg** nocte (Maudsley Prescribing Guidelines; KDT; Practical Psychopharmacology). The verified timing anchor for daridorexant is that it is taken within 30 minutes of going to bed with at least **7 hours** remaining before the planned waking time, precisely to keep the next-morning residual effect down; the same "leave a full sleep window" logic applies across the class.

AGENT (INTERNATIONAL BRAND)	NIGHTLY DOSE (MG PER DAY)	KEY POINT
Suvorexant (Belsomra)	**10 to 20**	First DORA; CYP3A4-metabolised, mean half-life about 12 hours; a stopping taper is not required
Lemborexant (Dayvigo)	**5 to 10**	Dual OX1/OX2 antagonist; cap at 5 nocte and use caution above it in patients 65 years and older (fall risk)
Daridorexant (Quviviq)	**25 to 50**	Most recent agent; take within 30 minutes of bed with at least 7 hours of sleep opportunity remaining

The three marketed dual orexin receptor antagonists and their once-nightly dose ranges; the numbers rise as the agents get newer.

12 SUVOREXANT MEAN HALF-LIFE (HOURS)	**10 to 20** SUVOREXANT DOSE (MG PER DAY)	**25 to 50** DARIDOREXANT DOSE (MG PER DAY)	**7** MINIMUM SLEEP WINDOW REMAINING (HOURS)

TRAP **Dosing without a full night ahead.** Taking a DORA when fewer than about seven hours of sleep remain, or the morning before driving, invites next-morning somnolence and impaired driving; the drug switches wakefulness off, and that suppression has to be allowed to wear off before the patient needs to be alert.

11.4 Place in therapy, cautions and the India reality

Not first-line, and still a controlled hypnotic. CBT-I is first-line for chronic insomnia; a DORA is a pharmacological option only where CBT-I fails, is unavailable or is declined, and the accompanying figure sketches the orexin wake-switch and where the class acts. BAP 2019 (Wilson et al.) names suvorexant among the evidence-based pharmacological choices in that scenario, and the class initiates *and* maintains sleep. Despite the lower dependence signal relative to GABAergic hypnotics, these agents are still handled as controlled/scheduled drugs, and the examinable cautions are next-morning somnolence and driving impairment, the sleep-paralysis and hypnagogic-hallucination/cataplexy-like phenomena that follow from the mechanism, complex sleep behaviours as a class labelling concern shared with the Z-drugs, and CYP3A4 interactions for suvorexant. Their positioning against CBT-I sits in the Eating & sleep-wake disorders notes, and the benzodiazepine dependence they are designed to sidestep in the Substance use disorders notes.

INDIA

The genuine Indian angle for this class is an absence. Indian insomnia and anxiety prescribing still defaults reflexively to a benzodiazepine, with alprazolam (alprazolam; Alprax or Restyl) the habitual first reach and often continued long-term, which is exactly the over-prescription problem the Indian Psychiatric Society position and the BAP/NICE short-course rule are trying to correct. A non-GABAergic hypnotic that carries far less dependence liability is precisely what that pattern needs, yet the dual orexin receptor antagonists remain a boutique, largely unavailable and prohibitively priced option in Indian practice as of 2026, so they do not yet displace the alprazolam habit. The exam-safe line is to know the mechanism and name the class as the dependence-sparing future of hypnotic prescribing, while noting it is not yet the ground reality in India.

GOOD TO REMEMBER

- **Suvorexant (Belsomra):** the first dual orexin receptor antagonist, blocking OX1 and OX2 to remove the orexin wake drive; dosed 10 to 20 mg nocte, CYP3A4-metabolised with a mean half-life of about 12 hours, and no taper needed on stopping.
- **Lemborexant (Dayvigo):** a dual OX1/OX2 antagonist for insomnia at 5 to 10 mg nocte, with the specific caution to cap at 5 mg and use care above it in patients 65 years and older because of fall risk.
- **Daridorexant (Quviviq):** the most recent DORA at 25 to 50 mg nocte, taken within 30 minutes of bed with at least 7 hours before planned waking to limit next-morning residual effect.

HOLD THIS

The DORAs (suvorexant 10 to 20 mg, lemborexant 5 to 10 mg, daridorexant 25 to 50 mg nocte) block both OX1 and OX2 to switch off the orexin/hypocretin wake system, promoting sleep by removing wakefulness rather than by GABAergic sedation, which is why they largely sidestep benzodiazepine-style dependence.

12 · Melatonin and ramelteon

These are the hypnotics the examiner uses to show you what a benzodiazepine is not. Melatonin and ramelteon are **melatonergic** agents: agonists at the MT1 and MT2 receptors of the suprachiasmatic nucleus, the brain's circadian pacemaker. They coax sleep by nudging the body clock rather than by depressing the cortex, so unlike a benzodiazepine or a z-drug they carry no dependence, no next-day cognitive impairment, no complex sleep behaviour and no controlled-substance status (Kaplan and Sadock, CTP 2024; Stahl; Kaufman's Clinical Neurology). That clean tail, set against a genuinely modest hypnotic effect, is the whole examinable delta.

Two facts carry most of the marks. First, prolonged-release **melatonin** is the guideline option in the patient over 55 and in the circadian sleep disorders, and it is the endorsed adjunct for insomnia *during a benzodiazepine taper* (BAP). Second, **ramelteon** is the prescription MT1/MT2 **circadian hypnotic** for sleep-onset insomnia. Keep both apart from agomelatine, the melatonergic *antidepressant*, which is developed in the Mood disorders: pharmacotherapy notes (agomelatine cross-ref).

12.1 Mechanism: MT1/MT2 melatonergic agonism

Melatonergic, not GABAergic. Endogenous **melatonin** is synthesised from serotonin in the pineal gland and signals darkness to the suprachiasmatic nucleus. Its two G-protein-coupled receptors divide the labour: stimulation of the MT1 receptor suppresses the firing of the suprachiasmatic pacemaker and so *promotes sleep onset*, while stimulation of the MT2 receptor mediates the *phase-shifting*, circadian-entraining effect (Stahl, Prescriber's Guide). Ramelteon is a full agonist at both MT1 and MT2. Because the drug works through the physiological sleep-timing system and not by opening the GABA-A chloride channel, it produces none of the sedation-by-CNS-depression, muscle relaxation, anticonvulsant cover, respiratory depression or cross-tolerance that define a GABAergic hypnotic. For the GABA-A receptor and the wider receptor systems, see the Neurochemistry, Neuroendocrinology, Neuroimaging & Basic Psychopharmacology notes.

MT1 receptor

Suppresses suprachiasmatic-nucleus firing; the sleep-*onset*-promoting arm of melatonergic signalling.

MT2 receptor

Mediates the *phase-shift* of the circadian clock; the entrainment arm used in jet lag and delayed sleep phase.

RULE **MT1 onset, MT2 phase, no dependence.** Melatonin and ramelteon are MT1/MT2 agonists acting on the circadian clock, not the GABA-A channel, so they cause no dependence, no cognitive impairment, no complex sleep behaviour and are not controlled substances.

12.2 Prolonged-release melatonin: the over-55 and circadian indications

The over-55 hypnotic and the body-clock drug. BAP names prolonged-release **melatonin** as an option to improve sleep-onset latency and sleep quality in patients over 55 years (BAP 2019, grade Ib), and the melatonergic agonists are the rational choice in the circadian rhythm sleep disorders, jet lag, shift work and delayed sleep phase, where the aim is to re-time rather than to sedate (Kaufman's Clinical Neurology; Kaplan and Sadock, CTP 2024). The licensed prolonged-release preparation is given as a **2 mg** bedtime dose; its effect on sleep latency is real but modest, comparable to other non-benzodiazepine hypnotics rather than to a benzodiazepine (Kaplan and Sadock, CTP 2024). Match a short-acting melatonergic agent to sleep-*onset* difficulty. Clinical insomnia, the sleep-wake disorders and CBT-I as the first-line are covered in the Eating & sleep-wake disorders notes.

GOOD TO REMEMBER

- **Melatonin (the drug):** an MT1/MT2 melatonergic agonist derived from serotonin in the pineal; the prolonged-release form is dosed at 2 mg at bedtime and is the BAP option for sleep-onset latency in patients over 55 and for the circadian sleep disorders; it does not enable benzodiazepine discontinuation on its own but is the endorsed adjunct for insomnia during the taper. Avoid in moderate-to-severe hepatic impairment.

12.3 Melatonin as an adjunct in benzodiazepine withdrawal

It settles the insomnia; it does not do the taper. BAP endorses **melatonin** as a useful adjunct for managing insomnia during benzodiazepine withdrawal (BAP 2025, grade A, strong). The important qualifier is that melatonin has *not* been shown to enable benzodiazepine discontinuation itself: a systematic review of six trials found it no better than placebo for that endpoint (Kaplan and Sadock, CTP 2024). So its role is symptomatic, to soften rebound insomnia while the actual work, consolidation onto a longer-acting benzodiazepine and a slow graded reduction, proceeds. The equivalence switch and the taper schedule, and the sedative or benzodiazepine use disorder in the addiction sense, are covered in the Substance use disorders notes.

TRAP **Leaning on melatonin to prevent withdrawal seizures.** Melatonin manages the insomnia of a benzodiazepine taper only; it does not cover the withdrawal syndrome or protect against the seizure. The slow graded reduction, never melatonin, is what prevents that.

12.4 Ramelteon: the MT1/MT2 circadian hypnotic

An 8 mg, sleep-onset, non-scheduled hypnotic. **Ramelteon** is a synthetic melatonin analogue and a full MT1/MT2 agonist, approved for insomnia characterised by difficulty with sleep *onset*. It is given as an **8 mg** dose about 30 minutes before bedtime (reports of efficacy span 4 to 64 mg), with no adjustment needed in renal impairment; use it cautiously in moderate hepatic impairment and avoid it in severe (Kaplan and Sadock, CTP 2024). The effect on sleep latency is small, roughly 4 minutes in a large meta-analysis, and is non-dose-dependent. Ramelteon is extensively metabolised by **CYP1A2**, so fluvoxamine, a potent CYP1A2 inhibitor, can raise ramelteon to toxic concentrations and is effectively contraindicated with it (Kaufman's Clinical Neurology). Its elimination half-life is short, under 2 hours, which is why it does not produce a next-day hangover. Being a melatonergic agonist, it is not a controlled substance.

2	8	55	< 2
PROLONGED-RELEASE MELATONIN (MG AT BEDTIME)	RAMELTEON (MG AT BEDTIME)	AGE FROM WHICH PR MELATONIN IS A BAP OPTION (YEARS)	MELATONERGIC AGONIST ELIMINATION HALF-LIFE (HOURS)

GOOD TO REMEMBER

- **Ramelteon (the drug):** a full MT1/MT2 melatonergic agonist for sleep-onset insomnia, dosed at 8 mg about 30 minutes before bedtime, with a short elimination half-life under 2 hours and no dependence or controlled-substance status; it is metabolised by CYP1A2, so co-prescription with fluvoxamine is dangerous, and it is used cautiously in hepatic impairment.

12.5 The class signature, and the agomelatine cross-ref

Clean where the GABAergic hypnotics are dirty. Set against a benzodiazepine or a z-drug, the melatonergic agonists reduce sleep latency and improve subjective sleep quality but, crucially, do not impair cognition, cause imbalance, induce dangerous complex sleep behaviour or fall into the controlled-substance category (Kaufman's Clinical Neurology). That is exactly the profile that makes them attractive where a benzodiazepine or a z-drug is hazardous, in the older adult, in respiratory disease and in anyone with a substance-misuse history, though the trade-off is a

decidedly gentler hypnotic effect. The wider family also includes tasimelteon (licensed for Non-24-Hour Sleep-Wake Disorder in the blind) and agomelatine, the melatonergic *antidepressant*, which combines MT1/MT2 agonism with 5-HT2C antagonism, is dosed at 25 mg at bedtime and needs liver-function monitoring; agomelatine is developed as an antidepressant in the Mood disorders: pharmacotherapy notes (agomelatine cross-ref). The z-drug complex-sleep-behaviour and dependence cautions that the melatonergic agents avoid are covered with the benzodiazepine-receptor hypnotics.

FEATURE	MELATONERGIC AGONIST (MELATONIN, RAMELTEON)	GABA-A HYPNOTIC (BENZODIAZEPINE, Z-DRUG)
Target	**MT1/MT2 on the suprachiasmatic clock**	**GABA-A chloride channel (PAM)**
Mode of action	Re-times sleep, promotes onset	Sedation by CNS depression
Hypnotic effect size	**Modest**	Larger, more reliable
Dependence, tolerance, withdrawal	**None**	Yes; seizure risk on abrupt stop
Cognitive impairment, imbalance	**None**	Yes
Complex sleep behaviour	**Not a feature**	Yes (notably the z-drugs)
Controlled substance	**No**	Yes

The melatonergic-versus-GABAergic contrast is the single most examinable point on these agents: clock-timing and clean against channel-opening and dependent.

INDIA

Melatonin is available over the counter in India (Meloset or Zytonin; verify the brand and strength locally), which is precisely why it matters against the real Indian problem: the over-prescription of benzodiazepines, with alprazolam (alprazolam; Alprax or Restyl) reached for reflexively as the default anxiolytic and hypnotic and too often continued long-term. A non-dependence-forming, non-controlled melatonergic hypnotic is a genuinely useful alternative in the patient who would otherwise be parked on alprazolam for sleep, and it is consistent with the Indian Psychiatric Society and BAP position that CBT-I is first-line and a benzodiazepine is a short-course measure only. Ramelteon is not widely marketed in India, so melatonin is the melatonergic agent you will actually reach for.

PEARL

Split the receptor to answer the mechanism question: MT1 quietens the suprachiasmatic pacemaker and brings sleep *on*, MT2 *shifts* the clock. That single distinction explains why these drugs help sleep-onset insomnia and jet lag but sedate far less forcefully than a benzodiazepine.

HOLD THIS

Melatonin and ramelteon are MT1/MT2 melatonergic agonists acting on the suprachiasmatic clock, not the GABA-A channel: prolonged-release melatonin 2 mg for the over-55 and as the taper-insomnia adjunct, ramelteon 8 mg for sleep-onset insomnia, both with a short half-life, a modest effect, and no dependence or controlled-substance status.

13 · Etifoxine and the non-benzodiazepine anxiolytics

This is the competitor-delta drug: the anxiolytic that quiets anxiety without being a benzodiazepine. Etifoxine is **a non-benzodiazepine anxiolytic** licensed in parts of Europe, and its whole exam value is a single claim, that it can match a benzodiazepine for short-term anxiety while carrying less of the benzodiazepine tail (rebound, central-nervous-system side effects). Kaplan and Sadock (CTP 2024) confirm it as a non-benzodiazepine that **modulates the GABA-A receptor**, and it is the one **novel anxiolytic** the examiner is likely to name against lorazepam and alprazolam.

Hold the frame that makes the marks. A benzodiazepine works fast but breeds tolerance, dependence and rebound. A translocator protein ligand such as etifoxine works on the same final channel by a different route, boosting the brain's own calming neurosteroids, so the trials show comparable anxiolysis with a cleaner discontinuation. The trap is to read "non-benzodiazepine" as "first-line": an SSRI remains first-line for generalised anxiety, and these agents are alternatives or short-course options, developed in the Anxiety, OCD & trauma-related disorders notes and the Mood disorders: pharmacotherapy notes.

13.1 What etifoxine is: a novel non-benzodiazepine anxiolytic

A European anxiolytic that is not a benzodiazepine. Etifoxine (a benzoxazine derivative) is marketed as an anxiolytic for the psychosomatic manifestations of anxiety and, in the trial literature, for the anxious subtype of adjustment disorder; Kaplan and Sadock (CTP 2024) describe it plainly as "a nonbenzodiazepine drug that modulates GABA-A receptors available in Europe" (New Oxford Textbook of Psychiatry likewise lists it as a non-BZD anxiolytic). It is not a controlled substance and it is not licensed in India through the mainstream pharmacopoeia, which is why the standard Indian textbooks (the Companion) do not carry a dose for it; treat it as the examinable European comparator drug rather than a routine Indian prescription.

13.2 Mechanism: GABA-A modulation plus the translocator protein

Two routes to the same chloride channel. Etifoxine acts by a dual mechanism. First, it is a direct positive modulator at the **GABA-A receptor** (Kaplan and Sadock, CTP 2024, confirm the GABA-A modulation). Second, and this is the part worth a mark, it is a ligand of the mitochondrial 18 kDa translocator protein (TSPO, the old peripheral benzodiazepine receptor), and by stimulating TSPO it drives **neurosteroidogenesis**, raising synthesis of the neurosteroid allopregnanolone, itself a powerful positive allosteric modulator of GABA-A. So etifoxine augments GABAergic inhibition both directly and indirectly through its own endogenous neurosteroid, a mechanism distinct from the benzodiazepine site. The GABA-A receptor and the

wider neurosteroid systems are developed in the Neurochemistry, Neuroendocrinology, Neuroimaging & Basic Psychopharmacology notes.

RULE **GABA-A directly, and again through the translocator protein.** Etifoxine is a non-benzodiazepine anxiolytic with a dual action, direct GABA-A modulation plus TSPO-driven neurosteroid (allopregnanolone) synthesis; it matches a benzodiazepine for short-term anxiety but is an alternative to it, never a substitute for a first-line SSRI.

13.3 The competitor-delta evidence: non-inferior to a benzodiazepine, better tolerated

Same anxiolysis, cleaner tail. The examinable data are head-to-head. A controlled protocol randomised **191** patients with DSM-IV adjustment disorder to etifoxine or lorazepam over **4 weeks**; on the Hamilton Anxiety Rating Scale (the primary outcome) etifoxine was *not inferior* to lorazepam, was better tolerated, produced more responders, and left fewer patients with **rebound anxiety** (Kaplan and Sadock, CTP 2024). A parallel comparison against alprazolam gave similar results, and after the drug was stopped the HAM-A scores kept falling in the etifoxine group while they rose again in the alprazolam group, which also carried more central-nervous-system adverse events. New Oxford records the same signal, a single-study superiority of etifoxine over lorazepam. The reading is that the benzodiazepine buys speed at the price of rebound and CNS load, while the translocator-protein route holds the gain after withdrawal.

AXIS	ETIFOXINE (GABA-A + TSPO)	A BENZODIAZEPINE (GABA-A PAM)
Site of action	**GABA-A modulation plus TSPO neurosteroid synthesis**	Benzodiazepine site on GABA-A
Short-term anxiolysis (HAM-A)	**Non-inferior to lorazepam / alprazolam**	Effective
Tolerability, CNS adverse events	**Better tolerated, fewer CNS events**	Sedation, psychomotor impairment
After discontinuation	**Gains maintained; less rebound anxiety**	Rebound anxiety, scores rise
Controlled-substance / dependence liability	Not scheduled; low reported abuse	Scheduled; dependence and withdrawal

The competitor-delta in one grid: etifoxine matches a benzodiazepine on anxiety scores but is better tolerated and holds the gain after stopping.

TRAP **Reading "novel" and "non-benzodiazepine" as "first-line".** A non-inferiority signal against lorazepam does not make etifoxine a first-line anxiolytic; an SSRI is first-line for generalised anxiety, and etifoxine (like hydroxyzine) is an alternative or short-course option, not the front of the ladder.

13.4 Dose and the Indian brand

The 50 mg capsule, given a few times a day. Etifoxine is supplied as a **50 mg** capsule and given in divided doses, with a usual daily dose of about **150 to 200 mg/day** (the standard European product information; the parsed textbook corpus confirms the drug and its mechanism but does not carry an exact dose, so treat the milligrams as standard-source rather than corpus-verified). In

India, Wilfred flags the brand **Tranxiety** (etifoxine 50 mg); the Indian brand and strength could not be independently confirmed against the Companion or the Maudsley Prescribing Guidelines, so it is carried as Wilfred-provided and flagged for a local check. A rare but recognised safety signal with etifoxine is idiosyncratic hepatocellular injury and severe cutaneous reactions, which is worth naming as the signature caution and is flagged as not corpus-confirmed.

50	150 to 200	191	4
ETIFOXINE CAPSULE STRENGTH (MG)	USUAL ETIFOXINE DOSE (MG PER DAY)	PATIENTS IN THE LORAZEPAM NON-INFERIORITY TRIAL	COMPARISON-TRIAL DURATION (WEEKS)

INDIA

Etifoxine matters in India as an answer to a genuine problem rather than as a common prescription. The problem is benzodiazepine over-prescription, with alprazolam (Alprax or Restyl) reached for reflexively as the default anxiolytic and continued far past any crisis. The Indian Psychiatric Society, in line with BAP and NICE, holds that an SSRI or SNRI is first-line for generalised anxiety and that a benzodiazepine is a short-course measure only, not a maintenance drug. A non-benzodiazepine anxiolytic that holds its gain after withdrawal is exactly the kind of agent that answers the alprazolam-default habit, and Wilfred flags a local brand (Tranxiety, etifoxine 50 mg); the exam-safe line is that etifoxine is a European comparator drug with a favourable discontinuation profile, not an established Indian first-line, and the brand and dose need local verification. The benzodiazepine dependence and withdrawal picture it is contrasted against is covered in the Substance use disorders notes.

13.5 The other non-benzodiazepine anxiolytics: a compact class

A small family, mostly historical or niche. Beyond etifoxine and the 5-HT1A azapirone buspirone, the label "non-benzodiazepine anxiolytic" gathers a scatter of agents. Chlormezanone is the historical one to name: a centrally acting drug with both anti-anxiety and neuro-hypnotic (muscle-relaxant) actions used for tension states (KDT, Essentials of Medical Pharmacology), which was largely withdrawn from world markets in the 1990s after reports of severe cutaneous reactions and hepatotoxicity, so it survives as an exam name rather than a live prescription (the withdrawal reason is flagged as not corpus-confirmed). Hydroxyzine (Atarax) is the H1-antihistamine anxiolytic that BAP names, with buspirone, as efficacious in acute generalised anxiety. Two further historical roots complete the picture: the carbamate meprobamate, the mid-century "minor tranquilliser" the benzodiazepines displaced, and tofisopam, an atypical 2,3-benzodiazepine promoted as a non-sedating daytime anxiolytic. Buspirone itself is developed in its own topic.

AGENT	CLASS / MECHANISM	STATUS
Etifoxine	**GABA-A modulator + TSPO neurosteroid ligand**	Licensed anxiolytic (Europe)
Buspirone	5-HT1A partial agonist (azapirone)	Current; acute GAD (own topic)
Hydroxyzine	H1 antihistamine	Current; acute GAD option (BAP)
Chlormezanone	**Central anxiolytic / muscle relaxant**	Historical; largely withdrawn
Meprobamate	Carbamate	Historical; displaced by benzodiazepines
Tofisopam	Atypical 2,3-benzodiazepine (non-sedating)	Niche; limited markets

The compact class: etifoxine is the live novel agent, chlormezanone and meprobamate are the historical names, hydroxyzine the current antihistamine option.

PEARL

The translocator protein has two lives on this paper. As a drug target it is how etifoxine raises its own GABA-modulating neurosteroid; as an imaging marker (TSPO PET tracers such as [11C]PK11195) it flags activated microglia in the neuroinflammation literature. Same protein, one pharmacological and one radiological. Say which you mean and the mark is yours.

GOOD TO REMEMBER

- **Etifoxine (the drug):** a non-benzodiazepine, novel anxiolytic acting by a dual mechanism, direct GABA-A modulation plus translocator-protein (TSPO)-driven neurosteroid (allopregnanolone) synthesis; supplied as a 50 mg capsule at about 150 to 200 mg/day, it was non-inferior to lorazepam and alprazolam on the HAM-A over 4 weeks with better tolerability and less rebound anxiety; the signature caution is rare hepatic and severe cutaneous reactions (dose and brand standard-source, not corpus-verified).
- **Chlormezanone (historical):** a centrally acting anxiolytic with muscle-relaxant / neuro-hypnotic properties for tension states, largely withdrawn from world markets for severe skin and liver reactions; an exam name, not a current prescription.
- **Hydroxyzine (the class option):** an H1-antihistamine anxiolytic that BAP names, alongside buspirone, as efficacious in acute generalised anxiety, with no dependence liability.

HOLD THIS

Etifoxine is a non-benzodiazepine anxiolytic that hits GABA-A two ways, directly and through translocator-protein-driven neurosteroid synthesis, and in adjustment-disorder anxiety it was non-inferior to lorazepam and alprazolam on the HAM-A while causing less rebound and fewer CNS effects, yet it is an alternative to a benzodiazepine, never a replacement for a first-line SSRI.

14 · Beta-blockers, antihistamines and gabapentinoids as anxiolytics

These are the adjunctive and off-label anxiolytics, and they earn their marks by testing one clinical reflex: can you match a drug to a symptom? Grouped here are three non-serotonergic,

non-benzodiazepine options reached for around the edges of anxiety management: a **beta-blocker anxiolytic** for the autonomic and performance-anxiety symptoms, a sedating **antihistamine anxiolytic** with genuine acute-generalised-anxiety evidence, and the two **gabapentinoid** agents, one of which is a licensed alternative first-line treatment for generalised anxiety disorder (GAD). None is a first-line agent for the psychic anxiety of GAD except pregabalin, and the single most current examinable point is that the gabapentinoids are no longer regarded as dependence-free.

Hold the group as a spread of receptor targets: propranolol at the peripheral **beta-adrenergic receptor**, hydroxyzine at the H1 histamine receptor, and pregabalin and gabapentin at the alpha-2-delta subunit of the voltage-gated calcium channel. Where each SSRI and SNRI sits as the true first-line anxiolytic belongs to the Mood disorders: pharmacotherapy notes, and the wider place of the anxiolytics across the anxiety disorders to the Anxiety, OCD & trauma-related disorders notes; this topic owns the adjuncts.

14.1 Propranolol: the beta-blocker anxiolytic

Blocks the body, not the mind. Propranolol (Ciplar or Inderal) is a non-selective **beta-adrenergic antagonist** whose anxiolytic action is peripheral: it abolishes the somatic, sympathetically driven symptoms of anxiety, the palpitations, tachycardia, tremor and dry mouth, without touching the cognitive dread itself (Kaplan and Sadock, CTP 2024; Practical Psychopharmacology). Its established anxiety niche is social anxiety disorder, performance type: a single dose of **10 to 40 mg** is taken about an hour before the feared performance, with a test dose tried on an ordinary occasion beforehand. Because relief comes from switching off the peripheral adrenergic surge rather than from sedation, it is a useful non-dependence-forming alternative to a benzodiazepine for the situational performer, the musician or the examinee with a pounding heart. It has a short half-life of about **3 to 5 hours** (immediate-release). Cautions are cardiorespiratory: avoid in asthma and COPD (beta-2 bronchoconstriction), in significant bradycardia or heart block, and do not withdraw abruptly in the cardiac patient. The beta-1-selective agent atenolol is an alternative. It has no useful effect on the pervasive worry of GAD.

> **PEARL**
>
> The beta-blocker treats the pulse, not the panic. Propranolol strips out the palpitations and tremor of the performance surge by blocking peripheral beta-adrenergic drive, but leaves the anticipatory dread intact, which is exactly why it shines for the time-limited somatic storm of stage fright and fails as a treatment for generalised, cognitively driven anxiety.

14.2 Hydroxyzine: the antihistamine anxiolytic

A sedating H1 antagonist with real acute-GAD evidence. Hydroxyzine (Atarax) is a first-generation piperazine antihistamine; its central antagonism of the **H1 histamine receptor** produces the sedation and anxiolysis that make it an **antihistamine anxiolytic** rather than merely an allergy drug. It carries a place most of this group lacks: BAP is explicit that hydroxyzine (alongside buspirone) is efficacious in the *acute* treatment of generalised anxiety disorder, though neither has published evidence for relapse prevention (BAP 2014, Baldwin et al.). The anxiety

dose is **50 to 100 mg** up to four times a day, and the elimination half-life is long at about **20 hours** (Stahl, Prescriber's Guide). It is not a controlled drug and does not cause dependence, so it is a reasonable short-term or as-needed alternative to a benzodiazepine. The examinable cautions are its sedation (warn about driving and machinery), its anticholinergic effects (dry mouth, constipation) and QT prolongation with cardiac conduction delay at higher doses.

RULE **Match the drug to the symptom.** Propranolol for the somatic autonomic surge of performance anxiety and hydroxyzine for short-term or acute generalised anxiety; of this whole group only pregabalin is a licensed alternative first-line agent for GAD, and an SSRI remains the true first-line drug.

14.3 The gabapentinoids: one mechanism, not a GABA drug

Alpha-2-delta ligands despite the name. The **gabapentinoid** class holds two agents, pregabalin and gabapentin, and the trap built into the name is that neither acts on the GABA-A receptor or on GABA metabolism at all (Kaplan and Sadock, CTP 2024; Stahl). Both bind the **alpha-2-delta subunit** of voltage-gated (P/Q-type) calcium channels on presynaptic terminals, reducing calcium influx and dampening the release of excitatory neurotransmitters such as glutamate, noradrenaline and substance P; the net effect is a reduction in neuronal excitability that translates into anxiolytic, analgesic and anticonvulsant activity. Both are excreted largely unchanged by the kidney rather than metabolised in the liver, so they carry few pharmacokinetic drug interactions but need dose reduction in renal impairment. The fast, frequency-increasing GABA-A mechanism they are so often confused with is the benzodiazepine's, developed in the Neurochemistry, Neuroendocrinology, Neuroimaging & Basic Psychopharmacology notes.

14.4 Pregabalin: the licensed alternative first-line agent

The one non-serotonergic drug licensed for GAD. Pregabalin (Pregeb or Pregastar) is licensed for generalised anxiety disorder in the UK and Europe, and both BAP and NICE place it as an alternative initial treatment where an SSRI or SNRI is unsuitable or not tolerated, and as an augmentation option after non-response to an SSRI or SNRI (BAP 2014; NICE CG113). Its different side-effect profile and faster onset than an SSRI are exactly why it is useful in the patient who cannot tolerate serotonergic agents (Shorter Oxford Textbook of Psychiatry). The dose is **150 to 600 mg** per day in two to three divided doses, and the half-life is short at about **5 to 7 hours** (Stahl). The signature caution, and the reason it is a scheduled/controlled drug (Schedule V in the United States), is a genuine dose-related misuse and dependence potential with euphoria and a withdrawal syndrome; it must never be stopped abruptly (seizure risk), and it can cause sedation, dizziness, peripheral oedema and weight gain, with the anticonvulsant-class suicidality signal to bear in mind.

14.5 Gabapentin: the off-label cousin

Off-label, weaker evidence, the same cautions. Gabapentin (Gabapin or Gabantin) is used off-label for anxiety, with controlled-trial evidence in social phobia (social anxiety disorder) and a post-hoc signal in panic disorder, but it is not licensed for GAD and does not carry pregabalin's guideline status (Kaplan and Sadock, CTP 2024). When used for anxiety the dose is broadly **900**

to 1800 mg per day in three divided doses, titrated upward over several days, with the same short half-life of about **5 to 7 hours** and the same renal excretion. Crucially it shares pregabalin's dependence and misuse liability and its abrupt-withdrawal seizure risk, so it is not the safe, consequence-free benzodiazepine substitute it is sometimes assumed to be. The sedative and benzodiazepine dependence picture these agents are compared against is developed in the Substance use disorders notes.

TRAP **Treating a gabapentinoid as dependence-free.** Pregabalin and gabapentin are now recognised drugs of misuse with a withdrawal syndrome; never stop either abruptly (seizure risk) and screen actively for misuse, especially alongside opioid or benzodiazepine use, rather than reaching for them as a "safe" alternative.

AGENT (INDIAN BRAND)	CLASS / TARGET	USUAL DOSE (MG PER DAY)	HALF-LIFE (HOURS)	PLACE IN ANXIETY
Propranolol (Ciplar, Inderal)	Non-selective beta-adrenergic antagonist	**10 to 40 (single pre-event dose)**	3 to 5 (IR)	**Somatic symptoms of performance / social anxiety**
Hydroxyzine (Atarax)	H1 antihistamine antagonist	**50 to 100, up to four times a day**	about 20	**Efficacious in acute GAD (no relapse-prevention data)**
Pregabalin (Pregeb, Pregastar)	Alpha-2-delta calcium-channel ligand	**150 to 600**	5 to 7	**Licensed alternative first-line for GAD; misuse potential**
Gabapentin (Gabapin, Gabantin)	Alpha-2-delta calcium-channel ligand	**900 to 1800**	5 to 7	Off-label (social phobia evidence); misuse potential

The adjunctive and off-label anxiolytics at a glance; the accompanying figure maps each agent to its receptor target and its symptom niche.

10 to 40	150 to 600	900 to 1800	5 to 7
PROPRANOLOL PRE-EVENT DOSE (MG PER DAY)	PREGABALIN DOSE (MG PER DAY)	GABAPENTIN DOSE (MG PER DAY)	GABAPENTINOID HALF-LIFE (HOURS)

INDIA

These agents matter in India as the answer to a real problem: benzodiazepine over-prescription, with alprazolam (alprazolam; Alprax or Restyl) the reflexive default anxiolytic, often begun from the outset and continued long-term. The Indian Psychiatric Society position, in line with BAP and NICE, is that an SSRI or SNRI is first-line for GAD and that a benzodiazepine is a short-course measure only. Propranolol for the situational performer, hydroxyzine for short-term anxiety, and pregabalin as the licensed alternative are all genuine non-benzodiazepine options in the patient who would otherwise be parked on alprazolam. The important caveat is that the gabapentinoids are themselves a recognised and rising drug of misuse, so they are a considered swap and not a free pass.

GOOD TO REMEMBER

- **Propranolol (Ciplar / Inderal):** a non-selective beta-adrenergic antagonist that treats the peripheral autonomic symptoms (palpitations, tremor) of performance / social anxiety at a single 10 to 40 mg dose about an hour before the event; short half-life about 3 to 5 hours, no effect on psychic anxiety, avoid in asthma and bradycardia.
- **Hydroxyzine (Atarax):** a sedating H1 antihistamine anxiolytic efficacious in acute GAD (BAP), dosed 50 to 100 mg up to four times a day with a long half-life of about 20 hours; not a controlled drug and no dependence, but sedating and anticholinergic.
- **Pregabalin (Pregeb / Pregastar):** an alpha-2-delta calcium-channel gabapentinoid, licensed and guideline-endorsed as an alternative first-line treatment for GAD, at 150 to 600 mg per day in divided doses (half-life about 5 to 7 hours); signature caution is a genuine misuse and dependence potential with a seizure-risk withdrawal, so never stop abruptly.
- **Gabapentin (Gabapin / Gabantin):** an off-label alpha-2-delta anxiolytic (evidence in social phobia) at about 900 to 1800 mg per day in three divided doses (half-life about 5 to 7 hours), sharing pregabalin's misuse liability and abrupt-withdrawal seizure risk.

HOLD THIS

Of the adjuncts, propranolol (a beta-adrenergic antagonist, 10 to 40 mg before a performance) treats only the somatic surge, hydroxyzine (an H1 antihistamine, efficacious in acute GAD) is a non-dependence-forming short-term option, and the gabapentinoids act on the alpha-2-delta calcium-channel subunit (not GABA-A), with only pregabalin licensed as an alternative first-line agent for GAD and both now recognised as drugs of misuse.

Apply and consolidate

15 · Worked cases

This closing set of cases lands where the paper actually lives, at the bedside and the prescription pad. Four **worked cases** gather the dissociative, conversion and anxiolytic threads into the four decisions the examiner most reliably tests: rule a **functional neurological disorder** in on a positive sign, separate a **dissociative** from an **organic** amnesia, taper a benzodiazepine dependence, and select the right anxiolytic or hypnotic for a specific patient. Each vignette is reasoned rather than recited, and each is a worked example of one two-beat method: name the positive finding that rules the decision in, then keep screening or apply the guideline anchor.

The textbook spine is the one carried through the block: Stone and Carson and DSM-5-TR for the conversion signs, DSM-5-TR and ICD-11 for the dissociative criteria, and BAP, NICE and the Maudsley Prescribing Guidelines for the taper and the agent choice, with the Indian Psychiatric Society for the Indian layer. Nothing new is introduced here; the cases only make the earlier topics decide something.

15.1 How to work a case: rule in, then keep screening

A positive finding first, an open mind second. Every case on this material is worked in two beats. The first beat is a **rule-in**: elicit the sign or the pattern that makes the diagnosis positively, a Hoover's sign, an entraining tremor, a retrograde memory loss with identity gone but new learning intact, or an interdose rebound that betrays dependence. The second beat is the

safeguard: a positive sign never closes the organic work-up, and a diagnosis never licenses the wrong drug. This is the Stone and Carson logic for conversion generalised to the whole block, and it is why the reflex sedative, reached for so readily in Indian practice, is so often the wrong answer. Two of the cases are diagnostic (conversion, dissociative amnesia) and two are managerial (the taper, the agent choice), but the shape is identical.

15.2 Case one: functional leg weakness and a positive Hoover's sign

Weak on command, strong on distraction. case: a woman in her late twenties develops a dense weakness of the right leg over several hours after a bitter family confrontation, with no sensory level, normal reflexes and a flexor plantar response. Direct hip extension of the "weak" leg is flaccid. You cup a hand under the right heel and ask her to flex the *left* hip against your other hand; as she does, the right heel drives firmly down into your palm. That is a positive Hoover's sign, the extensors she could not fire on command firing automatically when attention moves to the other leg (Kaufman; Kaplan and Sadock, CTP 2024). It rules a functional neurological disorder in at the bedside, in seconds and without a scanner. A give-way weakness (ratchety power that builds then suddenly collapses) supports the picture but is not specific, because pain and poor effort in genuine disease can produce it too.

RULE **Rule in, then still screen.** A functional disorder is diagnosed on a positive sign of internal inconsistency (weak on command, strong on distraction), never on the absence of a lesion or the presence of a stressor; the positive sign does not close the organic search in a progressive or atypical case.

WORKED EXAMPLE

The Hoover manoeuvre doubles as the first move of treatment. Having shown the patient that her heel pressed down of its own accord, you can say that a leg which moves automatically is a leg that *can* move, replacing "there is nothing wrong" with "here is what is wrong, and here is why it can recover". The demonstrated sign proves the diagnosis and its reversibility in one gesture.

15.3 Case one continued: the functional tremor that entrains

A tremor that copies the other hand is functional. The same patient, at a later review, has a coarse tremor of the right hand. You ask her to copy a slow rhythmical tapping with the *left* hand; the right-hand tremor shifts its frequency to match the tapping, then stops, and she cannot keep the copied rhythm going. That is a positive tremor entrainment test, the movement-domain equivalent of Hoover's sign: an organic tremor holds its own frequency regardless, a functional one entrains, stops or disrupts the copied rhythm (DSM-5-TR; New Oxford 2024). The unifying mechanism across both signs is that the symptom depends on abnormally focused attention, so diverting attention exposes the intact pathway. The visual analogue the examiner likes is the tubular field, a visual-field defect the same width at 1 metre as at 2 metres, which is physically impossible and so rules the functional picture in.

GOOD TO REMEMBER

- **Functional neurological disorder / conversion disorder (the syndrome):** defining criterion is a motor or sensory symptom, genuinely experienced, shown by a *positive* sign of internal inconsistency to be incompatible with neurological disease (Hoover's sign, tremor entrainment, tubular field); it is a *rule-in* diagnosis, not one of exclusion, no stressor is required (DSM-5-TR) and la belle indifference is non-diagnostic. First step: elicit a positive sign at the bedside, then keep screening for coexisting organic disease.

15.4 Case two: a fugue told apart from an organic amnesia

Direction of the loss, and the fate of identity. case: a man in his thirties is brought in by railway police, found several hundred kilometres from home, unable to give his name, address or occupation, and calm rather than distressed. The sensorium is clear, there are no focal neurological signs, and he learns and recalls a new list of three objects without difficulty; a relative later reports he left home the morning after a large debt notice arrived. The reasoning is a positive comparison, not a hunch. Intact new learning, a clear sensorium, a *lost personal identity* and a clear psychological precipitant point to a dissociative fugue with generalised dissociative amnesia, because the organic amnestic syndrome is the mirror image, an anterograde failure to form new memory with personal identity preserved. Loss of the name is a psychogenic flag until proven otherwise. Screening for dissociation itself uses the Dissociative Experiences Scale, where a mean around **30** flags a probable dissociative disorder, set out in the accompanying scale plate.

The rule-in does not end the work. Criterion C still requires the organic mimics to be excluded: transient global amnesia (an abrupt, isolated anterograde amnesia with repetitive questioning, identity preserved, resolving within some hours), a complex partial seizure or epileptic automatism (confusion, no assumption of a new identity, an abnormal EEG), the amnestic (Korsakoff) syndrome and a substance blackout. Only when those are cleared does the label fix, and the treatment is safety, contact with family and a gentle, phased recovery of the memory, never a sedative.

GOOD TO REMEMBER

- **Dissociative amnesia and fugue (the syndrome):** DSM-5-TR Criterion A is an inability to recall important autobiographical information, usually traumatic or stressful, that is inconsistent with ordinary forgetting (localised is the commonest type); fugue is the specifier "with dissociative fugue", apparently purposeful travel or bewildered wandering with amnesia for identity. The deficit is retrograde and reversible; the first step is to exclude an organic cause (Criterion C) and to check whether personal identity is lost, which points away from an organic amnesia.

15.5 Case three: consolidating an alprazolam dependence onto a long-acting agent

Consolidate, convert, then come down. case: a man has been taking alprazolam (Alprax, Restyl) for insomnia and worry, the dose creeping up over many months, and now describes anxiety and tremor 3 to 4 hours after each tablet that he reads as the illness returning. That interdose rebound, 3 to 4 hours after a short-acting high-potency agent, is the fingerprint of dependence, not relapse. The evidence-based taper (BAP 2025; Maudsley) begins by *consolidating* him onto a single long-acting benzodiazepine, diazepam (Valium, Calmpose) or clonazepam (Clonotril,

Rivotril), using the verified diazepam-equivalence below; where the liver is impaired, lorazepam (Ativan, Loraz) or oxazepam is used instead. The Maudsley table deliberately omits alprazolam, so no alprazolam equivalence is asserted here; in practice the difficult final alprazolam doses are eased by substituting clonazepam (Kaplan).

BENZODIAZEPINE	DOSE EQUAL TO DIAZEPAM 10 MG (MG)
Diazepam	10
Clonazepam	**0.5**
Lorazepam	**1**
Chlordiazepoxide	25

The consolidation switch uses the verified diazepam-equivalent doses (Maudsley Prescribing Guidelines, Table 3.29); alprazolam is not tabulated there, so its equivalence is not asserted.

15.6 Case three continued: reducing slowly and managing the withdrawal

Small proportional steps, and never an abrupt stop. Once consolidated, the dose comes down *gradually*: patients often tolerate reductions of about 10 percent of the last dose every 2 to 4 weeks (roughly 5 to 10 percent per month), the steps becoming smaller as the dose falls because the dose-to-effect relationship is hyperbolic, so the final reductions before cessation are often less than 1 mg of diazepam-equivalent (Maudsley). The usual maximum diazepam dose for anxiety is around 30 mg daily. Melatonin (Meloset, Zytonin) is a useful adjunct for the insomnia of withdrawal (BAP grade A). The withdrawal to manage is rebound anxiety and insomnia, autonomic arousal and perceptual disturbance, beginning within hours to a few days of stopping a short-acting agent but only 1 to 2 weeks after a long-acting one; the danger that governs the whole plan is *seizures*. The benzodiazepine use disorder as an addiction is developed in the Substance use disorders notes.

TRAP **Stopping the benzodiazepine abruptly.** Abrupt cessation risks a withdrawal syndrome of rebound anxiety, autonomic arousal and, dangerously, *seizures* (Maudsley: it can be fatal); the whole point of consolidating onto a long-acting agent and reducing in small proportional steps is to never stop suddenly.

10% USUAL TAPER STEP OF THE LAST DOSE EVERY 2 TO 4 WEEKS	**0.5 mg** CLONAZEPAM EQUAL TO DIAZEPAM 10 MG (MAUDSLEY)	**30** USUAL MAX DIAZEPAM FOR ANXIETY (MG PER DAY)	**3 to 4 h** INTERDOSE REBOUND AFTER A SHORT-ACTING AGENT

GOOD TO REMEMBER

- **Diazepam (Valium, Calmpose):** the long-acting anchor of the taper, oral 4 to 40 mg per day in divided doses; a GABA-A positive allosteric modulator with the long-lived active metabolite nordiazepam; verified equivalence, diazepam 10 mg equals clonazepam 0.5 mg equals lorazepam 1 mg equals chlordiazepoxide 25 mg (Maudsley Table 3.29).
- **Alprazolam (Alprax, Restyl):** short-to-intermediate high-potency benzodiazepine, anxiolytic range 1 to 4 mg per day, with 5 to 6 mg per day reserved for panic; the default Indian anxiolytic, the most toxic in overdose and the hardest to taper, with interdose rebound at 3 to 4 hours and a manufacturer short-course limit of 2 to 4 weeks.

15.7 Case four: selecting the anxiolytic to the patient and the goal

Match the agent to the target, and spare the benzodiazepine. case: three patients ask for "something for the nerves", and the right answer differs for each. A junior doctor with palpitations and hand tremor only before an examination viva needs the *somatic* surge blunted for a discrete event: propranolol (Ciplar, Inderal) 10 to 40 mg taken about 20 to 30 minutes before the performance blocks the peripheral autonomic symptoms without sedation or dependence (Kaplan and Sadock, CTP 2024). A woman with chronic generalised anxiety and mild COPD, already buying alprazolam from a chemist, needs a sustained non-dependence anxiolytic: an SSRI is the first-line agent, with buspirone (Buspin), a 5-HT1A partial agonist with no dependence or respiratory depression, as the benzodiazepine-sparing option, provided she is told it takes about a fortnight to work and is useless taken as-needed. A student with a short run of stress-related sleep-onset insomnia needs the briefest possible cover: zolpidem (Zolfresh, Nitrest) 10 mg at bedtime for 7 to 10 nights, or melatonin, with CBT for insomnia as the durable answer. The accompanying figure lays these choices out as an agent-selection map.

PATIENT AND GOAL	FIRST CHOICE (INDIAN BRAND)	DOSE (MG PER DAY)	WHY NOT A BENZODIAZEPINE
Performance or situational anxiety (palpitations, tremor)	propranolol (Ciplar, Inderal)	**10 to 40**	blunts the autonomic surge without sedation or dependence
Sustained GAD with respiratory disease or a substance history	SSRI first-line; buspirone (Buspin) as the non-dependence add-on	buspirone 15 to 30	no dependence, no respiratory depression, but two weeks to work
Short-term sleep-onset insomnia	zolpidem (Zolfresh, Nitrest) or melatonin (Meloset, Zytonin)	zolpidem 10	z-drug complex-sleep-behaviour and dependence caution; CBT-I is durable
Acute severe crisis, alcohol withdrawal, status epilepticus, catatonia	a benzodiazepine (diazepam or lorazepam)	**short course only**	this IS the benzodiazepine's genuine niche, time-limited

The agent-selection map: the anxiolytic is matched to the patient and the goal, and the benzodiazepine is spared for its genuine acute niche. The SSRIs that outrank all of these for sustained anxiety are developed in the Mood disorders: pharmacotherapy notes.

15.8 Case four continued: applying the short-course rule

Not first-line, not for maintenance. The anchor that decides all three sub-cases is the **short-course rule**: a benzodiazepine is not a first-line long-term anxiolytic or hypnotic. For generalised anxiety an SSRI is first-line (BAP 2014; NICE CG113 names sertraline first), and NICE says a benzodiazepine may be offered for generalised anxiety disorder only as a short-term crisis measure of no more than 2 to 4 weeks; for chronic insomnia CBT for insomnia is first-line (BAP 2019), with a z-drug or benzodiazepine only as a brief option matched to the pattern. Two corollaries fall out for this case. The delayed onset of buspirone means the woman must not be switched abruptly from alprazolam to buspirone, which does not cover benzodiazepine

withdrawal; she takes a therapeutic buspirone dose for two to four weeks first, and only then is the alprazolam tapered. And flumazenil, the benzodiazepine antagonist, is not a shortcut out of dependence, because it can precipitate seizures in a dependent patient. The wider anxiety pharmacology sits in the Anxiety, OCD & trauma-related disorders notes, and clinical insomnia and CBT-I in the Eating & sleep-wake disorders notes.

GOOD TO REMEMBER

- **Propranolol (Ciplar, Inderal):** a peripheral beta-adrenergic blocker for somatic and performance anxiety, 10 to 40 mg taken about 20 to 30 minutes before a performance (Kaplan and Sadock, CTP 2024); it blunts palpitations and tremor without sedation or dependence and has no effect on the psychic component.
- **Buspirone (Buspin):** a 5-HT1A partial agonist, 15 to 30 mg per day (maximum 60 mg per day), short half-life of about 2 to 3 hours but a delayed onset of two weeks or more, so never a PRN rescue; no dependence, sedation, anticonvulsant effect or abuse.
- **Zolpidem (Zolfresh, Nitrest):** a z-drug at the benzodiazepine-1 (omega-1) GABA-A subtype, 10 mg at bedtime for 7 to 10 nights (short half-life about 2.5 hours); the signature caution is complex sleep behaviours with dependence and next-morning impairment.

15.9 The single method behind all four

One move, four applications. Stand back and the four cases are one skill practised four ways. The two diagnostic cases rule a functional or dissociative disorder *in* on a positive finding, then keep the organic search open. The two managerial cases apply the short-course discipline, consolidating and tapering a dependence rather than continuing it or stopping it abruptly, and matching the anxiolytic to the patient rather than reaching for the default alprazolam. Across all four the reflex to resist is the same, the sedative given in place of an assessment, which is precisely the habit the Indian benzodiazepine-sparing position exists to correct.

INDIA

Every case here has an Indian edge. The benzodiazepine over-prescription problem is real, and **alprazolam** (Alprax, Restyl) is the default anxiolytic reached for reflexively and continued long-term; benzodiazepines are among the most frequently prescribed drugs, and a benzodiazepine should not ordinarily run beyond 2 to 4 weeks. The Indian Psychiatric Society position, in line with BAP and NICE, is that an SSRI or SNRI is first-line for generalised anxiety and that a benzodiazepine is a short-course measure only, so buspirone and propranolol are genuinely useful in the patient who would otherwise be parked on alprazolam. The culture-bound edge is just as genuine: possession and trance states, in which a deity, spirit or ancestor is felt to take over, are a common idiom of distress and can present with the amnesia and purposeful travel of case two; ICD-11 keeps these as separate categories (trance disorder 6B62, possession trance disorder 6B63), and a sanctioned, non-distressing ritual state is not a disorder at all. Read them through a cultural formulation, not a sedative, as developed in the Consultation-liaison, geriatric & transcultural psychiatry notes.

PEARL

The most powerful move in three of these four cases is a demonstration rather than a drug: the patient's own Hoover's sign or entraining tremor proves the functional diagnosis and its reversibility, the intact new learning proves the amnesia is not organic, and the interdose rebound proves the anxiety is dependence, not relapse. In each, the finding that rules the diagnosis in is also the thing you show the patient to explain it.

HOLD THIS

Win each case with a positive move: rule a functional disorder in on a sign that is weak on command but strong on distraction (Hoover, entrainment, tubular field), separate a dissociative from an organic amnesia by a retrograde loss with identity gone but new learning intact, and treat a benzodiazepine dependence by consolidating onto a long-acting agent (diazepam or clonazepam) and tapering slowly because abrupt cessation causes *seizures*, since a benzodiazepine is never the first-line long-term anxiolytic.

For the receptor detail behind the benzodiazepine mechanism see the Neurochemistry, Neuroendocrinology, Neuroimaging & Basic Psychopharmacology notes; for the video-EEG separation of dissociative from epileptic events the Epilepsy & psychiatry notes; for the lorazepam challenge and benzodiazepine management of catatonia the Other psychotic disorders, delusional syndromes & catatonia notes; for grounding, abreaction and hypnosis in the recovery of dissociative memory the Psychotherapies, clinical assessment, MSE & nosology notes; and for the somatic-symptom, functional and factitious boundary the Somatic-symptom, sexual, impulse-control disorders & suicide notes.

16 · Consolidation

The last step is not new material, it is retrieval. This closing topic exists to turn a chapter you have *read* into a chapter you can *reproduce* under exam pressure. The evidence is one-directional: testing yourself on half-learned material, **retrieval practice**, fixes it far more durably than reading it again, and the most efficient way to study this material is to **cover the answer** and force each fact out of memory before checking it. Everything below is built for that, a **mnemonic** that reassembles the whole chapter from one line, answer-free **retrieval prompt** lists, two answer vaults to check against, and a whole-chapter **synthesis map** to reproduce.

Use it actively, not by rereading. Say the master mnemonic once, then close the notes and work the retrieval prompts with the answer covered; only then uncover the Good-to-remember vaults and mark what you missed. Finish by reproducing the synthesis map on a blank sheet. Do those three things and the chapter is consolidated; the gaps you find are exactly where to go back. The wider study technique of active recall and spaced retrieval sits alongside the clinical material, and the grounding and hypnosis techniques touched on across the dissociative half are developed in the Psychotherapies, clinical assessment, MSE & nosology notes.

Fig 15.16 The whole-chapter synthesis map as a cover-the-columns grid: each dissociative entity reduced to its one discriminator and first step, and each anxiolytic-hypnotic class to its mechanism, use and key caution.

A. Dissociative and conversion: entity, discriminator, first step		
entity	**the one discriminator**	**the first step**
dissociative amnesia and fugue	retrograde loss, intact new learning; fugue is a specifier	exclude an organic amnestic cause
dissociative identity disorder	two or more identity states, plus recurrent amnesia	confirm the dissociative-amnesia criterion
depersonalisation-derealisation	detachment with intact reality testing ('as if')	confirm reality testing is intact (not psychosis)
conversion / functional neurological disorder	a positive rule-in sign, not a diagnosis of exclusion	elicit a positive sign
possession and trance	involuntary, outside accepted cultural or religious practice	apply the cultural-exclusion criterion

B. Anxiolytics and hypnotics: class, mechanism, use and key caution		
class	**mechanism**	**use and the key caution**
benzodiazepines	GABA-A positive allosteric modulator; frequency, not duration	short course only; dependence and seizure on abrupt withdrawal
z-drugs (zolpidem, zopiclone)	benzodiazepine-1 (omega-1) GABA-A subtype	short-term sleep onset; complex sleep behaviours
buspirone	5-HT1A partial agonist	sustained anxiety, spares BZD; delayed onset, no dependence
DORAs (suvorexant, lemborexant)	orexin (hypocretin) receptor antagonist	insomnia; blocks the wake-promoting orexin system
melatonergic (melatonin, ramelteon)	MT1 / MT2 receptor agonist	sleep onset; prolonged-release an option over age 55
adjuncts (propranolol, hydroxyzine, pregabalin)	beta-blocker, H1 antihistamine, alpha-2-delta ligand	somatic and acute anxiety; none is a GABA-A hypnotic

structure: section and column headers the exam anchor to hold the danger to hold

16.1 The master mnemonic, paid off

One line rebuilds the whole chapter. The chapter opened by seeding a single **mnemonic**, and this is where it is redeemed. *MIND SPLITS, BODY SPEAKS, GABA SLEEPS* is not decoration, each beat is a doorway into a third of the material, and saying the line should make the branches beneath it unfold. **MIND SPLITS** recovers the psychoform dissociative disorders of consciousness, memory and identity; **BODY SPEAKS** recovers conversion, the somatoform half; **GABA SLEEPS** hands over to the anxiolytic and hypnotic pharmacology that acts on the GABA-A receptor. If the line is solid, the chapter is recoverable from it.

MNEMONIC

MIND SPLITS, BODY SPEAKS, GABA SLEEPS

MIND SPLITS unfolds to the mind-side entities, dissociative *amnesia* (autobiographical memory), *identity* disorder and its partial form (identity), *depersonalisation-derealisation* (self and reality), and *trance* and *possession trance* (awareness and identity-replacement). **BODY SPEAKS** unfolds to the one body-side entity, conversion or dissociative neurological symptom disorder, diagnosed by positive signs. **GABA SLEEPS** unfolds to the benzodiazepine and its comparators, the mechanism (frequency, not duration), the half-life classes, dependence and the taper, flumazenil, and the short-course rule. Three beats, three branches, the whole chapter.

16.2 How to run the recall

Cover, retrieve, check, redraw. The mechanics of **active recall** for this chapter are fixed and worth stating so the rest of the topic is usable. First, **cover the answer**, keeping the two Good-to-remember vaults below hidden. Second, work each **retrieval prompt** out loud or on paper from memory. Third, uncover the vault and mark every miss. Fourth, close on the **synthesis map** and **redraw from memory** on a blank sheet. The order matters, because the effortful pull of retrieval is what lays down the memory, so a prompt you struggle with and then check is worth more than a paragraph reread. That is why the prompt lists below are deliberately answer-free.

RULE **Three anchors hold the chapter.** One split (dissociation of the mind versus dissociation of the body), one mechanism (the benzodiazepine raises the *frequency* of chloride-channel opening, not its duration), and one management rule (the benzodiazepine is a short-course drug, never a first-line long-term anxiolytic). Recover those three and the detail hangs off them.

16.3 Retrieval prompts: the dissociative discriminators

Cover the vaults below and answer from memory. Each prompt targets the single discriminator the examiner tests, not a general description. Work them as **retrieval practice**, then check against the criterion vault.

1. Name the seven ICD-11 dissociative types and, for each, the one integrative function that has failed.
2. What single discriminator separates dissociative amnesia from an organic amnestic syndrome, and is fugue a disorder or a specifier?
3. Beyond two or more distinct personality states, which criterion is mandatory for dissociative identity disorder, and what two competing models explain its cause?
4. What distinguishes partial dissociative identity disorder from the full disorder?
5. What keeps depersonalisation-derealisation disorder on the non-psychotic side of the line, and what scale threshold is conventionally diagnostic?
6. State the cultural-exclusion criterion that both trance disorder and possession trance disorder must satisfy, and how the two differ.
7. Where does conversion sit in ICD-11 versus DSM-5-TR, and why is that the pivotal filing difference?

16.4 Retrieval prompts: the conversion signs and the measure

Still covered. These carry the highest bedside yield of the mind-and-body half, the positive signs that rule conversion *in*, and the screen that flags dissociation for interview.

1. Name the five positive rule-in signs of a functional neurological symptom, and say what each one demonstrates.
2. Is conversion a diagnosis of exclusion, and is an identifiable psychological stressor required? What is the diagnostic status of la belle indifference?
3. Which single sign would you elicit first at the bedside for a functional leg weakness, and what is the positive finding?
4. What is the conventional Dissociative Experiences Scale (DES) screening cut-off, and what do you do for a patient who scores above it?
5. What does the DES-Taxon subscale add, and what does the SDQ-20 capture that the DES does not?

GOOD TO REMEMBER

- **Dissociative amnesia:** defining criterion is an inability to recall important autobiographical information inconsistent with normal forgetting; the deficit is *retrograde* with intact new learning (the discriminator from organic amnesia); fugue is a specifier. First step: exclude an organic amnestic cause.
- **Dissociative identity disorder:** two or more distinct personality states (or possession) *plus* recurrent dissociative amnesia; the amnesia criterion is the discriminator; trauma / structural-dissociation model versus the sociocognitive (fantasy) model.
- **Depersonalisation-derealisation disorder:** persistent detachment with *intact reality testing* and an "as if" quality, the intact reality check being the discriminator from psychosis; a Cambridge Depersonalisation Scale score of 70 or more is the conventional threshold.
- **Trance / possession trance disorder:** narrowed awareness with identity intact (trance) versus identity replaced by an external agent with amnesia (possession); both require the state to be involuntary, distressing and *outside accepted cultural or religious practice*. First step: apply the cultural-exclusion criterion.
- **Dissociative / functional neurological symptom disorder:** a neurological symptom with a *positive* sign of internal inconsistency (Hoover's sign, tremor entrainment, give-way weakness, tubular visual field, astasia-abasia); it is *not* a diagnosis of exclusion, no stressor is required, and la belle indifference is unreliable. First step: elicit a positive sign.

16.5 Retrieval prompts: the benzodiazepine mechanism and kinetics

Cover the dose vault below. The pharmacology half rewards the mechanism first, then the half-life sort, because everything clinical follows from those two.

1. State the benzodiazepine mechanism at the GABA-A receptor, which parameter of chloride-channel opening it raises, where its binding site lies, and how the barbiturate differs.
2. Why is a benzodiazepine relatively safe in a pure overdose while a barbiturate is not?
3. Sort lorazepam, alprazolam, clonazepam, diazepam and chlordiazepoxide into short-to-intermediate versus long-acting, and name the shared active metabolite of the long-acting agents.

4. Which three benzodiazepines have no active metabolite, making them the liver-safe choice, and what mnemonic names them?
5. Which receptor subtype carries sedation, and which carries anxiolysis?

16.6 Retrieval prompts: withdrawal, taper and selection

Still covered. These are the single most examinable management statements of the material, so retrieve them cleanly and check against the dose vault.

1. What are the dangerous features of benzodiazepine withdrawal, and why must the drug never be stopped abruptly?
2. Describe the taper, onto which agent you consolidate and at what rate you reduce.
3. Name the benzodiazepine antagonist, its half-life problem, and its signature hazard.
4. What is the first-line pharmacological treatment for generalised anxiety disorder, precisely where does the benzodiazepine sit, and what is the NICE ceiling on a benzodiazepine course?
5. What is first-line for chronic insomnia, and which non-benzodiazepine anxiolytic works only after a delay and carries no dependence?

30	0.5 to 6	20 to 50	10%
DES SCREENING CUT-OFF	ALPRAZOLAM ANXIETY DOSE (MG PER DAY)	DIAZEPAM ELIMINATION HALF-LIFE (HOURS)	TAPER: FRACTION OF LAST DOSE EVERY 2 TO 4 WEEKS

GOOD TO REMEMBER

- **Diazepam (Valium, Calmpose):** GABA-A positive allosteric modulator; 4 to 40 mg per day in divided doses; long-acting through the active metabolite nordiazepam; the consolidation anchor of the taper, with diazepam 10 mg equal to clonazepam 0.5 mg, lorazepam 1 mg and chlordiazepoxide 25 mg (Maudsley).
- **Alprazolam (Alprax, Restyl):** short-to-intermediate (half-life 6 to 20 hours), high-potency; anxiety 1 to 4 mg per day (5 to 6 mg per day is the panic figure, not the anxiolytic range); the most toxic benzodiazepine in overdose and the hardest to taper, and the Indian default anxiolytic despite both.
- **Clonazepam (Clonotril, Rivotril):** long-acting (half-life 30 to 40 hours), high-potency; panic 0.5 to 2 mg per day; the other taper-consolidation agent and the substitute that eases the final doses of alprazolam.
- **Lorazepam (Ativan, Loraz):** short-to-intermediate (half-life 10 to 20 hours), no active metabolite so liver-safe; oral 2 to 6 mg per day; the catatonia challenge agent at 1 to 2 mg.
- **Buspirone (Buspin):** a 5-HT1A partial agonist, 20 to 30 mg per day; a *delayed* onset of 2 weeks or more with no dependence, sedation or anticonvulsant effect, so it spares the benzodiazepine in sustained anxiety but is useless acutely.
- **Zolpidem (Zolfresh, Nitrest):** a z-drug at the benzodiazepine-1 (omega-1) GABA-A subtype, 10 mg at bedtime for short-term use; the signature caution is complex sleep behaviours, dependence and next-day impairment.
- **Flumazenil (the antagonist):** a competitive benzodiazepine-receptor antagonist with a short half-life of 41 to 79 minutes (so re-sedation and repeat dosing); it can *precipitate seizures* in benzodiazepine dependence and in mixed or cyclic-antidepressant overdose, so it is used selectively.

16.7 The whole-chapter synthesis map

Cover the branches and redraw from memory. The final and highest-value exercise is to reproduce the chapter as one picture. The accompanying figure sets out the **synthesis map** as a single tree, a trunk labelled by the master mnemonic, three primary branches (mind, body, GABA), and the named entities and anchors hanging off each. Study it once, then cover every branch and **redraw from memory** on blank paper, writing the discriminator or the dose at each leaf. The mind branch should regrow its five entities, each with its failed integrative function; the body branch its one entity with the positive-sign list; the GABA branch the mechanism, the half-life classes, the withdrawal-and-taper, flumazenil and the short-course rule. A branch you cannot regrow is a branch to reread. This cover-the-branches redraw is the most compact single test of whether the chapter is genuinely consolidated.

INDIA

Two Indian threads run the length of this chapter and belong on the synthesis map. On the pharmacology side, India carries a genuine benzodiazepine over-prescription problem, with **alprazolam** the reflex default anxiolytic despite being the most toxic in overdose and the hardest to taper; the Indian Psychiatric Society position and the wider benzodiazepine-sparing principle favour the SSRI or SNRI for sustained anxiety and CBT for insomnia, keeping the benzodiazepine to a genuine short course. On the dissociative side, trance, possession and conversion presentations are among the most frequent dissociative pictures in Indian practice, which makes the cultural-exclusion criterion and a proper cultural formulation, not a reflex sedative, the examinable core. The transcultural reading is expanded in the Consultation-liaison, geriatric & transcultural psychiatry notes.

TRAP **The chapter's recurring errors, in one line.** Missing an organic cause behind a "conversion" picture, diagnosing dissociative identity disorder without the dissociative-amnesia criterion, reading depersonalisation-derealisation as psychosis, starting a benzodiazepine for chronic anxiety or insomnia, and stopping a benzodiazepine abruptly and risking a seizure, five traps, one per section.

HOLD THIS

If you can say *MIND SPLITS, BODY SPEAKS, GABA SLEEPS* and, from it, regrow the mind-side discriminators, the conversion positive signs, the DES cut-off of 30, the frequency-not-duration mechanism and the never-abrupt, short-course-only benzodiazepine rule, the chapter is consolidated; wherever you cannot, that gap is the reread.

For the receptor systems behind the GABA-A detail see the Neurochemistry, Neuroendocrinology, Neuroimaging & Basic Psychopharmacology notes; for the sedative and benzodiazepine use disorder as an addiction the Substance use disorders notes; for the SSRIs and SNRIs that outrank the benzodiazepine as first-line anxiolytics the Mood disorders: pharmacotherapy notes; and for chronic insomnia and CBT for insomnia the Eating & sleep-wake disorders notes.

Previously asked

This territory is examined at two levels at once: the syndrome (the dissociative and conversion presentations, the positive signs that rule them in, the organic differential that must be excluded and the management that follows) and the pharmacology (the benzodiazepines and the wider anxiolytic and hypnotic agents, their receptor action and the dependence and withdrawal they carry). The dissociative and conversion questions on record are written in the older hysteria vocabulary, so the same case can be labelled hysterical unconsciousness, conversion disorder or functional neurological disorder across sittings, and a strong answer reconciles the ICD-11 and DSM-5 naming with the term used in the stem. Every long essay ends in a differential and a guideline-anchored management plan, so the organic-versus-functional decision and the first-line plan must be exam-ready. The genuine questions on record are grouped below. The clinical anxiety and obsessive-compulsive disorders these agents actually treat are developed in the Anxiety, obsessive-compulsive and trauma- and stressor-related disorders notes; the somatic-symptom and illness-anxiety boundary that sits beside conversion is developed in the Somatic-symptom, sexual, impulse-control disorders and suicide notes; and the GABA-A receptor pharmacology behind the anxiolytics and hypnotics is developed in the Neurochemistry, neuroendocrinology, neuroimaging and basic psychopharmacology notes, while the dissociative classification, the positive functional signs, the conversion management and the anxiolytic and hypnotic agents are owned here.

HOW THIS TERRITORY IS ACTUALLY TESTED

Q **Conversion disorder and the dissociative presentation of unconsciousness.** "Define consciousness. Differential diagnosis for unconsciousness in middle aged male. How to investigate and manage a case of Hysterical Unconsciousness?" has come as a full 25-mark essay, "Discuss etiology, clinical features and management of Hysterical Conversion Disorder" has come as a 25-mark essay, and "Clinical features and differential diagnosis of Conversion Disorder" has come as a 25-mark essay in its own right. Prepare the conversion and functional-neurological presentation, the positive signs that rule the disorder in (Hoover's sign, the hip-abductor and give-way patterns, tremor entrainment and the tubular visual field), the organic differential for unconsciousness that must be excluded first, the dissociative mechanism behind the symptom and the caveat that la belle indifference is neither sensitive nor specific, and the management line (exclude organic disease, explain the diagnosis as a real and reversible one, physiotherapy-led rehabilitation and treatment of the comorbid depression or anxiety). 25-mark essay, 2013 / 2014 / 2016

Q **Benzodiazepine dependence and the anxiolytic and hypnotic agents.** "Benzodiazepine Dependence" has come as a standalone 10-mark note. Prepare the receptor pharmacology (the GABA-A benzodiazepine site and its chloride-channel action), the tolerance and dependence that follow continued use, the withdrawal syndrome with its rebound anxiety, perceptual disturbance and seizure risk, the over-prescription context that drives the problem in Indian practice where a somatising anxious patient is handed alprazolam or clonazepam rather than started on the agent that treats the disorder, and the management (a slow graded taper, the switch to a long-acting agent such as diazepam, and the reservation of these drugs for short-term crisis use only). 10-mark note, 2016

Prepare this material to be diagnosed and treated, not just recited: the organic-versus-functional differential, the positive functional-sign figures, the dissociative classification set against the ICD-11 and DSM-5, the dose-anchored good-to-remember boxes and the benzodiazepine taper schedule in these notes are built to the way the block is examined. The dissociative amnesia and fugue, the depersonalisation and derealisation, the dissociative identity and the possession and trance

presentations are not on the question record but sit squarely inside the classification the stems ask you to apply, and the non-benzodiazepine anxiolytics and hypnotics (the Z-drugs, buspirone, melatonin and ramelteon, and flumazenil as the antidote) are catalogued as an essay only in the basic-pharmacology paper, so both are prepared here to the same depth. The clinical anxiety and obsessive-compulsive disorders these agents treat live in the Anxiety, obsessive-compulsive and trauma- and stressor-related disorders notes; the somatic-symptom and illness-anxiety boundary in the Somatic-symptom, sexual, impulse-control disorders and suicide notes; and the receptor-level pharmacology in the Neurochemistry, neuroendocrinology, neuroimaging and basic psychopharmacology notes.

Quick review in one table

THE DISSOCIATIVE DISORDERS OF THE MIND: THE DISCRIMINATOR AND THE FIRST STEP	
THE ORGANISING SPLIT	Dissociation of the **mind** (consciousness, memory, identity) versus the **body** (motor and sensory control). ICD-11 keeps conversion inside the family (6B60); DSM-5-TR exports it to the somatic disorders. First step: name which integrative function came apart and the diagnosis names itself.
DISSOCIATIVE AMNESIA (AND FUGUE)	Discriminator: a **retrograde** loss of autobiographical memory with **new learning intact** and identity often lost (the mirror of organic amnesia); localised is commonest, fugue is a specifier. First step: exclude an organic amnestic cause.
DISSOCIATIVE IDENTITY DISORDER	Discriminator: two or more distinct identity states **plus recurrent dissociative amnesia** (the required, most-tested criterion; drop it and it is other specified dissociative disorder). First step: confirm the amnesia criterion. Debate: trauma model versus sociocognitive (fantasy) model.
PARTIAL DISSOCIATIVE IDENTITY DISORDER	Discriminator: one dominant state runs daily life, intruded on by non-dominant states that do **not** take executive control (full disorder = states seize control, partial = they only intrude); an ICD-11 category, filed under other specified dissociative disorder in DSM-5-TR.
DEPERSONALISATION-DEREALISATION DISORDER	Discriminator: persistent detachment from self and/or world with an "as if" quality and **intact reality testing** (the separator from psychosis). First step: confirm reality testing is preserved. A Cambridge Depersonalisation Scale score of 70 or more is the conventional threshold.
TRANCE DISORDER	Discriminator: narrowed awareness of surroundings with a small, seemingly uncontrolled behavioural repertoire, the **self still intact** (no identity replacement); normal EEG even during episodes. First step: apply the cultural-exclusion criterion and clear the organic mimics.
POSSESSION TRANCE DISORDER	Discriminator: the sense of identity is **replaced by an external possessing agent** (spirit, deity, demon) with amnesia; the external attribution separates it from dissociative identity disorder. First step: apply the cultural-exclusion criterion (a sanctioned, non-distressing ritual is not a disorder).
CONVERSION, ITS SEIZURE FORM, AND MEASURING DISSOCIATION	
CONVERSION (DISSOCIATIVE NEUROLOGICAL SYMPTOM DISORDER)	Discriminator: a motor or sensory symptom with a **positive sign of internal inconsistency** (Hoover's sign, tremor entrainment, tubular field), weak on command but strong on distraction; a **rule-in** diagnosis, no stressor required, la belle indifference unreliable. First step: elicit a positive sign.

CONVERSION, ITS SEIZURE FORM, AND MEASURING DISSOCIATION	
DISSOCIATIVE (NON-EPILEPTIC) CONVULSIONS	Discriminator: a seizure-like attack with preserved awareness in bilateral shaking, closed and resisted eyes, a long fluctuating course, no post-ictal prolactin rise, and a **normal ictal video-EEG** (the gold standard). Tongue-biting and incontinence do not distinguish it. First step: capture the attack on video-EEG.
MEASURING DISSOCIATION (DES)	The Dissociative Experiences Scale is the self-report screen; a **mean of 30 or more** flags a probable dissociative disorder and prompts a structured interview (SCID-D, DDIS). The DES-Taxon isolates pathological dissociation; the SDQ-20 captures somatoform dissociation. A high score is a flag, never a diagnosis.

THE GABA-A SEDATIVE-HYPNOTICS: MECHANISM, USE AND CAUTION	
BENZODIAZEPINES (THE CLASS)	A **positive allosteric modulator** at the GABA-A receptor (benzodiazepine site, alpha-gamma interface): raises the **frequency** of chloride-channel opening only when GABA is present (barbiturates raise the **duration**). GABA-dependence gives a ceiling, so relatively safe in pure overdose. Alpha-1 sedation, alpha-2 anxiolysis.
AGENTS AND HALF-LIFE	Short-to-intermediate: lorazepam (10 to 20 h, no metabolite, liver-safe), **alprazolam** (12 to 15 h, high-potency). Long-acting through shared nordiazepam: diazepam, chlordiazepoxide; clonazepam (30 to 40 h). LOT group (lorazepam, oxazepam, temazepam) has no active metabolite. Alprazolam **1 to 4 mg per day for anxiety** (5 to 6 mg per day only for panic), most toxic in overdose, hardest to taper.
WITHDRAWAL AND TAPER	Withdrawal: rebound anxiety, perceptual disturbance and autonomic arousal, with the criterion-level dangers of **seizures**, psychosis and delirium. **Never stop abruptly.** Taper: consolidate onto a long-acting agent (diazepam or clonazepam), reduce about 10% of the last dose every 2 to 4 weeks (diazepam 10 = clonazepam 0.5 = lorazepam 1 = chlordiazepoxide 25 mg).
FLUMAZENIL (THE ANTAGONIST)	The competitive benzodiazepine-receptor **antagonist**; short half-life 41 to 79 minutes, so re-sedation and repeat dosing. Signature caution: it can **precipitate seizures** in benzodiazepine dependence and in mixed or cyclic-antidepressant overdose, so it is used selectively, not routinely.
Z-DRUGS (ZOLPIDEM, ZOPICLONE, ZALEPLON, ESZOPICLONE)	Non-benzodiazepine hypnotics that still modulate the GABA-A benzodiazepine site, selective for the **omega-1 (alpha-1)** subtype. Use: a short-term hypnotic after CBT for insomnia, matched by half-life (zolpidem 5 to 10 mg for onset, zopiclone for maintenance). Caution: **complex sleep behaviour**, dependence, next-day impairment.

THE NON-GABA ANXIOLYTICS AND THE OTHER HYPNOTICS	
BUSPIRONE (AZAPIRONE)	A **5-HT1A partial agonist**, not a GABA drug; 15 to 30 mg per day (short half-life 2 to 3 h). Use: acute GAD, sitting after an SSRI and before a benzodiazepine. Caution: a **delayed onset of 2 weeks or more**, so useless as a PRN, but no dependence, sedation or anticonvulsant effect.
GABAPENTINOIDS (PREGABALIN, GABAPENTIN)	**Alpha-2-delta calcium-channel ligands** (despite the name, not GABA drugs). Pregabalin 150 to 600 mg per day is the licensed **alternative first-line** for GAD; gabapentin 900 to 1800 mg per day is off-label. Caution: now recognised drugs of **misuse and dependence**, never stop abruptly (seizure).
PROPRANOLOL (BETA-BLOCKER)	A peripheral **beta-adrenergic antagonist**: strips the palpitations and tremor, not the dread. Use: the somatic symptoms of **performance and social anxiety**, a single 10 to 40 mg dose about an hour before the event. Caution: no effect on psychic anxiety; avoid in asthma and bradycardia.
HYDROXYZINE (ANTIHISTAMINE)	A sedating **H1 antagonist**; 50 to 100 mg up to four times a day (half-life about 20 h). Use: efficacious in **acute GAD** (BAP), no dependence, not controlled. Caution: sedation, anticholinergic effects, and QT prolongation at higher doses.
ETIFOXINE	A non-benzodiazepine anxiolytic with a **dual action**: direct GABA-A modulation plus translocator-protein (TSPO)-driven neurosteroid (allopregnanolone) synthesis; about 150 to 200 mg per day. Non-inferior to lorazepam and alprazolam over 4 weeks with less rebound. Caution: rare hepatic and severe cutaneous reactions; an alternative, not a first-line SSRI.
MELATONERGIC AGONISTS (MELATONIN, RAMELTEON)	**MT1/MT2 agonists** on the suprachiasmatic clock (MT1 onset, MT2 phase-shift), not the GABA channel. Use: prolonged-release melatonin 2 mg for the over-55 and as a taper-insomnia adjunct; ramelteon 8 mg for sleep-onset. Caution: a modest effect, no dependence; ramelteon with fluvoxamine is dangerous (CYP1A2).
DUAL OREXIN RECEPTOR ANTAGONISTS (DORAS)	**Dual OX1/OX2 orexin (hypocretin) antagonists** that promote sleep by subtracting wakefulness, not by adding GABAergic sedation. Use: insomnia when CBT for insomnia is not the route (suvorexant 10 to 20, lemborexant 5 to 10, daridorexant 25 to 50 mg nocte). Caution: next-morning somnolence, so leave a 7-hour sleep window.
THE GUIDELINE SPINE AND THE HARD RULES	
ANXIETY, FIRST-LINE	**An SSRI or SNRI is first-line** for GAD; pregabalin and buspirone are the alternatives, hydroxyzine and buspirone cover acute anxiety, and propranolol the performance type. A benzodiazepine is not first-line and not for maintenance.

THE GUIDELINE SPINE AND THE HARD RULES	
INSOMNIA, FIRST-LINE	**CBT for insomnia is first-line** for chronic insomnia; a hypnotic (benzodiazepine, z-drug, melatonin or a DORA) is a short-term option only, matched by half-life to the onset-versus-maintenance pattern.
THE BENZODIAZEPINE SHORT-COURSE RULE	A benzodiazepine is a **2 to 4 week crisis measure** at most (NICE), then tapered, and is **never stopped abruptly** because withdrawal seizures can be fatal. India's alprazolam-default habit is exactly the pattern the benzodiazepine-sparing position corrects.
THE DISSOCIATIVE FIRST-MOVE	For a possession, trance or dramatic dissociative presentation the first move is a **cultural formulation and exclusion of an organic cause**, not a reflex sedative; a sanctioned, non-distressing ritual is not a disorder, and dissociation has no benzodiazepine indication.
THE FIVE TRAPS	Missing an organic cause behind a "conversion"; diagnosing dissociative identity disorder **without the amnesia** criterion; reading depersonalisation-derealisation as psychosis; starting a benzodiazepine for chronic anxiety or insomnia; and stopping a benzodiazepine abruptly.

References

The dissociative, conversion and anxiolytic-and-hypnotic content is grounded in the standard psychiatry and psychopharmacology sources (the source hierarchy below), with Kaplan and Sadock as the depth bar for the dissociative phenomenology, the three pathogenesis models and the scale cut-offs, the New Oxford Textbook (Stone and Carson) for the positive-sign, rule-in approach to functional neurological disorder, and the Maudsley Prescribing Guidelines and Stahl as the depth bar for the receptor mechanisms, the half-life classes, the doses, the diazepam-equivalence table and the taper. The management is guideline-first, led by the British Association for Psychopharmacology (anxiety 2014, insomnia 2019, substance dependence), with NICE and the Indian Psychiatric Society. Every criterion, receptor detail, dose, half-life, equivalence and first-line or short-course statement was checked against these sources and the adversarial content pass; anything that could not be confirmed was omitted and flagged rather than guessed. Each journal PMID below was verified against PubMed this build and matched on title, first author and year; identifiers that resolved to the wrong paper were corrected or dropped. Books, classifications and guideline documents without a MEDLINE record are cited by author, title and year without a PMID.

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PART IX

IX

Personality Disorders

The personality disorders: how each is recognised, told apart from the others, and understood.

01 Framework and classification

02 The personality disorders by cluster

03 Aetiology, assessment and treatment

04 Apply and consolidate

PAPER II

Personality disorders: framework, types and treatment

Three sections . one complete notes document

This material gathers the personality disorders into one document, first the framework and the classification, then the disorders themselves, then how they are assessed and treated. The first band is **the framework and classification**: the definition and the general diagnostic criteria that must hold before any type is named, the ICD-11 dimensional model that abolished the categorical types for a severity gradient and a set of trait domains, the DSM-5 categorical clusters and their ten types with the alternative hybrid model alongside, and the comparison of the two approaches. The second band is **the personality disorders by cluster**: the cluster A odd and eccentric disorders, borderline personality disorder as the highest-yield type with its features, course and complications, antisocial personality disorder and its forensic significance, the histrionic and narcissistic disorders, the cluster C anxious and fearful disorders, and the borderline-versus-bipolar-II differential that examiners return to. The third band is **aetiology, assessment and treatment**: the genetic, neurobiological and developmental aetiology and the Linehan biosocial model, the assessment instruments and structured interviews, and the treatment block, dialectical behaviour therapy, schema therapy, mentalisation-based and transference-focused psychotherapy, the symptom-targeted pharmacotherapy, and the integrated borderline plan. The examinable skill is the safe, guideline-anchored diagnosis and treatment of each disorder: which criteria gate a personality-disorder diagnosis, how the classification shifted and why exams still test the categorical names, which disorder behind which presentation, the borderline-versus-bipolar-II boundary, which structured psychotherapy for which patient, and the rule that a drug is not the first-line treatment for borderline personality disorder.

HOW TO USE THESE NOTES

Read the three bands as one continuous account of how the personality disorders are classified, recognised and treated. The **framework and classification** band builds the frame: the general criteria that gate every diagnosis, the headline nosology shift where ICD-11 replaced the categorical types with a dimensional model of severity and trait domains, the DSM-5 categorical clusters and their ten types cross-mapped, and why exams still test both. The **personality disorders by cluster** band teaches the disorders themselves, cluster A, borderline personality disorder in full, antisocial personality disorder and its forensic frame, the histrionic and narcissistic disorders, cluster C, and the borderline-versus-bipolar-II differential. The **aetiology, assessment and treatment** band teaches the aetiology and the Linehan biosocial model, the assessment instruments, and the treatment block, where structured psychological therapy is primary and dialectical behaviour therapy, schema therapy, mentalisation-based and transference-focused psychotherapy are owned and fully taught here. Every management recommendation is guideline-anchored, led by NICE with the Indian Psychiatric Society and WFSBP positions stated, on the where-to-treat, target-by-phase, modes-of-treatment spine; every named disorder ends with a **Good to remember** box giving the defining criterion, the discriminator and the first step, and every named therapy ends with one giving the mechanism, the indication and the signature caution. Figures declare one axis and code it in colour: **petrol** marks structure and the neutral case, **coral** marks the trap or the danger, and **marigold** highlights the number to hold. Several boundaries are stated up front and cross-referenced by chapter name: the deep pharmacology of the mood stabilisers, low-dose antipsychotics and serotonin reuptake inhibitors used in symptom-targeted treatment is taught in the Mood disorders: pharmacotherapy notes and the Schizophrenia: management, antipsychotics and adverse effects notes; the bipolar-II side of the differential in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes; the forensic frame of antisocial personality disorder in the Mental health legislation and forensic psychiatry notes; the complex-PTSD boundary in the Anxiety, OCD and trauma-related disorders notes; the schizotypal-versus-schizophrenia boundary in the Schizophrenia: aetiology, phenomenology, classification and course notes; and the wider psychotherapy models in the Psychotherapies, clinical assessment, MSE and nosology notes. This is doctor-facing revision, so the full technical vocabulary is used, brand names lead with the Indian brand, and every criterion, trait domain, cluster mapping, severity anchor, dose and guideline rule is verified against a source or omitted and flagged.

Framework and classification

1 . Definition, concept and general diagnostic criteria

Why this leads the chapter. Every personality-disorder question turns on one gate that most candidates skip. Before any of the ten named types can be diagnosed, a set of **general diagnostic criteria** must ALL hold: an **enduring pattern** of inner experience and behaviour that is **pervasive and inflexible**, deviates markedly from the person's culture, begins by adolescence, is stable over time, is not better explained by another disorder or a substance, and causes clinically significant impairment or distress. A personality disorder is not diagnosed by pattern-matching a vignette to a type; it is diagnosed by first clearing this general threshold and only then asking

which type fits. Get the gate right and the whole family, however you later classify it, becomes a disciplined exercise; get it wrong and you will pin a lifelong label on a situational mood state.

This fragment sets the **definition of personality disorder**, walks the six-part general threshold criterion by criterion, and isolates the four features an examiner rewards: the **ego-syntonic** quality, the trait-versus-state caution, the cultural reading, and the rule that no type is named until the general criteria are met. The accompanying figure lays the same content out as a general-criteria decision map to be carried as one image. The forward split into the ICD-11 dimensional model and the DSM-5-TR categorical clusters is developed in the topics that follow; the borderline-versus-bipolar-II boundary is cross-referenced to the Mood disorders: classification, depressive & bipolar syndromes, neurobiology notes, the forensic weight of antisocial personality disorder to the Mental health legislation & forensic psychiatry notes, the complex-PTSD boundary to the Anxiety, OCD & trauma-related disorders notes, and the wider technique of the psychological therapies to the Psychotherapies, clinical assessment, MSE & nosology notes.

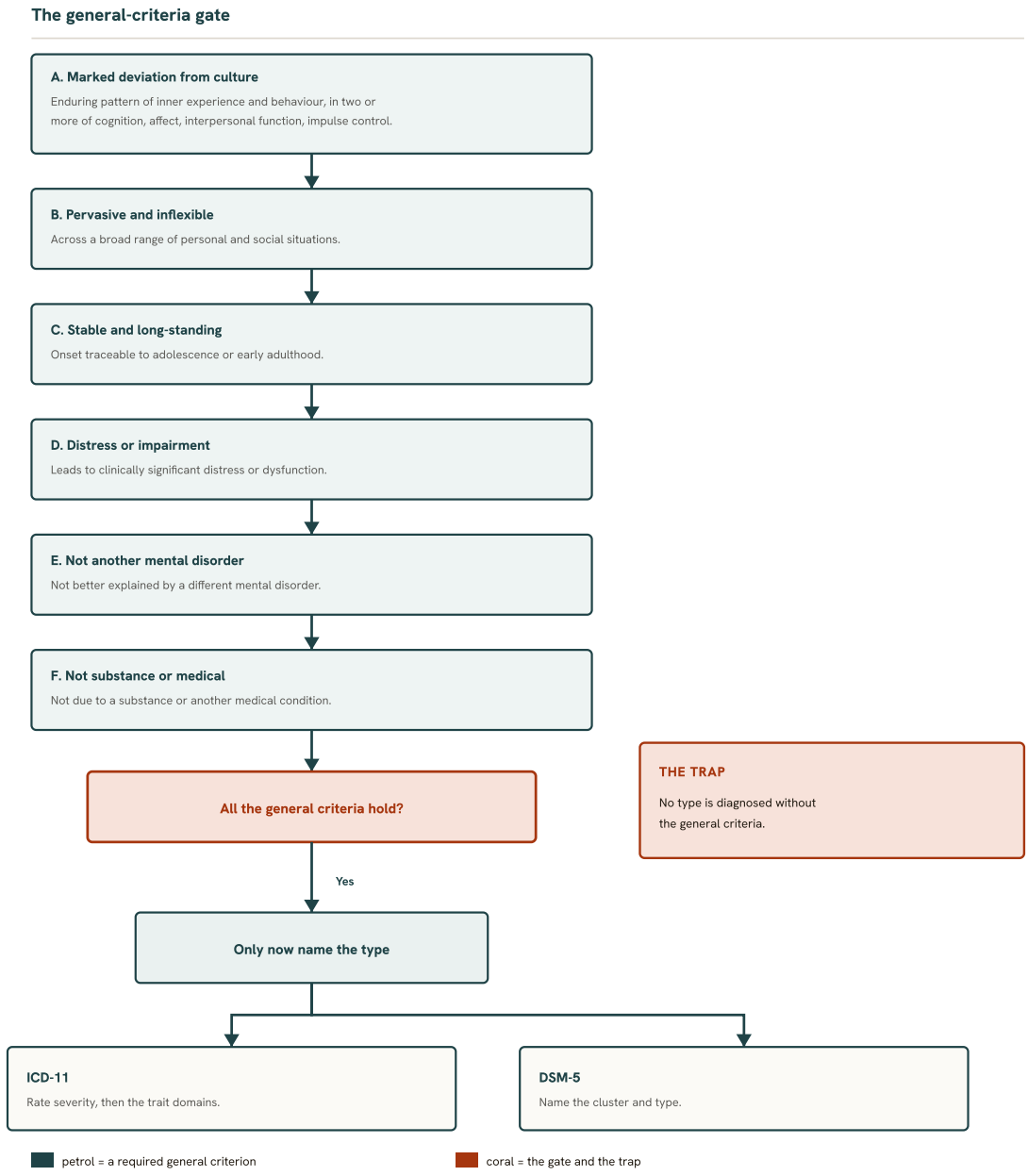


Fig 16.1 The general criteria for a personality disorder are a gate: the pattern must be enduring, pervasive and inflexible, deviate from cultural expectation, begin by adolescence or early adulthood, cause distress or impairment, and not be better explained by another disorder or a substance before any specific type is named.

1.1 Personality, trait, and what makes a disorder

A disorder is the maladaptive extreme of a normal continuum. Personality is the characteristic, deeply ingrained pattern of perceiving, relating to and thinking about oneself and the environment (DSM-5-TR). *Personality traits* are the normal, prominent aspects of that pattern; they become a disorder only when they are inflexible and maladaptive and cause significant functional impairment or subjective distress (DSM-5-TR). That single hinge, from normal-but-prominent to inflexible-and-impairing, is the working **definition of personality disorder**. The concept has a long descriptive spine: Kurt Schneider defined the abnormal (psychopathic) personalities as those who suffer from their abnormality or make society suffer, dissolving the older moral reading into a clinical one. ICD-11 phrases the modern definition as a

marked disturbance in personality functioning, with the central manifestations being impairments in aspects of the *self* (identity, self-worth, capacity for self-direction) and in *interpersonal* functioning (forming and keeping close relationships, understanding others, managing conflict). Hold both halves, self and other, because the dimensional model that follows is built on exactly this pair.

PEARL

The two manuals fight over how to sub-type personality pathology but barely differ on what it *is*: DSM-5-TR and the ICD systems give very similar GENERAL definitions of personality disorder, each locating the core pathology in cognition about self and others, emotional experience and regulation, interpersonal relating and behavioural control (Companion). Learn the general definition once; it survives every classification change.

1.2 The general diagnostic criteria: the six-part gate

All six must hold before any type. The DSM-5-TR general personality disorder criteria are the cleanest checklist to memorise, and the ICD equivalents map onto them almost one to one. They run: an enduring pattern deviating markedly from cultural expectation, shown in at least two areas of functioning (Criterion A); the pattern is inflexible and pervasive across situations (B); it causes clinically significant distress or impairment (C); it is stable and long-standing with onset traceable to adolescence or early adulthood (D); it is not better explained by another mental disorder (E); and it is not due to a substance or another medical condition (F). Reproduce the block as one table; this is the highest-yield single object in the chapter.

CRITERION	WHAT IT REQUIRES
A - Pattern and areas	**An enduring pattern of inner experience and behaviour deviating markedly from the person's culture, shown in two or more of four areas: cognition, affectivity, interpersonal functioning, impulse control**
B - Pervasiveness	The pattern is inflexible and pervasive across a broad range of personal and social situations
C - Impairment	It leads to clinically significant distress or impairment in social, occupational or other important functioning
D - Onset and stability	The pattern is stable and of long duration, with onset traceable back at least to adolescence or early adulthood
E - Not another disorder	Not better explained as a manifestation or consequence of another mental disorder
F - Not organic or substance	Not attributable to the physiological effects of a substance or another medical condition (for example head trauma)

The DSM-5-TR general criteria for a personality disorder (A to F); the ICD-11 essential features map closely onto the same requirements.

RULE **Clear the gate, then name the type.** No specific personality disorder is diagnosed unless every general criterion (enduring, pervasive and inflexible, culturally deviant, onset by adolescence, impairing, and not better explained) is first satisfied. The type is a sub-question that only opens once the gate is passed.

1.3 The four channels of deviation (Criterion A)

Two or more of four must be involved. Criterion A is not satisfied by trouble in one domain of life; the enduring pattern must show up in **two or more of the four** channels below. Learning these four is what lets you defend a diagnosis, because they force you to demonstrate that the disturbance is broad rather than a single symptom.

Cognition

Ways of perceiving and interpreting self, other people and events (for example pervasive suspiciousness, or a chronically fragile self-image).

Affectivity

The range, intensity, lability and appropriateness of emotional response (for example constricted flat affect, or rapidly reactive mood).

Interpersonal functioning

The characteristic pattern of relating (for example detachment and avoidance, or intense and unstable relationships).

Impulse control

The regulation of urges and behaviour (for example recurrent recklessness, aggression or self-damaging impulsivity).

1.4 Enduring, pervasive and inflexible, with onset by adolescence (Criteria B and D)

Trait-like breadth and lifelong reach are what separate a disorder from an episode. The words are load-bearing. *Enduring* and *stable* mean the pattern has run for years, not weeks; ICD-11 asks for a disturbance persisting over an extended period, typically two years or more. *Pervasive and inflexible* mean it holds across a broad range of personal and social situations rather than being triggered by one relationship or setting, and that the person cannot flex out of it when circumstances change. *Onset by adolescence* or early adulthood means the roots are developmental: an **enduring pattern** that first appears in mid or late adult life is a red flag for a personality change due to another medical condition or an unrecognised substance use disorder, not a primary personality disorder (DSM-5-TR). A pattern that is genuinely pervasive and inflexible with onset by adolescence is the developmental signature you are hunting for.

1.5 Deviation from cultural expectation (the cultural criterion)

The yardstick is the person's own culture, not the clinician's. Criterion A demands **deviation from cultural expectation**: the pattern must depart markedly from what the individual's *own* culture expects in cognition, affect, relating and impulse control. DSM-5-TR is explicit that personality disorder must not be confused with problems of acculturation after migration, or with habits, customs, and religious or political values rooted in the person's background; behaviour that looks rigid or dysfunctional may in fact be an adaptive response to real cultural

constraints. This is not a soft caveat but part of the criterion itself, and it is where cross-cultural over-diagnosis happens.

TRAP **Reading personality through one culture's norms.** Scoring deference, family-embeddedness, religiously framed experience or protest that risks the person's own safety as pathological dependence, oddness or callousness, when it is normative in their community, converts a cultural difference into a false diagnosis. Judge deviation against the patient's culture, with an informant if needed.

1.6 Impairment or distress, and the two exclusions (Criteria C, E and F)

Deviance alone is not a disorder. A culturally deviant, enduring, pervasive pattern still is not a personality disorder unless Criterion C is met: it must cause clinically significant **impairment or distress** in social, occupational or other important functioning. Many people have marked, inflexible traits and function well; without the impairment or distress they carry a personality *style*, and ICD-11 formalises this as personality difficulty (QE50.7), a factor influencing health status rather than a mental disorder. The final two criteria are exclusions that protect against mislabelling: the pattern must not be better explained by another mental disorder (E), and must not be attributable to a substance or medical condition such as head trauma (F).

COMMON TRAP

The mirror error to over-diagnosis: reading the enduring interpersonal and cognitive changes of a chronic Axis I illness (long-standing depression, an anxiety disorder, early psychosis, a frontal lesion or ongoing substance use) as a personality disorder. Criteria E and F exist precisely to catch this. If a supposedly lifelong pattern in fact tracks the course of another disorder or a drug, the personality label is wrong.

1.7 The ego-syntonic quality, and trait versus state

The patient rarely complains of the very thing you are diagnosing. Classically the abnormal personality traits are **ego-syntonic**: they are experienced as part of the self and are not felt as problematic, in sharp contrast to the ego-dystonic symptoms of the neurotic disorders, which distress the patient and drive help-seeking. Two consequences follow. First, people with a personality disorder often do not present for the personality disorder itself, but for a comorbid depression, anxiety or crisis, so the diagnosis is easy to miss and easy to make only from collateral history. Second, and the single commonest error, the traits must be distinguished from *states*: features that emerge in response to a specific situational stressor or a transient mental state (a mood episode, an anxiety disorder, or substance intoxication) are not personality (DSM-5-TR). Because the pattern is developmental, in a person under eighteen the features must have been present for at least one year before a personality disorder is diagnosed, and antisocial personality disorder is never diagnosed before eighteen (DSM-5-TR), a rule with direct medico-legal force.

TRAP **Calling a state a trait.** The affective lability, impulsivity and stormy relationships of an acute mood episode, an intoxication or a fresh crisis are not a personality disorder unless the same pattern is enduring, pervasive and predates the current state. Diagnose personality when the patient is at baseline, not mid-storm.

INDIA

Personality disorders are substantially under-recognised in Indian practice, and the ego-syntonic quality is a large part of why: patients present for the comorbid depression, self-harm or family conflict, not for the personality pattern, so it is recorded only when it is actively looked for. Two further Indian angles are genuine. The cultural criterion bites hardest here: deference, joint-family interdependence and religiously framed experience are normative and must not be read as dependent, avoidant or odd pathology. And the disorder-specific psychotherapies are arriving but unevenly available: dialectical behaviour therapy and schema therapy are being delivered and culturally adapted at Indian tertiary and private centres rather than being widely accessible, which shapes what a realistic management plan can offer. The forensic reading of antisocial personality disorder in the Indian court context is carried in the Mental health legislation & forensic psychiatry notes.

1.8 The rule that governs the whole chapter, and the forward map

General criteria first; classification second. With the gate cleared, the chapter splits into two ways of describing what lies beyond it, both cross-mapped in the topics that follow. DSM-5-TR keeps the familiar *categorical* system: the ten types grouped into three clusters (A odd or eccentric, B dramatic or erratic, C anxious or fearful), plus a Section III alternative hybrid model. ICD-11 takes the opposite route, abolishing the categorical types for a *dimensional* model that rates a severity level first and then adds trait-domain qualifiers and an optional borderline pattern. Whichever framework an examiner uses, it is downstream of the same general criteria you have just cleared. The ten categorical types are worth carrying as a single skeleton from the outset.

CLUSTER	TYPE	DESCRIPTOR
A	Paranoid	Odd or eccentric
A	Schizoid	Odd or eccentric
A	**Schizotypal**	Odd or eccentric (schizophrenia-spectrum edge)
B	Antisocial	Dramatic, emotional or erratic
B	**Borderline**	Dramatic, emotional or erratic
B	Histrionic	Dramatic, emotional or erratic
B	Narcissistic	Dramatic, emotional or erratic
C	Avoidant	Anxious or fearful
C	Dependent	Anxious or fearful
C	Anankastic (obsessive-compulsive)	Anxious or fearful

The three DSM-5-TR clusters and ten categorical types; ICD-11 abolishes these types for a dimensional model, developed in the topics that follow.

WORKED EXAMPLE

A woman in her twenties is referred after an overdose following a break-up, described as having "borderline personality disorder". You do not accept the label yet; you run the gate. Is the pattern of stormy relationships, identity instability and impulsivity *enduring* and traceable to adolescence, or does it date from a recent depressive episode (Criterion D, and E)? Is it *pervasive* across settings, or confined to one relationship (B)? Does it cause impairment at baseline, not only in crisis (C)? Only when every general criterion holds do you move to the type-specific criteria. If the pattern proves to be a first depressive episode with situational distress, you have prevented a lifelong misdiagnosis.

GOOD TO REMEMBER

- **Personality disorder (general):** defining requirement is an enduring pattern of inner experience and behaviour, pervasive and inflexible, deviating markedly from cultural expectation in two or more of cognition, affectivity, interpersonal functioning and impulse control, with onset by adolescence, causing impairment or distress, and not better explained by another disorder, a substance or a medical condition. Discriminator from a personality *style*: the impairment or distress (Criterion C); ICD-11 codes the style short of this as personality difficulty. First diagnostic step: clear all the general criteria before naming any type.

1.9 The master hook for the whole chapter

One scaffold to reassemble the day. The chapter has four countable skeletons: the clusters and types, the ICD-11 trait domains, the borderline criterion count, and the core skills therapy. Carry them as one mnemonic now and every later topic hangs off it; the pieces are paid off in full at consolidation.

MNEMONIC

MAD BAD SAD, FIVE DOMAINS, NINE-FOR-FIVE, FOUR TO COPE

MAD BAD SAD are the three clusters holding the ten types: *mad* = Cluster A odd or eccentric (Paranoid, Schizoid, Schizotypal); *bad* = Cluster B dramatic or erratic (Antisocial, Borderline, Histrionic, Narcissistic); *sad* = Cluster C anxious or fearful (Avoidant, Dependent, Anankastic). **FIVE DOMAINS** are the ICD-11 trait qualifiers, hooked as *New Dogs Do Dig Antiques*: Negative affectivity, Detachment, Dissociality, Disinhibition, Anankastia (plus the optional borderline pattern). **NINE-FOR-FIVE** is borderline personality disorder, defined by **five or more of the nine** criteria. **FOUR TO COPE** is dialectical behaviour therapy and its four skills modules (mindfulness, interpersonal effectiveness, emotion regulation, distress tolerance). Four numbers, and the chapter rebuilds from one line.

3	10	5	4
DSM-5-TR CLUSTERS	CATEGORICAL PERSONALITY TYPES	ICD-11 TRAIT DOMAINS	DBT SKILLS MODULES

HOLD THIS

The general diagnostic criteria are a gate, not a description: an enduring, pervasive and inflexible pattern, deviating from cultural expectation, with onset by adolescence, causing impairment or distress, and not better explained otherwise, must all hold before any specific personality-disorder type is diagnosed.

2 · ICD-11 dimensional classification: severity and trait domains

Why this matters. This is the single highest-yield nosology point of the personality-disorders chapter, and the examiner knows it. The **ICD-11 dimensional** system did something no previous classification dared: it **abolished the categorical personality-disorder types altogether**. There is no ICD-11 code for paranoid, schizoid, dissocial, histrionic, anankastic, avoidant or dependent personality disorder. In their place stands a model that first rates **severity** and then, optionally, describes style. Get the architecture of that model straight, the severity gradient that leads and the five trait domain qualifiers that follow, and you can answer almost any framework stem the paper sets.

The governing idea is a reversal of habit. The old question was "which type is this?"; the ICD-11 question is "how severe is the personality dysfunction, and what is its flavour?". Severity is rated **first and leads** because the degree of disturbance in self and interpersonal functioning predicts outcome, service need and risk far better than any type label ever did (ICD-11 CDDR; New Oxford Textbook of Psychiatry). The alternative model of personality disorders in DSM-5-TR Section III (the hybrid AMPD) and the retained DSM-5-TR categorical clusters are cross-mapped here so the two systems can be held side by side, and a legacy ICD-10 box records exactly what was removed and why the categorical names still get tested. The accompanying figure lays the whole model out as one object: the severity gradient down one axis and the trait-domain qualifiers across the other, with the borderline pattern qualifier hung off to the side.

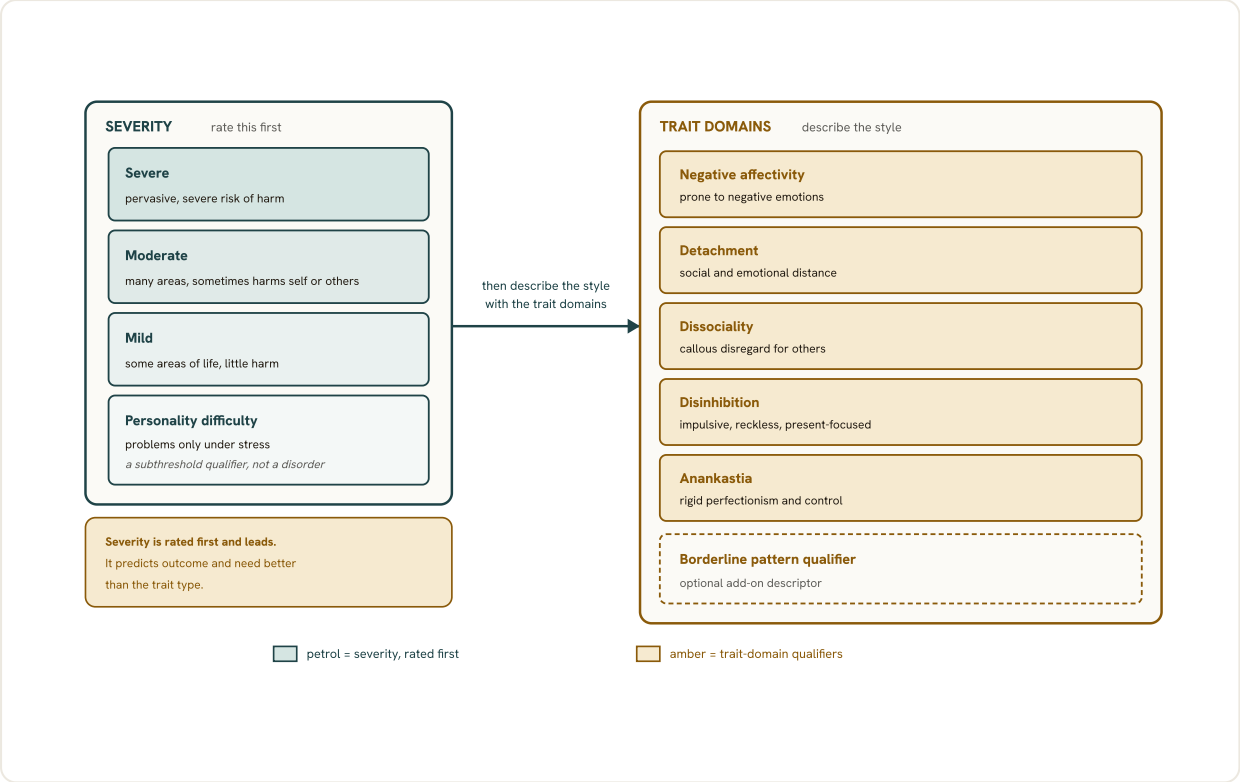


Fig 16.2 The ICD-11 model abolished the categorical types: rate severity first (personality difficulty, then mild, moderate or severe on a harm gradient), then describe the style with the five trait-domain qualifiers, negative affectivity, detachment, dissociality, disinhibition and anankastia, plus the optional borderline pattern qualifier.

2.1 The headline shift: types out, a dimensional model in

The ICD-11 dimensional model replaces the entire list of named types with a single diagnostic pathway (ICD-11 CDDR, grouping 6D10 to 6D11). You confirm the general criteria of a personality disorder (an enduring, pervasive, inflexible pattern of the self and of relationships, deviating from cultural expectation, with onset by adolescence or early adulthood and causing distress or impairment, all taught in the general-framework topic alongside), and then you make three moves in order. **First, rate severity** on a graded scale. **Second, add any of the five trait-domain qualifiers** that best describe the style of the disturbance. **Third, add the borderline pattern qualifier** if that specific picture is present. The type has vanished; the diagnosis is now a severity level plus a set of descriptive qualifiers. This is why the model is called dimensional rather than categorical: personality pathology is placed on continua of severity and trait, not sorted into boxes.

RULE **Severity is rated first and leads.** In the ICD-11 personality classification the degree of self-and-interpersonal dysfunction, not the type, is the primary axis, because severity predicts outcome and need better than any category.

2.2 How severity is defined, and why it carries the weight

Severity is judged on two linked capacities and one consequence. The capacities are **self functioning** (the stability and accuracy of identity, self-worth, self-direction and self-view) and **interpersonal functioning** (the desire and ability to form and sustain relationships, to grasp others' perspectives, and to manage conflict). The consequence is the associated **risk of harm** to self or others together with the breadth of functional impairment (ICD-11 CDDR). The rater asks

how pervasively these are disturbed, across how many domains of life, and with what danger attached. That single graded judgement then does the work the ten separate type-diagnoses used to do. The empirical case, built by Tyrer and the ICD-11 working group, is that the old categories overlapped so heavily that "type" was unreliable, whereas a simple severity rating tracks concurrent and prospective impairment robustly (New Oxford Textbook of Psychiatry).

PEARL

The reason severity leads is not administrative tidiness but prediction. Across longitudinal data the *severity* of personality dysfunction, more than its stylistic type, forecasts self-harm, suicide risk, service use, relationship breakdown and occupational failure. Rate severity well and you have already said the most prognostically useful thing about the patient.

2.3 The severity gradient: personality difficulty, then mild, moderate and severe

The gradient has a subthreshold rung and three disorder rungs. Personality difficulty (coded QE50.7, and deliberately placed not among the mental disorders but in the chapter on factors influencing health status) is **not a diagnosis of disorder**: it flags pronounced personality features that colour presentation or treatment without reaching the threshold. Above it sit mild personality disorder (6D10.0), moderate personality disorder (6D10.1) and severe personality disorder (6D10.2), separated by how many areas of functioning are affected and how much harm attaches. The table is the object to memorise; the highlighted cell in each row is the feature that fixes that level against its neighbours.

LEVEL (ICD-11 CODE)	SELF AND INTERPERSONAL FUNCTIONING	HARM AND IMPAIRMENT
Personality difficulty (QE50.7)	Pronounced features below the disorder threshold; some relevance to health or treatment	**Not a mental disorder; a health-status qualifier, not a diagnosis**
Mild personality disorder (6D10.0)	**Some areas of functioning affected, others spared; many relationships and expected roles still maintained**	Usually not associated with substantial harm to self or others
Moderate personality disorder (6D10.1)	**Marked problems in most relationships and most expected role functions; most areas of functioning affected**	May be associated with harm to self or others
Severe personality disorder (6D10.2)	**Severe disturbance of the sense of self (identity unstable or incoherent) and of nearly all relationships**	High risk of harm to self or others; severe functional impairment

The ICD-11 severity gradient: the subthreshold rung plus three disorder levels, read by degree of self-and-interpersonal dysfunction and attached risk of harm.

2.4 The five trait-domain qualifiers: describing the style once severity is set

Once severity is rated, one or more **trait-domain qualifiers** (postcoordinated codes 6D11.0 to 6D11.4) describe the prominent style of the disturbance. Each trait domain is a broad dimension,

not a type; a patient may carry several. The five, verbatim in construct, are set out below. Note the mnemonic order and hold them as a closed set: a sixth invented domain, or a missing one, is the classic slip.

Negative affectivity (6D11.0)
A tendency to experience a broad range of negative emotions (anxiety, anger, self-loathing, emotional lability, mistrust).

Detachment (6D11.1)
A tendency to maintain interpersonal and emotional distance: social withdrawal, aloofness, limited emotional expression and experience of pleasure.

Dissociality (6D11.2)
Disregard for the rights and feelings of others; self-centredness and lack of empathy, with grandiosity or callousness.

Disinhibition (6D11.3)
Acting rashly and impulsively on immediate stimuli, without consideration of consequences; recklessness and poor planning.

Anankastia (6D11.4)
A rigid focus on one's own and others' standards, commonly shown as perfectionism and emotional and behavioural constraint.

MNEMONIC

"N, then D-D-D, then A"

The five ICD-11 trait domains in order: **N**egative affectivity, then the three D's, **D**etachment, **D**issociality, **D**isinhibition, and finally **A**nankastia. The three D's are easy to muddle, so anchor them: detachment is *distance*, dissociality is *disregard for others*, disinhibition is *daring impulsivity*. The borderline pattern is a sixth token that sits apart, an optional add-on qualifier, not one of the five domains.

2.5 The borderline pattern qualifier: the one pattern that survived

The single named picture the ICD-11 kept is the borderline pattern qualifier (6D11.5), added for clinical utility and continuity with a large treatment literature (ICD-11 CDDR). It is an **additional qualifier**, not a type and not a trait domain, and it typically overlaps the domains (especially negative affectivity and disinhibition). It marks a pervasive pattern of instability of interpersonal relationships, self-image and affect together with marked impulsivity, defined by **five or more of the nine** features: frantic efforts to avoid abandonment; unstable, intense relationships that swing between idealisation and devaluation; identity disturbance; impulsivity that is potentially self-damaging; recurrent self-harm or suicidal behaviour; affective instability; chronic emptiness; inappropriate intense anger; and transient stress-related paranoid ideation or dissociation (Kaplan & Sadock CTP 2024). The threshold and the nine features are the same set the DSM-5-TR uses for borderline personality disorder, which is why the borderline construct crosses cleanly between the systems while the other types do not. The boundary with complex post-traumatic

stress disorder, a distinction ICD-11 sharpened by introducing both, is drawn in the Anxiety, OCD and trauma-related disorders notes.

GOOD TO REMEMBER

- **ICD-11 personality classification:** no types; rate severity first (personality difficulty, then mild, moderate, severe by self-and-interpersonal dysfunction and risk of harm), then add trait qualifiers.
- **The five trait domains:** negative affectivity, detachment, dissociality, disinhibition, anankastia; they describe style, not severity, and several may co-occur.
- **Borderline pattern qualifier (6D11.5):** the one retained pattern; an add-on qualifier defined by five or more of the nine borderline features; overlaps the domains, not a type.

2.6 Assembling a diagnosis: how the pieces combine in practice

A finished ICD-11 personality diagnosis is a severity level with any qualifiers appended, coded by postcoordination. You never stop at a trait: a qualifier without a rated severity is an incomplete diagnosis. The clinical value is that the same language scales from a screening judgement to a detailed formulation, and that severity, the part that drives the management plan and the risk assessment, is stated up front rather than buried inside a type label. The bipolar-II differential that so often shadows an affectively unstable presentation is worked in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes; the forensic reading of a prominent dissociality trait belongs to the Mental health legislation and forensic psychiatry notes.

WORKED EXAMPLE

A woman in her twenties has an incoherent sense of who she is, stormy relationships that collapse repeatedly, recurrent self-cutting after perceived abandonment, chronic emptiness and stress-related dissociation. Work the model in order. General criteria met. Severity: the self is severely disturbed and almost all relationships are affected with a high risk of self-harm, so this is severe personality disorder (6D10.2). Trait qualifiers: prominent negative affectivity and disinhibition. Pattern: the picture meets five or more of the nine borderline features, so add the borderline pattern qualifier (6D11.5). The diagnosis is "severe personality disorder with negative affectivity, disinhibition and a borderline pattern", not "borderline personality disorder" as a type.

2.7 Cross-map to DSM-5-TR: the categorical clusters and the AMPD hybrid

DSM-5-TR did not follow the ICD-11 all the way. Its main text **retains the categorical system**: three clusters (A the odd or eccentric, B the dramatic or erratic, C the anxious or fearful) holding ten types. In parallel, Section III offers the **alternative model of personality disorders**, a hybrid that mirrors the ICD-11 logic: Criterion A rates self and interpersonal functioning on the Level of Personality Functioning Scale (self as identity and self-direction; interpersonal as empathy and intimacy), and Criterion B specifies five pathological trait domains with 25 facets (Kaplan & Sadock CTP 2024). The two dimensional systems are close cousins but their trait sets are not identical, and the mismatch is examinable. The grid below is the discriminator to hold.

ICD-11 TRAIT DOMAIN	DSM-5-TR AMPD COUNTERPART	NOTE
Negative affectivity	Negative affectivity	Shared construct
Detachment	Detachment	Shared construct
Dissociality	Antagonism	**Same construct, different name**
Disinhibition	Disinhibition	Shared construct
Anankastia	(no AMPD domain)	**ICD-11 only; a constraint pole absent from the AMPD**
(no ICD-11 domain)	Psychoticism	**DSM only; ICD-11 places schizotypal with the psychoses, so it has no psychoticism domain**

The two dimensional trait sets: four align, but ICD-11 carries anankastia and the AMPD carries psychoticism; the highlighted rows are where they part.

TRAP **Do not equate the ICD-11 five with the DSM-5 AMPD five.** Anankastia is ICD-11-only and psychoticism is DSM-only; the schizotypal-versus-schizophrenia placement is set out in the Schizophrenia: aetiology, phenomenology, classification and course notes.

2.8 The legacy ICD-10 box: what changed and why the old names still get tested

The break from ICD-10 is total, which is exactly why the categorical vocabulary refuses to die. Knowing what was removed is itself the exam point.

ICD-10 TO ICD-11: WHAT CHANGED

ICD-10 (F60) **kept the categorical specific types**: paranoid, schizoid, dissocial, emotionally unstable (impulsive and borderline subtypes), histrionic, anankastic, anxious or avoidant, and dependent personality disorder, with schizotypal sitting separately under the schizophrenia grouping. ICD-11 **removed all of these named types** and rebuilt the diagnosis as a severity level plus trait-domain qualifiers, keeping only the borderline pattern as an optional qualifier. Exams still test the categorical names because DSM-5-TR retains them in its main text and clinicians still speak in them, so you must read fluently in both the dimensional and the categorical languages.

COMMON TRAP

Rating a trait qualifier while skipping severity, or naming "borderline personality disorder" as an ICD-11 type. In ICD-11 borderline is a *pattern qualifier* appended to a rated severity, never a standalone type; and no trait domain is a diagnosis on its own.

2.9 India and the cultural frame

Two India-specific cautions attach to this model. The first is **under-recognition**: personality disorders are diagnosed far less often in Indian clinical practice than Western prevalence would predict, an under-detection documented in Indian samples (Gupta & Mattoo, on personality-disorder prevalence and demography). A severity-led system that begins with a graded judgement of self-and-interpersonal dysfunction, rather than demanding a full type match, is well suited to

catching the milder end that Indian services routinely miss. The second is the **cultural expression of pathology**: the general criteria require deviation from what the person's own culture expects, so a self that is deeply embedded in family and community, or a deference and interdependence that would look like dependence through a Western lens, must not be read as disorder. The medico-legal weight of a prominent dissociality trait, which surfaces most sharply in offender assessment, is handled in the Mental health legislation and forensic psychiatry notes.

INDIA

Access to the structured psychotherapies that this severity framing points toward is uneven. Dialectical behaviour therapy and schema therapy are available and being culturally adapted in Indian metros and academic centres but remain scarce elsewhere, so a severe rating that mandates intensive structured therapy can outrun what a given service can deliver. Rate honestly, then match the plan to what is actually accessible, and never read collectivist family-embeddedness as a personality disorder.

5	3	5+	3 / 10
ICD-11 TRAIT DOMAINS	SEVERITY LEVELS (MILD, MODERATE, SEVERE)	OF NINE BORDERLINE-PATTERN FEATURES	DSM-5-TR CLUSTERS / TYPES (RETAINED)

HOLD THIS

ICD-11 has no personality-disorder types: rate severity first (personality difficulty, then mild, moderate, severe by self-and-interpersonal dysfunction and risk of harm), then add any of the five trait domains, negative affectivity, detachment, dissociality, disinhibition, anankastia, and the borderline pattern qualifier.

3 · DSM-5 categorical clusters and the alternative model

Two classifications of personality live side by side inside one manual. **dsm-5-tr** keeps, in its official Section II, the familiar **categorical clusters** and the **ten types** inherited almost unchanged from DSM-IV; and it offers, in its research Section III, an **alternative model**, a dimensional-categorical **hybrid model** (the **ampd**) that scores how badly the personality functions and profiles the traits that colour it. Knowing both, and being able to cross-map them onto the ICD-11 dimensional system, is the single highest-yield task on the personality-disorders paper.

Why it matters, and what this note owns. This note owns the DSM-5-TR side of the nosology: the three **categorical clusters** and their ten types with each type under its correct cluster, and the Section III **alternative model** in full, its Criterion A **level of personality functioning** scale and its Criterion B **pathological trait domains**. The ICD-11 dimensional model (the severity gradient and the five trait qualifiers) is taught forward in its own sibling note and only cross-mapped here; the deeper per-disorder phenomenology of each type lives in the cluster notes, and the general diagnostic criteria that gate any personality-disorder diagnosis are stated here only as the framing rule. The accompanying figure maps the ten types under the three clusters; a second figure alongside it lays the DSM-5 alternative model against the ICD-11 domains.

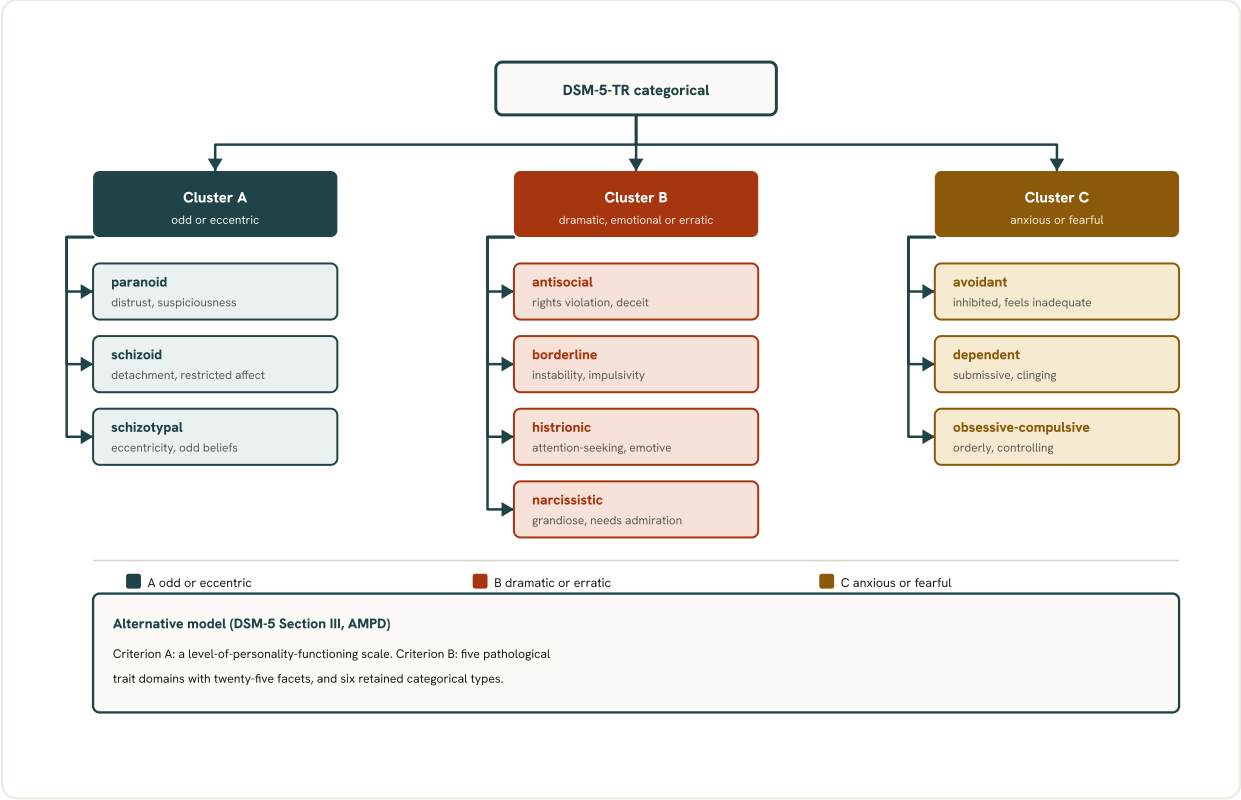


Fig 16.3 The DSM-5-TR keeps the ten categorical types in three clusters, A odd or eccentric, B dramatic or erratic, C anxious or fearful, with the Section III alternative model (a functioning scale plus pathological trait domains) alongside; ICD-10 kept these categories, which is why exams still test them.

3.1 Two systems in one manual: Section II categorical, Section III alternative

The structural fact to state first. dsm-5-tr carries *both* a categorical and a dimensional account of personality disorder. Section II, the official classification for routine clinical use, retains the ten categorical types grouped into three **categorical clusters**, virtually unchanged from DSM-IV-TR (DSM-5-TR 2022). Section III, "Emerging Measures and Models", houses the alternative model (also called the **hybrid model** or **ampd**, the Alternative **dsm-5** Model for Personality Disorders), placed there for further study rather than official use. The APA Board of Trustees kept both deliberately: the categorical set to preserve continuity with clinical practice, and the hybrid model to answer the categorical system's well-known failings (excessive comorbidity between types, and "other specified" being the commonest and least informative diagnosis).

Why the split is examinable. The examiner wants you to be fluent in the official categorical vocabulary (paranoid, borderline, and the rest) *and* able to explain the model that is expected to replace it. That is the through-line of the whole chapter: teach the dimensional direction of travel (ICD-11 has already abolished the categorical types entirely), but master the categorical names because Section II, everyday communication and most examinations still run on them.

GOOD TO REMEMBER

- **DSM-5-TR dual structure:** Section II retains the official categorical system, three clusters and ten types unchanged from DSM-IV-TR; Section III offers the alternative (hybrid AMPD) model for further study; both are printed in the same manual by deliberate APA decision, the categorical for continuity, the dimensional to fix comorbidity and the uninformative "unspecified" default.

3.2 The gate before any label: the general criteria for a personality disorder

The pattern precedes the type. No cluster and no type may be assigned until the general criteria for a personality disorder are met: an enduring, pervasive, inflexible pattern of inner experience and behaviour that *deviates markedly from the expectations of the individual's culture*, is stable over time, traceable to **adolescence or early adulthood**, and leads to distress or impairment, and is not better explained by another mental disorder, a substance, or a medical condition (DSM-5-TR 2022). The same seven general criteria (A to G) sit at the head of the Section III model, where Criterion A is reframed as moderate or greater impairment in personality functioning and Criterion B as one or more pathological traits, but the enduring, pervasive, culturally-deviant, early-onset spine is identical.

Deviation is judged against the person's own culture. The cultural clause is not decorative; the pattern must deviate from the norms of the individual's *own* cultural, ethnic and social reference group, and manifest across cognition, affectivity, interpersonal functioning and impulse control. Reading a migrant's habits, a subculture's mores, or a life-stage's turbulence as personality pathology is the classic misdiagnosis this criterion exists to block.

RULE **The enduring pattern before the label.** Establish the general personality-disorder criteria first, an inflexible, pervasive, culturally-deviant pattern stable since adolescence or early adulthood with distress or impairment, and only then place the cluster and the type; the cluster or the AMPD trait profile is meaningless without that gate.

TRAP **State mistaken for trait.** Do not label situational or episodic features a personality disorder: calling a passing affective lability "borderline" without the enduring identity disturbance and abandonment features, or reading a cultural or developmental norm as pathology, breaks the general criteria and is the commonest error on this topic.

3.3 Cluster A, the odd or eccentric cluster

The cluster and its three types. **cluster a** groups the personality disorders whose sufferers "often appear odd or eccentric" (DSM-5-TR 2022): paranoid personality disorder (a pervasive distrust and suspiciousness, reading others' motives as malevolent), schizoid personality disorder (detachment from social relationships with a restricted, flattened emotional range, the person is a genuine loner who does not want closeness), and schizotypal personality disorder (acute social discomfort with cognitive and perceptual distortions and eccentricities, ideas of reference, odd beliefs and magical thinking, unusual perceptions). The cluster's phenomenology shades toward the schizophrenia spectrum.

The boundary that is tested. Schizotypal is the one to place carefully: its cognitive-perceptual eccentricities are attenuated, not frank psychosis, so it stays a personality disorder in DSM-5-TR (though it is cross-listed with the schizophrenia spectrum), and mislabelling it as schizophrenia is a standard error, developed in the Schizophrenia: aetiology, phenomenology, classification and course notes.

GOOD TO REMEMBER

- **Cluster A (odd or eccentric):** paranoid (pervasive distrust and suspiciousness), schizoid (detachment with restricted emotion, a contented loner), schizotypal (social discomfort plus cognitive-perceptual distortions, ideas of reference, magical thinking); the discriminator from the schizophrenia spectrum is that the distortions are attenuated, not frankly psychotic.

3.4 Cluster B, the dramatic, emotional or erratic cluster

The cluster and its four types. **cluster b** groups those who "often appear dramatic, emotional, or erratic" (DSM-5-TR 2022): antisocial personality disorder (a pervasive disregard for and violation of the rights of others, deceit, impulsivity, aggression and lack of remorse, requiring evidence of conduct disorder before the age of fifteen years), borderline personality disorder (instability of relationships, self-image and affect with marked impulsivity), histrionic personality disorder (pervasive excessive emotionality and attention seeking), and narcissistic personality disorder (grandiosity, need for admiration and lack of empathy). This is the cluster that dominates the clinic and the examination, borderline above all.

Two exam anchors. Antisocial personality disorder is the one type DSM-5-TR will not diagnose before the age of eighteen years and only with a documented childhood conduct disorder, and it carries the forensic weight of the chapter (offender assessment, court reports), developed in the Mental health legislation and forensic psychiatry notes. Borderline is the flagship carried in detail below and across the day.

GOOD TO REMEMBER

- **Cluster B (dramatic, emotional or erratic):** antisocial (disregard for and violation of others' rights; needs conduct disorder before age fifteen and diagnosis only from age eighteen), borderline (instability of relationships, self-image and affect with impulsivity), histrionic (excessive emotionality and attention seeking), narcissistic (grandiosity, need for admiration, lack of empathy); it is the highest-yield cluster.

3.5 Cluster C, the anxious or fearful cluster, and the full ten-type map

The cluster and its three types. **cluster c** groups those who "often appear anxious or fearful" (DSM-5-TR 2022): avoidant personality disorder (social inhibition, feelings of inadequacy and hypersensitivity to negative evaluation, the person wants closeness but is too afraid of rejection to risk it), dependent personality disorder (a pervasive, excessive need to be taken care of, submissive and clinging behaviour, fear of separation), and obsessive-compulsive personality disorder (a preoccupation with orderliness, perfectionism and control at the expense of flexibility and efficiency). Avoidant is separated from social anxiety disorder by its pervasive, trait-level character, and obsessive-compulsive personality disorder is separated from OCD by the absence of true obsessions and compulsions, the confusion of the anankastic character with the anxiety disorder being a stock trap.

The ten under the three. The mapping to reproduce cold, three **categorical clusters** holding **ten types**, is set out in the table and the accompanying figure. DSM-5-TR itself warns that the clustering, though useful for teaching and research, "has serious limitations and has not been

consistently validated": types from different clusters co-occur freely, which is exactly the comorbidity problem the alternative model was built to solve.

CLUSTER	CHARACTER	TYPE	ONE-LINE SIGNATURE
Cluster A	**Odd or eccentric**	Paranoid	Pervasive distrust and suspiciousness; reads motives as malevolent
Cluster A	Odd or eccentric	Schizoid	Detachment from relationships; restricted emotion; a contented loner
Cluster A	Odd or eccentric	Schizotypal	**Social discomfort plus cognitive-perceptual distortions and eccentricity**
Cluster B	**Dramatic, emotional or erratic**	Antisocial	Disregard for and violation of others' rights; deceit, impulsivity, no remorse
Cluster B	Dramatic, emotional or erratic	Borderline	**Instability of relationships, self-image and affect; marked impulsivity**
Cluster B	Dramatic, emotional or erratic	Histrionic	Excessive emotionality and attention seeking
Cluster B	Dramatic, emotional or erratic	Narcissistic	Grandiosity, need for admiration, lack of empathy
Cluster C	**Anxious or fearful**	Avoidant	Social inhibition, feelings of inadequacy, fear of negative evaluation
Cluster C	Anxious or fearful	Dependent	Excessive need to be cared for; submissive, clinging; fear of separation
Cluster C	Anxious or fearful	Obsessive-compulsive	**Preoccupation with order, perfectionism and control; not OCD**

The DSM-5-TR Section II categorical system: three clusters holding ten types; the discriminator cells flag the boundaries most often tested (schizotypal versus schizophrenia, borderline as the flagship, obsessive-compulsive personality versus OCD) (DSM-5-TR 2022).

MNEMONIC

Weird, Wild, Worried

The three clusters by feel. **Cluster A** is **Weird** (odd or eccentric: Paranoid, Schizoid, Schizotypal, the three "P-S-S" types). **Cluster B** is **Wild** (dramatic, emotional or erratic: Antisocial, Borderline, Histrionic, Narcissistic). **Cluster C** is **Worried** (anxious or fearful: Avoidant, Dependent, Obsessive-compulsive). Three, four, three, adding to the ten types.

GOOD TO REMEMBER

- **Cluster C (anxious or fearful):** avoidant (social inhibition and fear of negative evaluation; wants but fears closeness), dependent (excessive need to be cared for, clinging, fear of separation), obsessive-compulsive personality (orderliness, perfectionism and control without true obsessions or compulsions); the whole set is three clusters and ten types, a clustering DSM-5-TR itself flags as weakly validated.

ICD-10 LEGACY: WHAT CHANGED

The old ICD-10 KEPT a categorical list of personality disorders largely paralleling the DSM types (paranoid, schizoid, dissocial for antisocial, emotionally unstable with an impulsive and a borderline type, histrionic, anankastic for obsessive-compulsive, anxious for avoidant, and dependent), with two familiar divergences: narcissistic sat only under "other specific personality disorder", and schizotypal was placed in the schizophrenia and delusional-disorders grouping, not among the personality disorders. ICD-11 then made the sharpest break of all: it *abolished* every one of these discrete categorical types, replacing them with a single personality-disorder diagnosis rated by severity (personality difficulty, then mild, moderate or severe) plus five trait qualifiers and a borderline pattern qualifier. Examinations still test the categorical names because DSM-5-TR Section II retains them, decades of literature and clinical communication use them, and the dimensional transition is recent, so the vocabulary of clusters and types remains the shared currency even where the official classification has moved on.

3.6 Borderline personality disorder: the flagship type and the five-of-nine threshold

The criterion to state cold. borderline personality disorder is "a pervasive pattern of instability of interpersonal relationships, self-image, and affects, and marked impulsivity, beginning by early adulthood", diagnosed when **five or more of the nine** criteria are present (DSM-5-TR 2022). The nine are: frantic efforts to avoid abandonment; a pattern of unstable, intense relationships alternating between idealisation and devaluation; identity disturbance; impulsivity in at least two potentially self-damaging areas; recurrent suicidal or self-mutilating behaviour; affective instability due to marked reactivity of mood; chronic feelings of emptiness; inappropriate, intense anger; and transient, stress-related paranoid ideation or severe dissociative symptoms.

Why the threshold is worth memorising. The **five or more of the nine** rule is the count most likely to be asked, and it is the reason a polythetic categorical system produces so many symptom combinations: two people can each carry the borderline label while sharing only one of the nine features. That combinatorial sprawl is the empirical case for the dimensional models. The borderline-versus-bipolar-II discrimination (do not start a mood stabiliser for personality-based

instability) and the biosocial and psychotherapeutic detail are developed elsewhere in the day and in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes.

GOOD TO REMEMBER

- **Borderline personality disorder:** a pervasive pattern of instability of relationships, self-image and affect with marked impulsivity from early adulthood; diagnosed on five or more of the nine criteria (abandonment fears, idealisation-devaluation, identity disturbance, impulsivity, recurrent self-harm or suicidality, affective instability, chronic emptiness, intense anger, transient paranoia or dissociation); the first diagnostic step is the enduring pattern, and the five-of-nine polythetic threshold is why the same label covers very different presentations.

3.7 The alternative model (AMPD): a dimensional-categorical hybrid

What the hybrid does. The Section III alternative model for personality disorders redefines a personality disorder as the combination of two things: *impairment in personality functioning* (Criterion A) and one or more *pathological personality traits* (Criterion B) (DSM-5-TR 2022). It is a **hybrid model** because it fuses a dimensional severity axis (how impaired the personality is) with a dimensional trait profile (which traits are elevated), then still allows six named categorical diagnoses to be reconstructed from those dimensions. The general criteria C to G (inflexible and pervasive, stable since adolescence or early adulthood, not better explained by another disorder, a substance or a developmental or cultural norm) carry over unchanged.

The two determinations. Diagnosing under the **ampd** requires two assessments in order: first rate the level of impairment in personality functioning (Criterion A) on the Level of Personality Functioning Scale, then evaluate the pathological personality traits (Criterion B) across the trait domains. A *moderate* or greater impairment in personality functioning is the entry threshold; below it, no personality disorder is diagnosed however the traits fall.

GOOD TO REMEMBER

- **Alternative model (AMPD):** the DSM-5 Section III dimensional-categorical hybrid; a personality disorder is impairment in personality functioning (Criterion A) plus one or more pathological personality traits (Criterion B), retaining general criteria C to G; diagnosis runs A then B, with moderate or greater functional impairment the required entry threshold; it exists to cure the categorical system's comorbidity and its uninformative "unspecified" default.

3.8 Criterion A: the Level of Personality Functioning scale (self and interpersonal)

The self and interpersonal axes. Criterion A grades disturbance in *self* and *interpersonal* functioning on the Level of Personality Functioning Scale (DSM-5-TR 2022). Self functioning has two elements, identity and self-direction; interpersonal functioning has two, empathy and intimacy. The scale differentiates five levels of impairment, from little or no impairment (healthy) through some, moderate and severe to extreme; moderate impairment is the threshold that a personality disorder must reach. The severity of impairment also predicts whether the person has more than one personality disorder or one of the more severe types, which is why the **level of personality functioning** is rated first and leads.

Identity (self)

A stable, bounded sense of self; regulated self-esteem and accurate self-appraisal; capacity to experience and modulate a range of emotion.

Self-direction (self)
Pursuit of coherent short-term and life goals; constructive, prosocial internal standards; the ability to self-reflect productively.

Empathy (interpersonal)
Comprehension of others' experiences and motives; tolerance of differing perspectives; awareness of one's effect on others.

Intimacy (interpersonal)
Depth and duration of connection; the desire and capacity for closeness; mutuality of regard in relationships.

The four elements of personality functioning that anchor Criterion A of the alternative model; two are self elements, two interpersonal, graded across five severity levels with moderate impairment the diagnostic threshold (DSM-5-TR 2022).

GOOD TO REMEMBER

- **Criterion A (Level of Personality Functioning):** the AMPD severity axis, self functioning (identity, self-direction) and interpersonal functioning (empathy, intimacy) across five levels from little-or-no to extreme; moderate or greater impairment is required to diagnose any personality disorder, and severity predicts multiplicity and the more severe types, so it is rated first.

3.9 Criterion B: the five pathological trait domains, and the ICD-11 cross-map

The five domains and their facets. Criterion B profiles the personality across five broad pathological trait domains: **negative affectivity**, **detachment**, **antagonism**, **disinhibition** and **psychoticism**, which subdivide into twenty-five specific trait facets (DSM-5-TR 2022). Each named disorder's B criterion is a defined subset of those facets, for example antisocial personality disorder draws on Antagonism and Disinhibition, avoidant on Negative Affectivity and Detachment. The five domains are the maladaptive-range extensions of the Big Five personality dimensions.

The cross-map to ICD-11, the point examiners love. The ICD-11 dimensional model, taught forward in its own note, uses its own five trait qualifiers, and four broadly correspond to the DSM-5 **pathological trait domains**: negative affectivity, detachment, dissociality (aligning with DSM-5 Antagonism) and disinhibition are shared. The fifth is where they part: DSM-5 has **psychoticism** (which ICD-11 has no equivalent domain for), while ICD-11 has **anankastia** (which DSM-5 folds into low Disinhibition rather than naming). ICD-11 then adds a borderline pattern qualifier on top of its domains, a feature the DSM-5 trait set does not carry.

DSM-5 ALTERNATIVE-MODEL DOMAIN	ICD-11 TRAIT QUALIFIER	WHAT IT CAPTURES
Negative affectivity	Negative affectivity	Frequent, intense negative emotions (anxiety, insecurity, emotional lability)
Detachment	Detachment	Social and emotional withdrawal, avoidance of intimacy, restricted emotion
Antagonism	**Dissociality**	Disregard for others; grandiosity, deceit, callousness, manipulation
Disinhibition	Disinhibition	Impulsivity, irresponsibility, recklessness, distractibility
Psychoticism (no ICD-11 domain)	**Anankastia (no DSM-5 domain)**	DSM-5: odd beliefs, unusual perceptions, eccentricity. ICD-11: rigidity, perfectionism, constraint

Cross-mapping the two dimensional trait systems: four domains broadly correspond, but the fifth differs, DSM-5 names Psychoticism where ICD-11 names Anankastia, and ICD-11 adds a borderline pattern qualifier the DSM-5 set lacks (DSM-5-TR 2022; ICD-11 CDDR).

COMMON TRAP

Do not treat the two dimensional systems as identical five-domain sets. Four domains align (negative affectivity, detachment, antagonism as ICD-11 dissociality, disinhibition), but the fifth is different in each: the DSM-5 alternative model has *psychoticism* and no anankastia domain, whereas ICD-11 has *anankastia* and no psychoticism domain. Naming psychoticism as an ICD-11 domain, or anankastia as a DSM-5 domain, is a straight error.

GOOD TO REMEMBER

- **Criterion B (pathological trait domains):** five domains, negative affectivity, detachment, antagonism, disinhibition and psychoticism, with twenty-five facets, each disorder's B criterion a defined subset; four align with the ICD-11 qualifiers (antagonism maps to dissociality), but DSM-5's fifth is psychoticism while ICD-11's is anankastia, and only ICD-11 adds a borderline pattern qualifier.

3.10 The six retained types and the trait-specified diagnosis

Ten collapse to six, plus a residual. Where the categorical system names ten types, the **alternative model** retains only six that can be diagnosed by their own criteria sets: antisocial, avoidant, borderline, narcissistic, obsessive-compulsive and schizotypal personality disorders (DSM-5-TR 2022). Each is defined by a characteristic Criterion A functioning impairment plus a specified Criterion B trait subset. The four categorical types dropped from the named list (paranoid, schizoid, histrionic, dependent) are not lost: when a personality disorder is present but no specific set is met, it is diagnosed as *personality disorder, trait specified* (PD-TS), recording the impairment level and the elevated trait domains directly.

How a diagnosis is built. To diagnose, say, avoidant personality disorder under the hybrid model, the clinician confirms moderate or greater impairment across the relevant functioning elements (Criterion A) and the specified maladaptive traits, here in Negative Affectivity and Detachment (Criterion B), then checks the general criteria C to G. The system's promise is that the profile itself, the severity level and the domain scores, carries the clinical information even when no tidy category fits, which is precisely the case in most real patients.

GOOD TO REMEMBER

- **The six AMPD types and PD-TS:** the alternative model diagnoses six specific types, antisocial, avoidant, borderline, narcissistic, obsessive-compulsive and schizotypal, each an A-functioning impairment plus a B-trait subset; the other cases (including the dropped paranoid, schizoid, histrionic and dependent) become personality disorder, trait specified, recorded by severity level and trait domains.

3.11 The India lens: under-recognition, cultural expression and the medico-legal frame

An under-recognised group read through the wrong culture. Personality disorders are markedly under-recognised in routine Indian practice: they present through their comorbidities (a mood or anxiety disorder, a substance problem, repeated self-harm) rather than as a personality diagnosis, they are under-coded, and the personality label is often avoided for fear of stigma. The cultural clause in the general criteria matters acutely here, deviation must be judged against the patient's own cultural, familial and social norms, so that collectivist family embeddedness is not misread as dependent personality, culturally sanctioned religious or ritual practice is not misread as schizotypal eccentricity, and gendered social scripts are not misread as histrionic or avoidant traits. The cultural expression of personality pathology is genuine and must be weighed before any type is fixed.

Where the label carries force. Antisocial personality disorder is the type with the sharpest medico-legal edge in Indian practice, surfacing in offender assessment, fitness and court reports, where a careful, non-pejorative formulation matters, and it is developed in the Mental health legislation and forensic psychiatry notes. On the treatment side, the structured psychotherapies that the borderline diagnosis calls for, dialectical behaviour therapy and schema therapy, are available only patchily outside the metros and are being culturally adapted for Indian settings; that availability gap, not the classification, is usually what limits care once the diagnosis is correctly made.

INDIA

Personality disorders are under-recognised in Indian practice, surfacing through comorbid mood, anxiety, substance or self-harm presentations and often left uncoded for fear of stigma. The general criteria's cultural clause is the safeguard: judge deviation against the patient's own cultural and social norms, so family embeddedness is not scored as dependency, religious practice not as schizotypal eccentricity, and social scripts not as histrionic or avoidant pathology. Antisocial personality disorder carries the medico-legal weight (offender and court work, cross-referenced to the forensic notes), and the structured psychotherapies borderline needs, dialectical behaviour therapy and schema therapy, are unevenly available and still being culturally adapted for India.

3	10	5	five
CATEGORICAL CLUSTERS (A ODD, B DRAMATIC, C ANXIOUS)	CATEGORICAL PERSONALITY-DISORDER TYPES ACROSS THE CLUSTERS	PATHOLOGICAL TRAIT DOMAINS IN THE DSM-5 ALTERNATIVE MODEL	OF THE NINE CRITERIA NEEDED TO DIAGNOSE BORDERLINE PERSONALITY DISORDER

HOLD THIS

DSM-5-TR keeps the categorical clusters in Section II (Cluster A odd or eccentric: paranoid, schizoid, schizotypal; Cluster B dramatic, emotional or erratic: antisocial, borderline, histrionic, narcissistic; Cluster C anxious or fearful: avoidant, dependent, obsessive-compulsive, ten types in all) and offers, in Section III, the alternative hybrid model (AMPD): Criterion A the Level of Personality Functioning scale (self: identity, self-direction; interpersonal: empathy, intimacy) plus Criterion B the five pathological trait domains (negative affectivity, detachment, antagonism, disinhibition, psychoticism), diagnosing six specific types; ICD-11 has abolished the categorical types for a severity-led dimensional model whose fifth domain is anankastia, not psychoticism, yet the categorical names remain the examinable vocabulary.

4 · Categorical versus dimensional approaches

Why this matters. This is the conceptual hinge of the whole personality-disorders chapter, and it is the stem an examiner reaches for when a single question has to test understanding rather than recall. The sibling notes teach the two live classifications in full, the DSM-5-TR categorical clusters and the ICD-11 dimensional model; this note owns the argument *between* them. The **categorical versus dimensional** debate asks a prior question: is a personality disorder a distinct kind of thing that you either have or do not, or a position on a set of continua that shade imperceptibly into ordinary personality? Answer that, and you can explain every failing of the old system and every design choice of the new one.

Held tightly, the **comparison of approaches** is a small object: two definitions, a short list of **strengths and weaknesses** on each side, and the reason the evidence tilted one way. The categorical approach trades validity for familiarity; the dimensional approach trades familiarity for validity and coverage; and the modern manuals split the difference, ICD-11 committing fully to dimensions while DSM-5-TR keeps the categories in front and files the dimensional model behind them for study. The accompanying figure lays the two approaches out as one grid, discrete boxes on one side against graded continua on the other, and it is the single image to carry for this

topic. The detailed severity gradient, the trait domains and the cluster map are developed in the sibling framework notes and only invoked here as evidence.



Feature	Categorical (DSM-5-TR, ICD-10)	Dimensional (ICD-11, DSM-5 AMPD)
Unit	Discrete named types	Severity and trait continua
Comorbidity and thresholds	Excessive comorbidity, arbitrary cut-offs	Handled on continua
Communicability	Familiar, easy to convey in a word	Less familiar, harder to convey
Validity and coverage	Within-type heterogeneity, a large not-otherwise-specified group	Covers the subthreshold majority, better validity
Exam bottom line	Still tested and clinically familiar	The direction the field moved

Paradigm header Deciding contrast for the row

Fig 16.4 Categorical classification names discrete types (familiar, but with excessive comorbidity, arbitrary thresholds and a large residual group), while dimensional classification grades severity and traits on continua (better validity and coverage of the subthreshold majority); the field moved dimensional, though the categories are still examined.

4.1 Two ways to carve personality: kinds versus degrees

The distinction to state first. The categorical approach holds that personality disorders are *qualitatively distinct clinical syndromes*, discrete kinds that a person either meets or does not, sorted into named types (DSM-5-TR 2022). The dimensional approach holds the opposite: that personality pathology represents *maladaptive variants of personality traits that merge imperceptibly into normality and into one another*, so that difference from health is one of degree, not of kind (DSM-5-TR 2022). One view draws boundaries and puts patients in boxes; the other places them on continua of severity and trait and reads their position. Everything else in the debate follows from this single fork, kinds against degrees.

Why the fork is not merely philosophical. The choice determines what the diagnosis can say. A category returns a name; a dimension returns a profile. Where a categorical system must decide a threshold above which a person "has" the disorder, a dimensional system can describe exactly how far along each continuum the person sits, and can keep describing the many people who fall below any categorical cut-off. The five-factor model of normal personality supplies the trait scaffolding the dimensional side builds on, its maladaptive poles becoming the pathological trait domains of the modern models (New Oxford Textbook of Psychiatry).

RULE **Kinds versus degrees is the whole debate.** The categorical approach treats a personality disorder as a discrete type you have or lack; the dimensional approach treats it as a position on continua of severity and trait that grade smoothly into normal personality. Every strength and weakness on either side is a consequence of this one choice.

4.2 The categorical approach: where it is strong

Familiarity and communicability are its real assets. The categorical approach is the default of clinical medicine: a diagnosis is a name, and a name is fast to assign, easy to record, and instantly communicable to another clinician in a single phrase (Tasman Psychiatry). Saying "borderline personality disorder" transmits a rich prototype in two words; there is a century of description, a large treatment literature and an examination vocabulary all built on the named types. The explicit operational criteria introduced from DSM-III onward gave the categories a further, genuine payoff: they let the field *document* substantial community and clinical prevalence, high rates of social and occupational impairment, and a more chronic course for co-occurring disorders (New Oxford Textbook of Psychiatry). These are not trivial gains, and they are why the categories have survived every attempt to retire them.

The prototype is the mechanism. Clinicians reason by pattern-matching a patient to a remembered exemplar, and the categorical types are ready-made prototypes. That cognitive fit, not evidence of natural boundaries, is the categorical system's durable strength: it maps onto how doctors actually think and talk.

PEARL

The categorical system persists because of its *communicative* value, not its scientific validity. The single most defensible thing to say for it is that a type name carries a whole clinical picture in one phrase, which is exactly what a busy clinic and a shared record need. Hold that as its strength, and its weaknesses become easier to name honestly.

4.3 The categorical approach: where it fails

Four failings, and they are examinable as a set. The problems are the mirror image of the discrete-kinds assumption, and the New Oxford Textbook lists them cleanly: *extensive co-occurrence of personality disorders* (excessive comorbidity, patients routinely meeting several type criteria at once), *considerable heterogeneity within categories* (two people can share a diagnosis while sharing almost none of its features), *arbitrary diagnostic thresholds without empirical bases* (the cut-off between disorder and no-disorder is a convention, not a natural join), and *incomplete coverage of the full range of personality pathology* (the many patients whose difficulty is real but does not match any single type). Temporal instability of the categories and their limited validity and clinical utility round out the indictment (New Oxford Textbook of Psychiatry).

Borderline is the worked case of heterogeneity. Because borderline personality disorder is polythetic, diagnosed on **five or more of the nine** criteria, two patients can each carry the label while overlapping on only one feature. That combinatorial sprawl is the categorical system's within-category heterogeneity made concrete, and it is the empirical case the dimensional models

were built to answer. The unstable, affectively reactive presentation also blurs into bipolar-II, a boundary drawn in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes.

The residual category tells the story. The clearest sign of incomplete coverage is that the residual not-otherwise-specified diagnosis (personality disorder not otherwise specified in DSM-IV, and the "other specified" and "unspecified" categories in DSM-5-TR) has been among the most frequently assigned of all the personality-disorder diagnoses, and is also the least informative one (DSM-5-TR 2022; New Oxford Textbook of Psychiatry). A system whose commonest verdict is "a personality disorder, but none of the ones we named" is telling you its named types do not cover the territory.

TRAP **Reading the types as non-overlapping natural kinds.** The categorical model implies the types are distinct and separable, but they co-occur freely and blur at every edge; treating a tidy single-type label as the natural truth of a patient, rather than a convenient summary, is the error the dimensional case exists to correct.

COMMON TRAP

Mistaking the frequency of the not-otherwise-specified diagnosis for clinician laziness. It is a structural signal, not a shortcut: the residual category is common *because* most real personality pathology is subthreshold or mixed and falls between the named types. That is the coverage problem, not a documentation problem.

4.4 The dimensional approach: its strengths

It fixes what the categories broke. By placing severity and traits on continua, the dimensional approach retains the information a category discards: a profile records how impaired the personality is and which traits are elevated, so two patients who would share one categorical label are told apart, and a patient who matches no type is still fully described (Tasman Psychiatry). This is why the empirical structure favours it: a meta-analytic review of many latent-structure studies found little persuasive evidence for discrete taxa underlying the personality disorders, with schizotypal the only possible partial exception (New Oxford Textbook of Psychiatry). If the underlying reality is continuous, a continuous model has better *validity* and, crucially, covers the subthreshold majority that the categorical cut-offs leave out.

Severity leads because severity predicts. The single most useful dimension is overall severity of personality dysfunction, which forecasts self-harm, service use, relationship breakdown and occupational failure better than any type label; rating it first is the design principle both modern dimensional systems adopt. The schizotypal exception, the one construct with some categorical support, sits at the schizophrenia-spectrum edge and is developed in the Schizophrenia: aetiology, phenomenology, classification and course notes.

4.5 The dimensional approach: its price

Validity is bought with unfamiliarity. The dimensional model's weaknesses are the reciprocal of its strengths. It is *less familiar* and harder to communicate: a severity level plus a set of trait

qualifiers does not compress into a single memorable phrase the way "narcissistic personality disorder" does, and clinicians trained on the types find the profiles unintuitive at first (New Oxford Textbook of Psychiatry). There has also been decades of *controversy over the best dimensional representation*, how many domains, which ones, how to set the severity anchors, though considerable consensus has now settled on a small set of core trait domains. Notably, once clinicians use the dimensional models they tend to find them *more* clinically useful than the categories, so the unfamiliarity is a transitional cost rather than a permanent defect (New Oxford Textbook of Psychiatry).

GOOD TO REMEMBER

- **Categorical approach:** personality disorders as qualitatively distinct kinds sorted into named types; strengths are clinical familiarity and one-phrase communicability plus documented prevalence, impairment and course; weaknesses are excessive comorbidity, within-category heterogeneity, arbitrary thresholds, temporal instability, limited validity, and incomplete coverage of the subthreshold majority (a large not-otherwise-specified group).
- **Dimensional approach:** personality pathology as maladaptive variants of traits on continua of severity and trait that merge into normality; strengths are better validity, retention of individual profile information and coverage of the subthreshold majority; weaknesses are unfamiliarity, harder single-phrase communication, and past controversy over the best representation.
- **The discriminator to state:** kinds versus degrees; every strength and weakness on each side follows from that one assumption.

4.6 The comparison of approaches, side by side

The object to reproduce cold. The **comparison of approaches** is best held as a two-column ledger of matched trade-offs; the highlighted cells are the points most often tested. Read across each row and the reciprocal structure is obvious: what one approach gains, the other loses.

DIMENSION OF COMPARISON	CATEGORICAL APPROACH	DIMENSIONAL APPROACH
Core claim	Distinct kinds; a disorder you have or lack	**Degrees; maladaptive variants merging into normality**
Diagnosis returns	A type name	A severity level plus a trait profile
Communicability	**High; one phrase carries a prototype**	Lower; a profile is harder to state briefly
Clinical familiarity	**High; the default of medicine, a century of use**	Low; newer and initially unintuitive
Comorbidity	**Excessive; types co-occur freely**	Dissolved; overlap is expected on shared traits
Within-category variation	Large; polythetic criteria yield heterogeneous cases	**Captured; the profile separates similar-looking patients**
Thresholds	Arbitrary, without empirical basis	Graded; the cut is a chosen point on a continuum
Coverage of subthreshold pathology	Poor; a large not-otherwise-specified residual	**Good; the subthreshold majority is still described**

DIMENSION OF COMPARISON	CATEGORICAL APPROACH	DIMENSIONAL APPROACH
Empirical validity	Limited; little evidence for discrete taxa	**Better; matches the continuous latent structure**

The categorical and dimensional approaches as matched trade-offs; the highlighted cells mark each side's decisive advantage, and every row is a consequence of the kinds-versus-degrees choice.

MNEMONIC

Categories COMMUNICATE, dimensions VALIDATE

The one-line split. The **categorical** approach wins on **C**ommunicability and **C**linical familiarity but is **C**omorbidity-ridden and **C**rudely-thresholded. The **dimensional** approach wins on **V**alidity, **V**ariation captured and coverage, but is unfamiliar and hard to state in a phrase. Communicate versus validate is the trade-off, and the field has decided validity should lead.

4.7 Why the field moved to dimensional

The evidence tilted, then the manuals followed. The reason for the shift is not fashion but data. Latent-structure research found little support for discrete personality-disorder taxa, and by a 2007 survey a large majority of personality-disorder experts, some **eighty-seven per cent**, judged that personality pathology was dimensional in nature (New Oxford Textbook of Psychiatry). The verdict in the literature is that the classification of personality pathology has been "slowly but inexorably moving from a categorical to a dimensional model", because a dimensional model better reflects the continuous phenomena and better describes both the distance from normal personality and the degree of severity. That, in a phrase, is **why the field moved to dimensional**: the discrete kinds the categories assume do not appear to exist, and continua describe the reality and predict the outcomes better.

Two manuals, two speeds of change. ICD-11 made the full commitment: it abolished the categorical types outright and rebuilt the diagnosis as a severity rating (personality difficulty, then mild, moderate or severe) followed by the trait-domain qualifiers and an optional borderline pattern, the model taught forward in the ICD-11 dimensional-classification note. DSM-5-TR was more cautious, and its caution is itself the examinable compromise: it kept the familiar categorical clusters and ten types in Section II for everyday use, and placed the alternative model of personality disorders (the AMPD, a dimensional-categorical hybrid built on the Level of Personality Functioning Scale plus five trait domains) in Section III for further study, developed in the DSM-5 categorical-clusters note. The hybrid is the evidence-driven middle path: it scores personality functioning and traits dimensionally, yet still lets a handful of named types be reconstructed, so the field can move toward dimensions without discarding a century of clinical vocabulary at once.

ICD-10 TO ICD-11: WHAT CHANGED

ICD-10 (F60) **kept the categorical types**, paranoid, schizoid, dissocial, emotionally unstable, histrionic, anankastic, anxious and dependent, in step with the DSM tradition. ICD-11 **removed every one of them** and replaced the list with a severity-led dimensional diagnosis plus trait qualifiers and a borderline pattern qualifier. This is the field moving to dimensional in its purest form. Examinations still test the categorical names because DSM-5-TR Section II retains them, because decades of literature and clinical communication run on them, and because the transition is recent, so a candidate must read fluently in both the categorical and the dimensional languages.

WORKED EXAMPLE

Take the same patient through both approaches. A man in his thirties has rigid perfectionism and interpersonal coldness, plus marked suspiciousness, but does not fully meet any single type. The *categorical approach* stalls: he has features of obsessive-compulsive, paranoid and schizoid personality disorder, meets none cleanly, and is filed as a personality disorder, unspecified, a label that says almost nothing. The *dimensional approach* succeeds: rate moderate personality dysfunction and note prominent anankastia and detachment with some negative affectivity, and the profile describes him precisely and guides the plan. The contrast is the whole argument in one case: the category returns a shrug, the dimensions return a description.

4.8 The India lens and the cultural frame

Under-recognition meets a severity-led model. Personality disorders are markedly under-recognised in routine Indian practice: they surface through comorbid mood, anxiety, substance or self-harm presentations rather than as a personality diagnosis, and the personality label is often avoided for fear of stigma (Gupta and Mattoo, on Indian personality-disorder prevalence and demography). A severity-led dimensional system, which begins with a graded judgement of self-and-interpersonal dysfunction rather than demanding a full type match, is well suited to catching the milder and mixed presentations that categorical thresholds cause Indian services to miss. The categorical versus dimensional choice is therefore not only academic here; the dimensional route may materially improve detection.

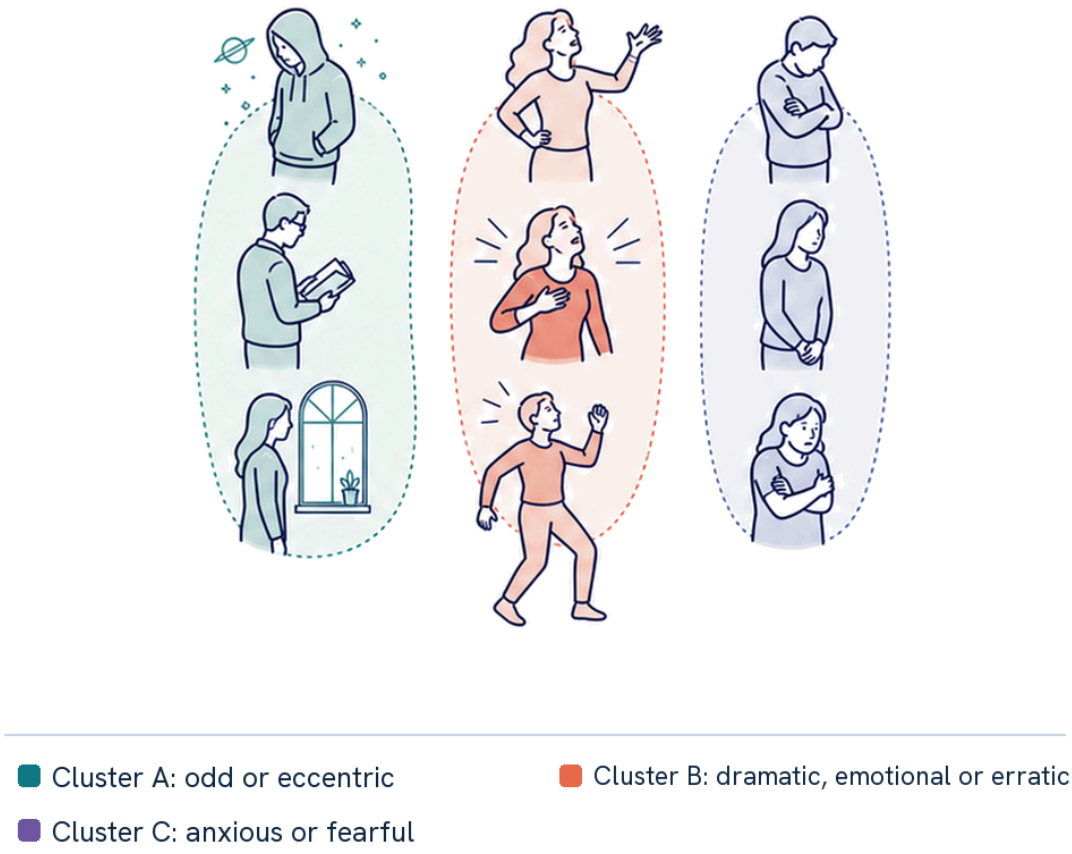


Fig 16.5 The legacy DSM categorical model groups personality disorders into Cluster A, odd or eccentric; Cluster B, dramatic, emotional or erratic; and Cluster C, anxious or fearful. ICD-11 instead prioritises severity and trait domains.

The cultural expression of pathology cuts across both. Whichever approach is used, the general criteria require deviation from what the person's *own* culture expects, so a self deeply embedded in family and community, or a deference and interdependence that would read as dependence through a Western lens, must not be scored as disorder; personality pathology must not be read through a single culture's norms. On the treatment side, the structured psychotherapies a dimensional severity rating points toward, dialectical behaviour therapy and schema therapy, are available and being culturally adapted in Indian metros and academic centres but remain scarce elsewhere, so a severe rating can outrun what a service can deliver. Antisocial personality disorder carries the sharpest medico-legal edge in Indian practice, and its offender and court framing is handled in the Mental health legislation and forensic psychiatry notes; the wider technique of the psychological therapies belongs to the Psychotherapies, clinical assessment, MSE and nosology notes.

INDIA

Personality disorders are under-recognised in Indian practice, presenting through their comorbidities and often left uncoded for fear of stigma; a dimensional, severity-first reading is better at catching the subthreshold and mixed cases that categorical cut-offs miss. Judge deviation against the patient's own cultural and social norms, so collectivist family-embeddedness is not scored as dependency and religiously framed experience not as schizotypal oddness. The structured psychotherapies that the dimensional model points to, dialectical behaviour therapy and schema therapy, are available and being culturally adapted in the metros and academic centres but unevenly accessible elsewhere; and antisocial personality disorder carries the medico-legal weight, cross-referenced to the forensic notes.

3 / 10	5	5+	87%
DSM-5-TR CATEGORICAL CLUSTERS / TYPES	DIMENSIONAL TRAIT DOMAINS (ICD-11 AND AMPD)	OF NINE BORDERLINE CRITERIA (THE POLYTHETIC THRESHOLD)	OF PD EXPERTS JUDGED PATHOLOGY DIMENSIONAL (2007 SURVEY)

HOLD THIS

The categorical approach treats a personality disorder as a discrete type (familiar and communicable, but comorbid, heterogeneous, arbitrarily thresholded and poor at covering the subthreshold majority); the dimensional approach treats it as severity plus traits on continua (better validity and coverage, but less familiar); the field moved to dimensional because the discrete kinds do not appear to exist, and ICD-11 abolished the types while DSM-5-TR keeps them in front with the AMPD hybrid behind as the evidence-driven compromise.

The personality disorders by cluster

5 . Cluster A: paranoid, schizoid and schizotypal

Why this cluster is worth its marks. **cluster a** is the **odd or eccentric** group, and it rewards a candidate who can do two things: give the one-line essential feature of each of its three types cold, and defend the boundaries that separate them from one another and from frank psychosis. The three are paranoid personality disorder (a pervasive distrust and suspiciousness in which others' motives are read as malevolent), schizoid personality disorder (detachment from social relationships with a restricted range of emotional expression), and schizotypal personality disorder (acute discomfort in close relationships together with cognitive or perceptual distortions and eccentricities of behaviour) (DSM-5-TR). The thread that ties them is a retreat from, or a distortion of, ordinary social relatedness, and at the schizotypal end that thread runs into the **schizophrenia spectrum**.

This fragment first frames the cluster on one grid, then takes each type through its defining criterion and the discriminator an examiner rewards, and finally isolates the single highest-yield boundary of the group, schizotypal versus schizophrenia, with the nosological twist that schizotypal is the one member that both manuals place, wholly or partly, among the psychotic disorders rather than the personality disorders. Two prior cautions carry over from the

framework topics of this chapter and are assumed throughout: the general personality-disorder criteria (an enduring, pervasive, inflexible pattern, culturally deviant, with onset by adolescence, causing impairment, and not better explained otherwise) must be cleared before any of these types is named; and ICD-11 has abolished the categorical types, so "paranoid" and "schizoid" as labels survive only in DSM-5-TR and in clinical shorthand. The deep pharmacology sits in the Schizophrenia: management, antipsychotics and adverse effects notes, the schizophrenia boundary in the Schizophrenia: aetiology, phenomenology, classification and course notes, and the wider psychotherapy technique in the Psychotherapies, clinical assessment, MSE and nosology notes.

5.1 The cluster on one frame

Three types, one thread, graded by how far from reality they drift. DSM-5-TR groups the three types whose sufferers "often appear odd or eccentric" (DSM-5-TR). Read the cluster as a gradient of departure from normal relatedness: paranoid personality disorder distrusts other people but keeps a firm hold on reality; schizoid personality disorder withdraws from other people without distorting them; schizotypal personality disorder adds to that withdrawal a layer of cognitive and perceptual oddness that shades toward, but never reaches, frank psychosis. Learning the three essential features and their thresholds as one block is the fastest route to every cluster A question.

TYPE	ESSENTIAL FEATURE (DSM-5-TR)	THRESHOLD	CORE DISCRIMINATOR
Paranoid	A pervasive distrust and suspiciousness such that others' motives are interpreted as malevolent	Four or more of the seven features	**Suspiciousness with reality intact; no cognitive-perceptual distortion**
Schizoid	Detachment from social relationships with a restricted range of emotional expression	Four or more of the seven features	**A contented loner: no desire for closeness at all**
Schizotypal	Acute discomfort in close relationships, plus cognitive or perceptual distortions and eccentricities of behaviour	Five or more of the nine features	**Odd cognition and perception; the schizophrenia-spectrum edge**

The three DSM-5-TR Cluster A types with their essential features, criterion thresholds and core discriminators; the accompanying figure lays the same three on a distrust-to-distortion gradient.

PEARL

A one-word tag per type keeps them apart under pressure: paranoid is *distrust*, schizoid is *detachment*, and schizotypal is *distortion* laid on top of detachment. The suspiciousness of paranoid and the aloofness of schizoid can both appear in schizotypal, but only schizotypal carries the odd beliefs, perceptions and speech; that added layer is the whole diagnosis.

5.2 Paranoid personality disorder

Malevolent motives read into a neutral world. The essential feature of paranoid personality disorder is a pervasive distrust and suspiciousness of others such that their motives are interpreted as malevolent, beginning by early adulthood and present across contexts, shown by **four or more of the seven** features (DSM-5-TR). The seven are: unjustified suspicion that others are exploiting, harming or deceiving them; preoccupation with doubts about the loyalty or trustworthiness of associates; reluctance to confide for fear the information will be used against them; reading hidden demeaning or threatening meaning into benign remarks or events; persistently bearing grudges; perceiving attacks on their character that are not apparent to others, with a quick angry counterattack; and recurrent unjustified suspicions about a partner's fidelity. The interpersonal signature is a person who scrutinises every action for hostile intent and cannot accept loyalty when it is shown. Crucially the beliefs are held with suspicion, not with delusional conviction: the patient can, at least in principle, acknowledge an alternative reading, which is exactly what separates this from a persecutory delusion (Companion).

GOOD TO REMEMBER

- **Paranoid personality disorder:** defining criterion is a pervasive distrust and suspiciousness in which others' motives are read as malevolent, four or more of the seven features present, from early adulthood. Discriminator upward from psychosis: the suspicions are not of delusional intensity and alternatives can be acknowledged (from delusional disorder and schizophrenia). Discriminator within the cluster: no cognitive-perceptual distortion or eccentricity, which would move it to schizotypal. First step: confirm the general personality-disorder criteria, then that the suspiciousness is pervasive and reality-based, not a fixed delusion.

5.3 Schizoid personality disorder

The genuine loner, not the frightened one. The essential feature of schizoid personality disorder is a pervasive pattern of detachment from social relationships and a restricted range of emotional expression in interpersonal settings, from early adulthood, shown by **four or more of the seven** features (DSM-5-TR). The seven are: neither desiring nor enjoying close relationships, including being part of a family; almost always choosing solitary activities; little interest in sexual experiences with another person; taking pleasure in few activities; lacking close friends or confidants other than first-degree relatives; indifference to praise or criticism; and emotional coldness, detachment or flattened affect. The person is a contented loner who does not want closeness, presenting a bland exterior with little visible emotional reactivity. The examiner's favourite contrast is with avoidant personality disorder: the avoidant person longs for relationships but is held back by fear of rejection, whereas the schizoid person has no desire for them in the first place. That single question, "do they want closeness?", separates the two.

GOOD TO REMEMBER

- **Schizoid personality disorder:** defining criterion is detachment from social relationships with a restricted, flattened range of emotional expression, four or more of the seven features, from early adulthood. Discriminator from avoidant: absence of any desire for closeness (avoidant desires it but fears rejection). Discriminator from schizotypal: detachment without cognitive-perceptual distortion or eccentricity. First step: establish that solitariness is preferred and pervasive, not a secondary retreat from anxiety, depression or psychosis.

5.4 Schizotypal personality disorder

Attenuated oddness, not frank psychosis. The essential feature of schizotypal personality disorder is a pervasive pattern of social and interpersonal deficits marked by acute discomfort with, and reduced capacity for, close relationships, together with cognitive or perceptual distortions and eccentricities of behaviour, shown by **five or more of the nine** features (DSM-5-TR). The nine are: ideas of reference (incorrect readings of casual events as having special personal meaning, but short of delusional conviction); odd beliefs or magical thinking influencing behaviour (superstition, belief in clairvoyance, telepathy or a "sixth sense"); unusual perceptual experiences including bodily illusions; odd thinking and speech (vague, digressive or over-elaborate, but without derailment or incoherence); suspiciousness or paranoid ideation; inappropriate or constricted affect; behaviour or appearance that is odd, eccentric or peculiar; lack of close friends other than first-degree relatives; and excessive social anxiety that does not ease with familiarity and is tied to paranoid fears rather than to negative self-judgement. Two distinctions matter. Ideas of reference are not delusions of reference: the difference is conviction. And the social anxiety, unlike the avoidant type's, does not settle as the person gets to know the setting, because it is driven by suspiciousness. Under stress these patients may have transient psychotic-like episodes lasting minutes to hours, usually too brief to meet the threshold for a brief psychotic disorder.

GOOD TO REMEMBER

- **Schizotypal personality disorder:** defining criterion is social and interpersonal deficits plus cognitive or perceptual distortions and eccentricity, five or more of the nine features, from early adulthood. Discriminator within the cluster: it is paranoid plus schizoid plus the distortion layer (odd beliefs, unusual perceptions, odd speech, eccentricity), which neither of the others has. Discriminator upward: the distortions are attenuated, ideas of reference not delusions, no sustained frank psychosis. First step: demonstrate the cognitive-perceptual oddness is enduring and trait-level, then that it never crosses into frank, sustained psychosis.

5.5 Schizotypal versus schizophrenia, and the schizophrenia-spectrum placement

The one member that belongs to the psychosis family. Schizotypal is the boundary the day is built to test. It is characterised by an enduring pattern of unusual speech, perceptions, beliefs and behaviours that resemble *attenuated* forms of the defining symptoms of schizophrenia (ICD-11 CDDR). The line from schizophrenia is drawn on intensity alone: schizophrenia is diagnosed when the symptoms are severe and sustained enough to meet its own threshold, and until then the presentation stays eccentric or peculiar rather than overtly psychotic. The familial evidence backs the kinship: schizotypal aggregates in the first-degree biological relatives of people with

schizophrenia and is regarded as part of the schizophrenia-related spectrum of psychopathology. This is why the classification treats it as a half-member of the personality-disorder family. DSM-5-TR lists it in the personality-disorders chapter but cross-lists it in the Schizophrenia Spectrum and Other Psychotic Disorders chapter and codes it F21. ICD-11 goes further and places schizotypal disorder (6A22) squarely within the schizophrenia and other primary psychotic disorders grouping, not among the personality disorders at all, continuing what ICD-10 did with F21. So while ICD-11 abolished paranoid and schizoid as categories, it kept schizotypal, but moved it out of the personality chapter entirely.

BOUNDARY	CLUSTER A SIDE	THE OTHER SIDE	DISCRIMINATOR
Schizotypal vs schizophrenia	Attenuated distortions; eccentric or peculiar; transient stress-related psychosis of minutes to hours	Frank, sustained delusions or hallucinations meeting threshold	**Intensity alone: attenuation versus frank sustained psychosis**
Schizotypal vs paranoid or schizoid	Cognitive-perceptual distortions and marked eccentricity present	Suspiciousness alone (paranoid) or detachment alone (schizoid)	Presence of the distortion and eccentricity layer
Schizoid vs avoidant	No desire for relationships; content in solitude	Desires relationships but fears rejection	Whether closeness is wanted at all
Paranoid vs delusional disorder	Suspicion not of delusional intensity; alternatives can be acknowledged	Fixed persecutory delusion held with conviction	Delusional conviction and intensity

The four boundaries most often tested around Cluster A; the highlighted cell is the single discriminator that decides schizotypal versus schizophrenia. The schizophrenia side is developed in the Schizophrenia: aetiology, phenomenology, classification and course notes.

RULE **Schizotypal is schizophrenia-spectrum, and the line is intensity.** ICD-11 codes schizotypal disorder 6A22 with the primary psychotic disorders, not the personality disorders; it is separated from schizophrenia by the attenuation of its symptoms alone, not by a different set of symptoms.

TRAP **Calling attenuated schizotypal features schizophrenia.** Ideas of reference, magical thinking, odd speech and eccentricity that never reach frank, sustained delusions or hallucinations are schizotypal, not schizophrenia; upgrading them to a psychotic diagnosis on their oddness alone is the classic error.

WORKED EXAMPLE

A man in his late twenties is referred as "possible schizophrenia". He has always been a fringe figure: he believes he can sense events before they happen, dresses in a way that does not quite fit together, speaks in a vague, over-elaborate way, and keeps to himself because he suspects colleagues mean him harm. There are no sustained delusions and no hallucinations; under stress he has had brief spells of feeling watched that pass within an hour or two. This is schizotypal personality disorder (or ICD-11 schizotypal disorder), not schizophrenia: the cognitive-perceptual features are attenuated and enduring, never crossing into frank, sustained psychosis. The label you avoid saves him a lifelong psychotic diagnosis and its treatment.

5.6 Management in outline, and the cultural reading

Engagement is the treatment; drugs are narrow and symptom-targeted. Cluster A is managed, not cured, and the deep detail is cross-referenced. No drug is disorder-specific for any of the three. The working mode is a structured, supportive psychotherapy delivered with a reliable, low-intensity, non-intrusive stance: for the paranoid and schizoid patient the whole difficulty is engagement, because suspiciousness or a genuine preference for solitude makes them slow to enter therapy and quick to leave it, and over-warmth or forced intimacy can rupture the alliance. For schizotypal personality disorder, a low-dose second-generation antipsychotic (for example, risperidone) can be used in a symptom-targeted, adjunctive way for the cognitive-perceptual features, with the dosing and adverse-effect detail carried in the Schizophrenia: management, antipsychotics and adverse effects notes rather than re-taught here. The broader psychotherapy technique sits in the Psychotherapies, clinical assessment, MSE and nosology notes.

GOOD TO REMEMBER

- **Structured supportive psychotherapy (Cluster A):** mechanism is a reliable, low-intensity working alliance that reduces isolation and reality-tests suspicion without forcing intimacy; indication is all three Cluster A types, chosen because they rarely tolerate intensive, emotionally demanding therapy; signature caution is that engagement itself is the obstacle, so over-familiarity or a pushed pace ruptures the alliance in the paranoid and schizoid patient. For schizotypal, a low-dose second-generation antipsychotic is adjunctive and symptom-targeted only, never disorder-specific.

INDIA

Two genuine India angles converge on Cluster A. First, under-recognition: these are the quietest personality disorders, ego-syntonic and rarely self-referred, so the paranoid and schizoid patient reaches services only through a comorbidity or a family crisis, and the diagnosis is made only when it is actively sought. Second, and more testable, the cultural reading of schizotypal features. Both DSM-5-TR and the ICD-11 CDDR warn explicitly that culturally sanctioned beliefs and practices, belief in the evil eye, a sixth sense, spirit visitation of a deceased relative, shamanic or trance experience, speaking in tongues, magical beliefs about health and illness, can look schizotypal to an uninformed clinician and must not be scored as cognitive-perceptual distortion when they are normative for the person's community. The cultural expression of personality pathology has to be weighed against the patient's own milieu, with an informant where needed, before any Cluster A type is fixed. Structured psychotherapy is available unevenly and mostly at tertiary and private centres.

5.7 The countable skeleton

One line rebuilds the cluster. Three types, two thresholds and one spectrum placement are the whole of Cluster A worth carrying into the hall. Hook them once and each type unpacks from the tag.

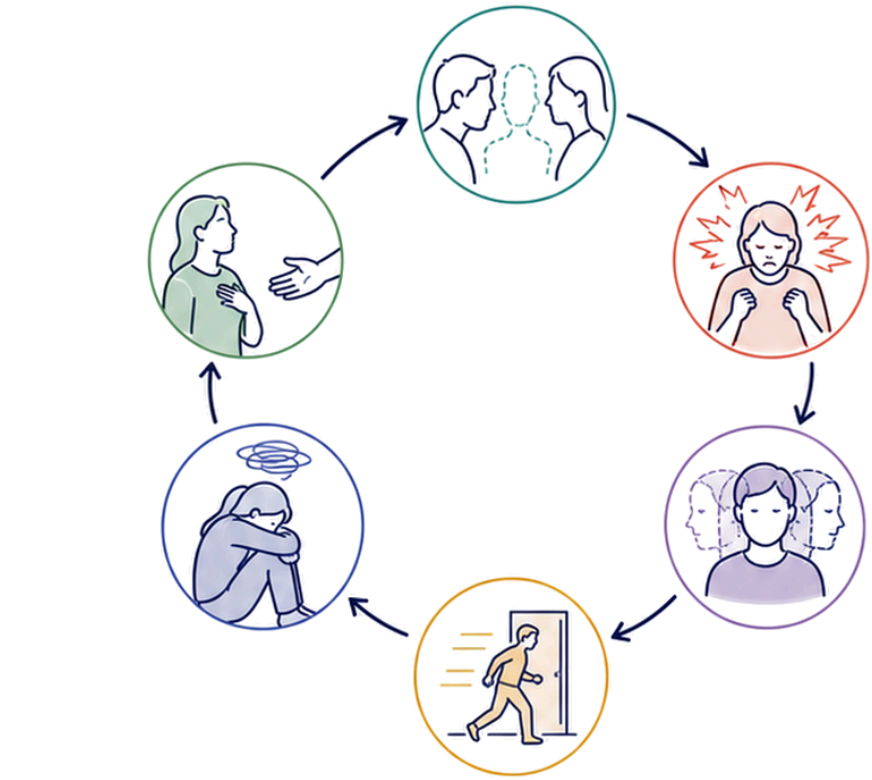


Fig 16.6 A common borderline personality dynamic links perceived attachment threat to rapid affective escalation, unstable self-other representations, impulsive action, shame or emptiness and renewed interpersonal sensitivity.

MNEMONIC

DISTRUST, DETACH, DISTORT

The three Cluster A types by their one-word core. **DISTRUST** is paranoid personality disorder (suspiciousness, motives read as malevolent, four or more of the seven, reality intact). **DETACH** is schizoid personality disorder (a contented loner, restricted emotion, four or more of the seven, no desire for closeness). **DISTORT** is schizotypal personality disorder (detachment plus cognitive-perceptual oddness and eccentricity, five or more of the nine, the schizophrenia-spectrum edge). Distrust keeps reality; detachment leaves it alone; distortion bends it, but never breaks it.

3 CLUSTER A TYPES (ODD OR ECCENTRIC)	**4** OF SEVEN FEATURES: PARANOID OR SCHIZOID THRESHOLD	**5** OF NINE FEATURES: SCHIZOTYPAL THRESHOLD	**6A22** ICD-11 SCHIZOTYPAL, IN THE SCHIZOPHRENIA SPECTRUM

HOLD THIS

Cluster A is odd or eccentric: paranoid is distrust with reality intact (four or more of the seven), schizoid is detachment with no wish for closeness (four or more of the seven), schizotypal is both plus cognitive-perceptual distortion (five or more of the nine); and schizotypal alone sits on the schizophrenia spectrum (ICD-11 schizotypal disorder 6A22), separated from schizophrenia by attenuation, not by a different symptom.

6 . Borderline personality disorder

The type every examiner returns to. Of the ten categorical types, borderline personality disorder (BPD) is the single highest-yield entity of the chapter: it carries as many criteria as any type, the most differentials, and the only personality-disorder treatment literature dense enough to examine on its own. The whole picture reduces to one **pervasive pattern of instability**, of interpersonal relationships, of self-image and of affect, welded to marked impulsivity, beginning by early adulthood and present across a variety of contexts. Learn it as a polythetic set of nine features from which **five or more of the nine criteria** must be present, and you can both make the diagnosis and defend it against the two presentations that most often masquerade as it, bipolar II disorder and complex post-traumatic stress disorder.

This fragment walks the nine criteria one by one, spells the threshold, teaches the **course** and the **complications**, and closes on the ICD-11 borderline pattern qualifier as the dimensional equivalent of the same construct. The **affective instability** boundary with the bipolar-II side is cross-referenced to the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes; the trauma boundary to the Anxiety, OCD and trauma-related disorders notes; and the depth of the disorder-specific psychotherapies (dialectical behaviour therapy, schema therapy, mentalisation-based treatment) to their own topics in this chapter. Everything here sits downstream of the general personality-disorder criteria, which must be cleared before the count begins.

6.1 The essential feature: instability across three domains plus impulsivity

Instability is the signature, in relationships, in the self and in affect. The essential feature of borderline personality disorder is a pervasive pattern of instability of interpersonal relationships, self-image and affects, together with marked **impulsivity**, that begins by early adulthood and is present in a variety of contexts (DSM-5-TR). Three domains are unstable, relationships, self and mood, and a fourth behavioural strand, impulsivity, cuts across all of them; the nine diagnostic criteria are simply these four strands unpacked. Holding the four-strand skeleton first is what stops BPD collapsing into a list to be memorised blind: abandonment and idealisation-devaluation are the *relationship* strand; identity disturbance and chronic emptiness are the *self* strand; reactive mood and inappropriate anger are the *affect* strand; and self-damaging impulsivity, recurrent self-harm and transient stress-related paranoia or dissociation are the *behaviour-under-load* strand. The instability is not situational turbulence but a lifelong, ego-syntonic pattern that the general criteria have already certified as enduring, pervasive and inflexible.

6.2 The nine criteria in full

Reproduce all nine; the count depends on it. The DSM-5-TR criteria (F60.3) are the cleanest form of the construct, and the ICD-11 borderline pattern list mirrors them almost word for word. Carry the block as one table, because a defensible diagnosis names *which* criteria are met, not merely that the patient "seems borderline".

NO.	CRITERION	WHAT IT REQUIRES
1	Abandonment	Frantic efforts to avoid real or imagined **abandonment** (self-harm and suicidal acts are counted separately, under criterion five)
2	Unstable relationships	A pattern of unstable and intense interpersonal relationships alternating between extremes of idealisation and devaluation
3	Identity disturbance	**Identity disturbance**: a markedly and persistently unstable self-image or sense of self
4	Impulsivity	Impulsivity in at least two areas that are potentially self-damaging (spending, sex, substance use, reckless driving, binge eating)
5	Self-harm / suicidality	Recurrent suicidal behaviour, gestures or threats, or self-mutilating behaviour
6	Affective instability	**Affective instability due to a marked reactivity of mood (episodic dysphoria, irritability or anxiety usually lasting a few hours and only rarely more than a few days)**
7	Chronic emptiness	Chronic feelings of emptiness
8	Inappropriate anger	Inappropriate, intense anger or difficulty controlling anger (frequent temper, constant anger, recurrent physical fights)
9	Paranoia / dissociation	Transient, stress-related paranoid ideation or severe dissociative symptoms

The nine DSM-5-TR borderline personality disorder criteria; the highlighted reactivity clause of criterion six is the pivot on which the bipolar-II discrimination turns. The ICD-11 borderline pattern list is materially identical.

6.3 The threshold, and why the disorder is heterogeneous

Five or more of the nine, in any combination. Borderline personality disorder is diagnosed when a pervasive pattern of instability and impulsivity is present, as shown by **five or more of**

the nine criteria. Because any five will do, the set is polythetic: two patients can both carry the diagnosis while sharing only one criterion between them, which is why the presentation ranges so widely, from the quietly empty and self-harming to the floridly angry and quasi-psychotic. The count is not the first step, though; the general personality-disorder criteria (enduring, pervasive and inflexible, onset by adolescence, not better explained by another disorder or a substance) are cleared first, and only then are the nine tallied. This is also why heterogeneity is examinable: naming the five you have counted forces the discipline that a pattern-matched label lacks.

MNEMONIC

AM SUICIDE

The nine criteria, one letter each: **A**bandonment fears; **M**ood instability (reactive affect); **S**uicidal or self-mutilating behaviour; **U**nstable, intense relationships (idealisation to devaluation); **I**mpulsivity in two or more self-damaging areas; **C**ontrol of anger poor (inappropriate intense anger); **I**dentity disturbance; **D**issociation or paranoia that is transient and stress-related; **E**mptiness (chronic). Nine letters, nine criteria, threshold five.

9	5	2
BORDERLINE CRITERIA (DSM-5-TR)	MINIMUM MET, OF THE NINE, TO DIAGNOSE	SELF-DAMAGING AREAS FOR THE IMPULSIVITY CRITERION

WORKED EXAMPLE

A woman in her early twenties presents after an overdose following a break-up. On history she describes terror of being left (one), relationships that swing from "he is perfect" to "he is cruel" within days (two), never knowing who she really is (three), recurrent cutting and this overdose (five), moods that flip within an afternoon in response to a text going unanswered (six), and a background sense of emptiness (seven). That is five of the nine met with room to spare, on an enduring pattern predating the current crisis. The diagnosis is defensible not because she "looks borderline" but because you can name the criteria and show they are trait, not a fresh state.

6.4 Abandonment, and the idealisation-devaluation of relationships

The relationship strand is driven by intolerance of aloneness. The frantic efforts to avoid real or imagined **abandonment** (criterion one) are cued by the mere perception of impending separation or the loss of external structure, so that a clinician ending a session on time or arriving a few minutes late can trigger panic or fury out of all proportion. The same sensitivity produces the unstable, intense relationships of criterion two: the patient idealises a new caregiver or lover at the first meeting, demands closeness, then switches abruptly to devaluation when the other is felt not to give or care enough. These sudden reversals in the view of another person, from all-good to all-bad, are the surface of the classical defence of splitting, in which contradictory images of self and other cannot be held together, so they alternate instead.

PEARL

Splitting is the mechanism the object-relations tradition (Otto Kernberg) places at the centre of the borderline structure: the inability to integrate good and bad representations of the same person, so that idealisation and devaluation swing back and forth rather than blending into a whole, ambivalent view. Naming splitting explains criterion two and the "you are the only one who understands me / you are just like all the others" whiplash that clinicians feel in the room.

6.5 Identity disturbance and chronic emptiness

The self strand is a self that will not hold still. **Identity disturbance** (criterion three) is a markedly and persistently unstable self-image or sense of self: values, goals, career direction, sexual identity and even the felt sense of existing can shift suddenly, and the person may report at times a feeling that they do not exist at all. It is worst in unstructured settings, where there is no external scaffold to borrow an identity from, which is why performance can collapse in open-ended work or study while holding up under close direction. Running underneath it is criterion seven, chronic feelings of emptiness, a persistent hollowness distinct from the sadness of depression: not "I feel low" but "there is nothing inside". The two together are the self-strand that the disorder-specific psychotherapies target most directly, and they are also the features most easily overlooked when attention fixes on the dramatic behaviours.

6.6 Affective instability and inappropriate anger, and the bipolar-II line

The affect is reactive, fast and interpersonally cued. **Affective instability** (criterion six) is defined by a marked reactivity of mood: episodic dysphoria, irritability or anxiety that is triggered, most often by an interpersonal event, and that usually lasts a few hours and only rarely more than a few days. Criterion eight, inappropriate and intense anger, belongs to the same strand: disproportionate temper, sustained anger, sometimes physical fights, frequently aimed at the very person whose closeness is most wanted. This is the criterion pair that collides with bipolar II disorder, and the collision is the highest-yield discrimination on the topic. Bipolar mood runs as sustained, autonomous episodes lasting days to weeks, carrying change in sleep, energy and goal-directed activity; borderline mood is reactive, brief and settles when the trigger resolves. The full grid sits on the bipolar-II topic; here, hold the discriminator.

RULE **Read the clock and the trigger on the mood.** Borderline affective instability is reactive, interpersonally cued and settles in hours; a mood that runs autonomously for days to weeks with change in sleep, energy and goal-direction is a bipolar episode, not a personality trait.

TRAP **Starting a mood stabiliser for personality-based instability.** Missing the borderline-versus-bipolar-II distinction and reading reactive, hours-long lability as bipolar II disorder medicalises a pattern whose primary treatment is structured psychotherapy; the drug then follows the misdiagnosis rather than the illness.

6.7 Impulsivity, recurrent self-harm and suicidality

The behaviour-under-load strand is where the risk lives. Criterion four requires **impulsivity** in at least two potentially self-damaging areas, spending, sex, substance use, reckless driving or

binge eating, and it is counted separately from the self-directed acts. Those acts are criterion five: **recurrent self-harm** and **suicidality**, which is to say recurrent suicidal behaviour, gestures or threats, or self-mutilating behaviour. Self-harm in borderline personality disorder frequently functions to regulate unbearable affect or to end dissociation rather than to end life, but the two intentions coexist and the mortality is real, so the presence of a regulatory function never downgrades the risk assessment. Chronic recurrent self-harm and acute suicidality must be held apart in the moment: the enduring pattern is expected, while a change from baseline, a new plan or a fresh stressor, is what escalates management.

6.8 Transient stress-related paranoia and dissociation

The quasi-psychotic criterion is transient and stress-bound. Criterion nine is **transient stress-related paranoia** (paranoid ideation) or severe **dissociation**, arising in states of high affective arousal, most often under the threat of abandonment, and resolving as the arousal subsides. The qualifiers are load-bearing: *transient* and *stress-related* separate these micro-psychotic experiences from the sustained, autonomous psychosis of a schizophrenia-spectrum disorder, and from the enduring cognitive-perceptual oddness of schizotypal personality. They are brief, reactive, and the patient usually retains some distance from them once calm. This criterion is also the one that overlaps most with the dissociative and hyperarousal features of complex post-traumatic stress disorder, which is the second great mimic of the syndrome.

> **COMMON TRAP**
>
> Collapsing complex post-traumatic stress disorder into borderline personality disorder. Both follow early adversity and share affect dysregulation, dissociation and unstable relationships, but complex post-traumatic stress disorder is built on the trauma triad (re-experiencing, avoidance, hyperarousal) plus disturbances in self-organisation, and its instability is trauma-cued rather than the enduring, abandonment-driven identity pathology of borderline personality disorder. The boundary and its therapeutic consequences are developed in the Anxiety, OCD and trauma-related disorders notes.

6.9 The course: waxing and waning, remission that outpaces recovery

The symptoms remit long before function returns. The **course** of borderline personality disorder is a waxing and waning one that trends, over years, toward **symptomatic remission**: in long-term prospective follow-up (the McLean Study of Adult Development led by Zanarini, and the Collaborative Longitudinal Personality Disorders Study), the majority of patients no longer meet full criteria after several years, and the acute, impulsive features, self-harm, quasi-psychotic episodes, stormy relationships, tend to attenuate earliest. The catch is that *functional* recovery, stable work and durable relationships, lags well behind symptomatic remission; a patient can stop meeting criteria yet remain vocationally and interpersonally disabled. This dissociation between symptom remission and functional recovery is the examinable heart of the prognosis, and it reframes the disorder as more remitting than its acute presentation suggests, while cautioning against calling a symptomatic remission a cure.

6.10 The complications, and the management orientation

The morbidity clusters in four places. The **complications** of borderline personality disorder are, first, repeated self-harm; second, completed suicide, whose lifetime rate is substantial and highest in the early acute years; third, comorbid substance use, mood and eating disorders that both worsen impulsivity and confound the diagnosis; and fourth, the corrosive impact on relationships and on work, which is the burden that outlasts the symptoms. The management orientation follows directly from the course: structured psychological therapy is the primary treatment, the disorder-specific models (dialectical behaviour therapy, schema therapy, mentalisation-based treatment) are taught on their own topics, and pharmacotherapy is symptom-targeted, adjunctive and time-limited rather than a treatment for the disorder itself; the deep drug detail sits in the Mood disorders: pharmacotherapy notes. Crucially, a diagnosis of borderline personality disorder is never grounds to exclude a patient from care.

INDIA

Borderline personality disorder is markedly under-recognised in Indian practice. Patients reach services through the self-harm or the overdose, which is coded as the attempt rather than the pattern, so the underlying disorder is captured only when it is deliberately sought. Two adaptations matter. First, cultural expression: transient dissociative and possession-trance presentations are normative idioms of distress in many Indian settings and must not be over-read as the criterion-nine dissociation, just as family interdependence must not be read as pathological abandonment fear; judge every criterion against the person's own culture. Second, access: dialectical behaviour therapy and schema therapy are being delivered and culturally adapted at Indian tertiary and private centres rather than being widely available, which is what a realistic management plan must reckon with.

6.11 The ICD-11 borderline pattern qualifier: the dimensional equivalent

The same construct, carried forward into the dimensional model. ICD-11 abolished the categorical types, but it did not abolish borderline; it preserved the construct as an optional *borderline pattern* specifier (6D11.5), applied on top of a rated severity level and the trait-domain qualifiers. A complete ICD-11 formulation reads, for example, "moderate personality disorder with negative affectivity, dissociality and disinhibition, borderline pattern": severity first, trait domains next, borderline pattern last. The specifier is defined by the same list of features, a pervasive pattern of instability of relationships, self-image and affects with marked impulsivity, and the CDDR applies the *same* formal threshold as DSM-5-TR, five or more of nine features, so the count is not a DSM-only device; it overlaps most with the negative affectivity, dissociality and disinhibition domains. It was retained for a frankly pragmatic reason, which examiners like: to flag the patients who respond to the established borderline-specific psychotherapies. The categorical name therefore survives inside the dimensional system, which is why both are testable.

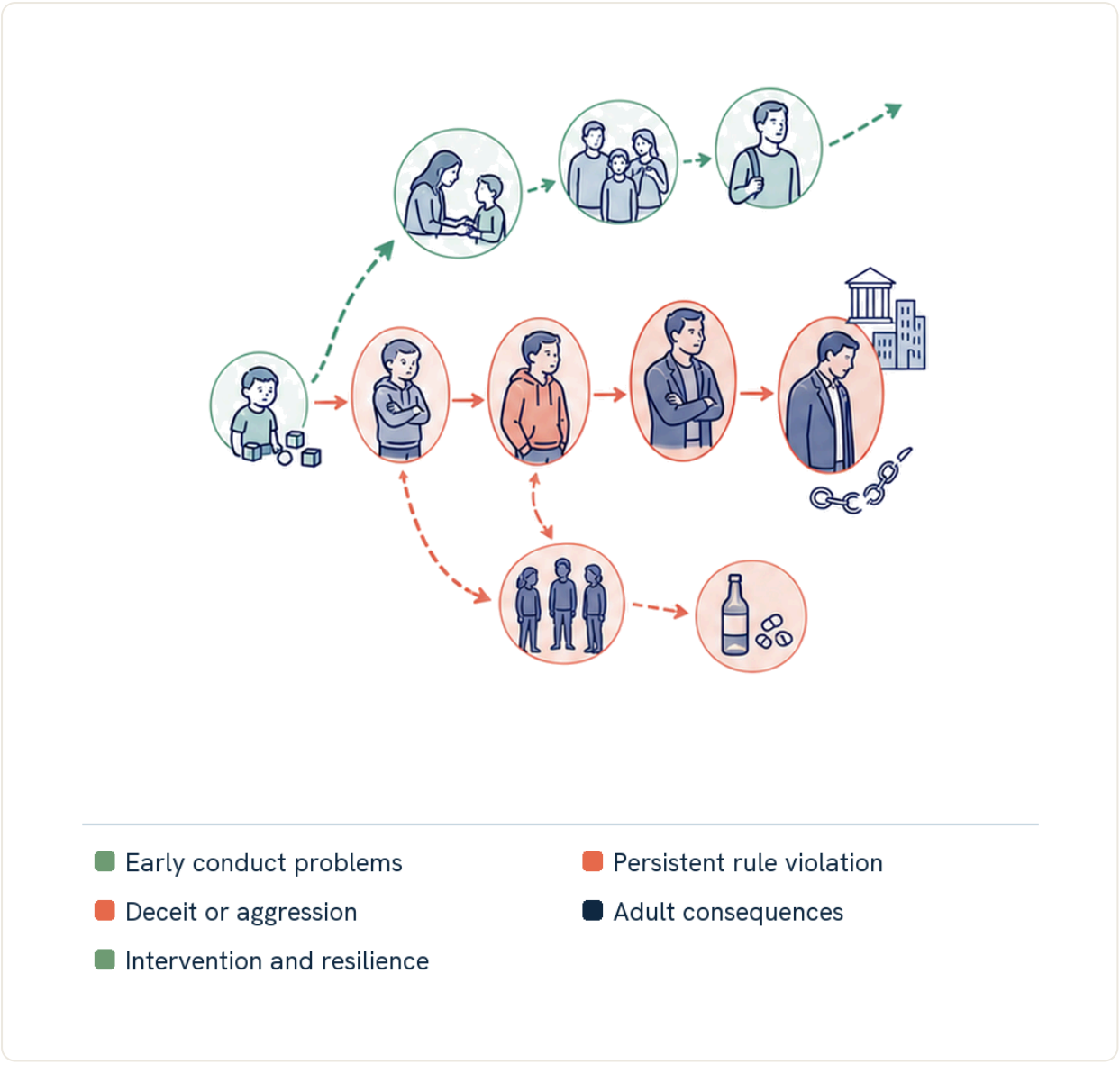


Fig 16.7 Antisocial personality disorder is developmentally anchored in earlier conduct problems, but progression is not inevitable; social context, comorbidity, intervention and resilience shape the adult pathway.

GOOD TO REMEMBER

- **Borderline personality disorder:** defining requirement is a pervasive pattern of instability of relationships, self-image and affect with marked impulsivity, meeting five or more of the nine criteria (abandonment, unstable idealising-devaluing relationships, identity disturbance, self-damaging impulsivity in at least two areas, recurrent self-harm or suicidality, reactive affective instability, chronic emptiness, inappropriate anger, transient stress-related paranoia or dissociation). Discriminator: the affect is rapidly reactive and interpersonally triggered and lasts hours, versus the sustained autonomous episodes of bipolar II disorder. First diagnostic step: clear the general personality-disorder criteria, then count the nine. ICD-11 keeps the construct as the optional borderline pattern qualifier on the dimensional model.

HOLD THIS

Borderline personality disorder is five or more of the nine, on a pervasive base of unstable relationships, unstable identity and reactive affect with impulsivity; the affect swings in hours and tracks interpersonal triggers, which is exactly what separates it from the sustained, autonomous episodes of bipolar II disorder.

7 . Antisocial personality disorder and forensic implications

The type the courts ask about. antisocial personality disorder (**aspd**; dissocial personality disorder in the older ICD terms) is the Cluster B type defined by a pervasive **disregard for and violation of the rights of others**, and it is the one personality disorder the examination reliably pushes into the medico-legal arena. Two features make it examinable beyond the criteria list. First, it is the only personality disorder with a hard developmental gate: it may not be diagnosed without evidence of conduct disorder before adolescence and it may not be diagnosed before adulthood, so the **age criterion** is part of the definition rather than a footnote. Second, it carries the **forensic implications** of the chapter, offending, the assessment of dangerousness, and the court report, and it forces the candidate to hold apart three things that are constantly conflated: the disorder, the construct of psychopathy, and criminality itself.

This fragment states the essential feature and walks the seven adult criteria, fixes the conduct-disorder precursor and the two ages, separates **aspd** from psychopathy and its **pcl-r** construct, cross-maps the categorical name onto the ICD-11 dimensional model, and then develops the two forensic tasks the psychiatrist is actually asked to perform, the structured assessment of dangerousness and the court report. The deep offender-management and legislative detail is carried in the Mental health legislation and forensic psychiatry notes; the general psychotherapy technique in the Psychotherapies, clinical assessment, MSE and nosology notes; and any symptom-targeted pharmacology in the Mood disorders: pharmacotherapy notes and the Schizophrenia: management, antipsychotics and adverse effects notes. Everything here sits downstream of the general personality-disorder criteria, which must be cleared before the count begins.

7.1 The essential feature: a pervasive disregard for the rights of others

The pattern violates the rights of others, and it began in childhood. The essential feature of antisocial personality disorder is a pervasive pattern of disregard for, and violation of, the rights of others, occurring since the age of fifteen years and continuing into adulthood (DSM-5-TR, F60.2). The manual notes in the same breath that this pattern has also been called **psychopathy**, sociopathy or dyssocial personality disorder, which is precisely the overlap the topic exists to disentangle. The behaviour is not a run of bad choices but an enduring, ego-syntonic trait structure: callous unconcern for others' feelings, a readiness to deceive and exploit, impulsive action without forethought, irritable aggression, reckless indifference to safety, chronic irresponsibility, and an absence of guilt. Because deceit and manipulation are central to the presentation, DSM-5-TR advises explicitly that the clinical account be corroborated from collateral and documentary sources rather than taken on the patient's word, a caution that matters even more when the assessment is destined for a court.

7.2 The seven adult criteria, and the three-of-seven threshold

Three or more of the seven, on the enduring pattern. Criterion A is met by **three or more of the seven** features below, present since the age of fifteen years (DSM-5-TR). Carry the block as one table, because a defensible antisocial diagnosis names which features are met, and the

affective item, **lack of remorse**, is the one that later separates the disorder from the narrower construct of psychopathy.

NO.	CRITERION (DSM-5-TR)	WHAT IT REQUIRES
1	Failure to conform to law	Failure to conform to social norms with respect to lawful behaviour, repeatedly performing acts that are grounds for arrest (whether or not arrest follows)
2	Deceitfulness	**deceitfulness**: repeated lying, use of aliases, or conning others for personal profit or pleasure
3	Impulsivity	Impulsivity or failure to plan ahead; decisions made on the spur of the moment without regard for consequences
4	Irritability and aggressiveness	Irritability and aggressiveness, indicated by repeated physical fights or assaults (acts in self-defence do not count)
5	Reckless disregard for safety	Reckless disregard for the safety of self or others (dangerous driving, high-risk behaviour, endangering a dependent)
6	Consistent irresponsibility	Consistent **irresponsibility**: repeated failure to sustain work or to honour financial obligations
7	Lack of remorse	**lack of remorse: being indifferent to, or rationalising, having hurt, mistreated or stolen from another**

The seven DSM-5-TR antisocial personality disorder criteria, of which three or more must be present; the highlighted affective item, lack of remorse, is the feature that most nearly touches the psychopathy construct and is the least likely to be present in ordinary offending.

MNEMONIC

CORRUPT

The seven criteria, one letter each. **C**onformity to law lacking (acts that are grounds for arrest); **O**bligations ignored (consistent irresponsibility, work and money); **R**eckless disregard for safety; **R**emorselessness (lack of remorse); **U**nderhandedness (deceitfulness, lying and conning); **P**lanning absent (impulsivity, failure to plan ahead); **T**emper (irritability and aggressiveness, repeated fights). Seven letters, seven criteria, threshold three.

Two exclusions close the definition. Two further clauses complete Criterion A's scaffolding. The individual must be at least eighteen years old (Criterion B) and must have shown evidence of conduct disorder with onset before fifteen years (Criterion C); and the antisocial behaviour must

not occur exclusively during the course of schizophrenia or a bipolar disorder (Criterion D), so that antisociality driven by mania or by psychosis is excluded from the personality diagnosis.

GOOD TO REMEMBER

- **Antisocial personality disorder:** defining requirement is a pervasive pattern of disregard for and violation of the rights of others since age fifteen, meeting three or more of the seven criteria (failure to conform to law, deceitfulness, impulsivity, irritability and aggressiveness, reckless disregard for safety, consistent irresponsibility, lack of remorse), with the individual at least eighteen and with documented conduct disorder before fifteen, and the behaviour not confined to schizophrenia or bipolar disorder. Discriminator: it is a trait pattern with a childhood-conduct-disorder precursor, not a synonym for a criminal record. First diagnostic step: clear the general personality-disorder criteria, confirm the conduct-disorder history and the age, then count the seven.

7.3 The conduct-disorder precursor and the age criterion

The developmental spine: oppositional to conduct to antisocial. The **age criterion** is what makes this a developmental diagnosis. The disorder cannot be given before eighteen years, and it cannot be given at all without evidence of conduct disorder with onset before fifteen years (DSM-5-TR). Conduct disorder is itself a repetitive, persistent violation of the basic rights of others or of major age-appropriate norms, and its behaviours fall into four groups, aggression to people and animals, destruction of property, deceitfulness or theft, and serious violation of rules; oppositional defiant disorder is a frequent earlier precursor of the childhood-onset type. The line runs, in the minority who progress, from oppositional through conduct disorder into the adult antisocial pattern, and the childhood-onset conduct disorder carries the worse prognosis. Most children with conduct disorder do not become antisocial adults, but essentially every antisocial adult has a conduct-disordered childhood, which is exactly why the history is a mandatory gate and not an optional descriptor. The developmental trajectory is laid out in the accompanying figure.

RULE **No conduct disorder before fifteen, no antisocial personality disorder.** Evidence of childhood conduct disorder and an age of at least eighteen are hard gates in the criteria; the antisocial diagnosis is a developmental one and cannot be built from an adult offending history alone.

TRAP **Reading a criminal record as antisocial personality disorder.** Offending, gang membership or survival-driven rule-breaking is not the disorder without the enduring, pervasive trait pattern and the conduct-disorder precursor; and antisociality seen only during mania or psychosis is excluded by Criterion D. Crime is neither necessary nor sufficient for the diagnosis.

7.4 Antisocial personality disorder versus psychopathy: the affective-interpersonal core and the PCL-R

Psychopathy is the narrower, affect-defined construct. psychopathy overlaps with antisocial personality disorder but is not the same thing, and treating them as interchangeable is the classic error. The categorical diagnosis is defined largely by observable antisocial *behaviour*; psychopathy is defined by an affective-interpersonal *core*, the glib superficial charm, grandiosity, pathological lying, callousness and, above all, the absence of guilt, remorse or empathy that Hervey Cleckley

described in *The Mask of Sanity* (1941). The construct has been dropped from the formal classifications but survives in forensic psychology and the prison service, where it is assessed with the Hare Psychopathy Checklist-Revised (the **pcl-r**; Robert Hare, 1991), a rater-scored instrument of twenty items, each scored zero to two, to a maximum of forty. The items load onto two factors: an interpersonal-affective factor (the charm, callousness and exploitation, the true psychopathic core) and a lifestyle-antisocial factor (the impulsive, irresponsible and violent behaviour that overlaps heavily with the antisocial criteria). Most people who meet the antisocial criteria do *not* reach a high psychopathy score; psychopathy is the smaller, affect-defined subset carrying the interpersonal-affective factor, and it is that factor, not the criminal record, that predicts the most instrumental and remorseless offending. The overlap and the nesting are shown in the figure alongside.

PEARL

Karpman, paralleling Cleckley's clinical description, distinguished *primary* from *secondary* psychopathy: the primary psychopath acts without anxiety, guilt or autonomic arousal, the mark of the affective deficit, while the secondary psychopath reports guilt and fear but offends through poor impulse control and emotional lability. The distinction maps loosely onto the two PCL-R factors, and it is why "psychopathy" is best reserved for the affective-interpersonal core and, as the general-psychiatry texts advise, largely avoided as a loose synonym for antisocial personality disorder.

GOOD TO REMEMBER

- **Psychopathy and the PCL-R:** the defining feature is the affective-interpersonal core, callousness and the absence of guilt, remorse and empathy (Cleckley), which the behaviour-based antisocial criteria do not require; the instrument is the Hare Psychopathy Checklist-Revised, twenty items scored zero to two to a maximum of forty, with an interpersonal-affective factor and a lifestyle-antisocial factor. Discriminator from antisocial personality disorder: psychopathy is the smaller, affect-defined subset, so most antisocial patients are not psychopathic; the two terms are not interchangeable, and psychopathy is not a diagnostic category in DSM-5-TR or ICD-11.

7.5 The classification frame: DSM-5-TR categorical, ICD-10 dissocial, ICD-11 dissociality

The same construct across three systems. In DSM-5-TR Section II the disorder is the antisocial type in Cluster B (the dramatic, emotional or erratic cluster). ICD-10 kept an almost identical categorical entity under the name dissocial personality disorder, requiring at least three of six traits, callous unconcern for others' feelings, gross and persistent irresponsibility and disregard for social norms, incapacity to maintain enduring relationships, very low frustration tolerance with a low threshold for aggression, incapacity to experience guilt or to profit from experience or punishment, and a marked proneness to blame others, with a childhood conduct-disorder history offered as supporting evidence. ICD-11 then abolished the categorical types altogether: there is now a single personality-disorder diagnosis rated first by severity (personality difficulty, then mild, moderate or severe) and qualified by the five trait domains. The antisocial construct is captured dimensionally by prominent **dissociality** (the ICD-11 domain 6D11.2, whose core feature is a disregard for the rights and feelings of others, self-centredness and lack of empathy),

usually together with **disinhibition** (impulsivity, irresponsibility, recklessness), at a moderate or severe level. The forward teaching of the ICD-11 dimensional model, its severity gradient and its five domains, is developed on the framework topics; here, hold the cross-map. The categorical names still dominate the examination and the courtroom because DSM-5-TR retains them and the case-law is written in them, which is why "antisocial" and "dissocial" remain testable even after ICD-11 has moved on.

7.6 Forensic implications: offending and the assessment of dangerousness

The task is a structured, defensible estimate of future risk. The **forensic implications** begin with offending: antisocial personality disorder is far commoner in men and is markedly over-represented in prison populations, and it frequently co-occurs with substance misuse, which amplifies impulsive aggression. The recurring clinical demand is the **assessment of dangerousness**, an estimate of the risk of future violence. Three approaches exist, and the examinable point is which is preferred. Unstructured clinical judgement is variable and biased; purely actuarial scoring is reliable but ignores the individual's own risk and protective factors; the recommended middle path is **structured professional judgement**, in which the clinician rates empirically derived risk factors systematically and then integrates them with the individual case (Clinical Methods in Psychiatry, AIIMS 2024). The most researched such instrument is the HCR-20, a twenty-item scheme across three scales, ten Historical (static) factors including past violence, young age at first violence, psychopathy and personality disorder, five Clinical (dynamic) factors, and five Risk-Management (dynamic) factors; each item is scored absent, partial or present, and the clinician then makes a summary rating of low, moderate or high, which is deliberately *not* a mechanical sum of ticks. A high PCL-R psychopathy score is itself one of the strongest single predictors of violent recidivism, which is why the two instruments are used together. Whenever risk is judged to be directed at an identifiable person, the duty to protect can override confidentiality. The three approaches are contrasted in the accompanying figure.

RULE **Structure the risk estimate, then judge it; never tick and total.** Dangerousness is assessed by structured professional judgement, empirically derived factors rated systematically and then weighed for the individual, ending in a reasoned low, moderate or high rating, not by the raw count on any checklist.

7.7 Forensic implications: court reports and the medico-legal frame

Antisocial personality disorder is a matter of disposal, not of exculpation. The second forensic task is the court report, and its central caution is that the antisocial diagnosis rarely excuses a crime. The insanity defence turns on a defect of reason from unsoundness of mind such that the accused did not know the nature of the act or that it was wrong, and the courts distinguish this *legal* insanity sharply from any *medical* diagnosis; a personality disorder, being a stable trait pattern rather than a disorder that clouds the knowledge of nature or wrongfulness, seldom meets that test. Psychiatric evidence is treated as relevant, not determinative. So the forensic weight of antisocial personality disorder falls on the assessment of dangerousness, on fitness to stand trial, and on disposal and sentencing, and on the psychiatric prediction of future dangerousness that the law can demand before an insanity-acquitted person is discharged, rather

than on culpability itself. In the report the clinician is an expert assisting the court: the opinion must be evidence-based, non-pejorative, carefully recorded (what is not written is treated as not done), and explicit about the limits of prediction. This medico-legal frame, the statutes, the fitness assessment, the disposal pathways and the report structure, is developed in the Mental health legislation and forensic psychiatry notes.

Criminal responsibility (insanity defence)
Whether unsoundness of mind prevented the accused knowing the nature of the act or that it was wrong; a legal test, judged against medical evidence, that antisocial personality disorder rarely satisfies.

Fitness to stand trial
Whether the accused can understand the charge and proceedings and instruct a defence; assessed before culpability is considered.

Assessment of dangerousness
A structured, professionally judged estimate of the risk of future violence, informing bail, disposal, discharge and management, not guilt.

The expert witness / court report
The psychiatrist assists the court with an impartial, evidence-based, well-documented opinion; relevant to the court's decision but never determinative of it.

The four medico-legal points where antisocial personality disorder meets the court; note that all four concern process, risk and disposal, not the excusing of the offence, whose statutory detail sits in the Mental health legislation and forensic psychiatry notes.

WORKED EXAMPLE

A man in his thirties is remanded after a violent robbery and referred for a court report and a "diagnosis of psychopathy". The history shows truanting, cruelty and theft from before the age of twelve, expulsions, repeated adult convictions, a chaotic work record, unpaid debts, and a flat indifference to the people he has hurt. He meets the antisocial criteria comfortably, with conduct disorder well before fifteen. The report says three things and no more than it can defend: the diagnosis is antisocial personality disorder (not, on this assessment, formally psychopathy, which would need a rated PCL-R); the disorder does not amount to the unsoundness of mind that founds an insanity defence, so it does not reduce his responsibility for the act; and his risk of future violence, assessed by structured professional judgement, is high and should guide disposal. The value of the report lies in what it declines to claim as much as in what it asserts.

RULE **Antisocial personality disorder is not an insanity defence.** As a stable trait pattern it seldom meets the legal test of unsoundness of mind; its forensic relevance is to dangerousness, fitness and disposal, not to exculpation, and the psychiatric opinion is relevant to the court, never determinative.

7.8 Management: guideline-anchored, psychological-first, and drug-sparing

Structured psychological work leads; no drug treats the personality. Management is modest and guideline-anchored, and the deep detail is cross-referenced. NICE recommends offering people with antisocial personality disorder group-based cognitive and behavioural interventions, involving the person in choosing their duration and intensity, and delivered where relevant in

criminal-justice as well as health settings, and it stresses a structured clinical assessment to make the diagnosis in the first place (NICE 2015). No drug is recommended or licensed for the antisocial personality itself; pharmacotherapy is reserved for a comorbid mental disorder, and where impulsive aggression is a treatment target it is addressed adjunctively and off-licence, for example with a mood stabiliser such as divalproex (Valprol, Encorate) or a second-generation antipsychotic, with the dosing and adverse-effect detail carried in the Mood disorders: pharmacotherapy notes and the Schizophrenia: management, antipsychotics and adverse effects notes rather than re-taught here. Engagement is the perennial obstacle: the condition is ego-syntonic, motivation is external, and manipulation of the therapeutic frame is expected, so treatment leans on structure, clear limits and realistic goals. Mentalisation-based treatment, adapted for antisocial personality disorder (Bateman and Fonagy), is an emerging structured option under trial; its general technique sits in the Psychotherapies, clinical assessment, MSE and nosology notes.

GOOD TO REMEMBER

- **Group cognitive-behavioural therapy for antisocial personality disorder:** mechanism is a structured, skills-based group intervention targeting the cognitions and behaviours that drive offending, delivered with firm limits; indication is antisocial personality disorder, especially with an offending history, and it is the NICE-recommended mainstay (NICE 2015), the person sharing the choice of duration and intensity; signature caution is that no drug is recommended for the personality itself, that medication is only for a comorbid disorder or, adjunctively and off-licence, for impulsive aggression, and that poor engagement and manipulation of the frame are the rule, not the exception.

INDIA

Three genuine India angles converge on antisocial personality disorder. First, under-recognition: personality disorders are markedly under-recognised in routine Indian practice, and the antisocial pattern in particular surfaces through its comorbidities, a substance-use disorder, repeated violence, or a legal referral, rather than as a personality diagnosis, so it is captured only when actively sought and a corroborated developmental history is taken. Second, the medico-legal frame is where the label carries the most force in India: the insanity defence rests on the unsoundness-of-mind test derived into the Indian Penal Code, which antisocial personality disorder rarely satisfies, so the psychiatrist's work is court reports, fitness assessment and the prediction of dangerousness rather than exculpation, and the dedicated forensic and secure-service infrastructure to support it is thin, developed in the Mental health legislation and forensic psychiatry notes. Third, the cultural expression of personality pathology: deviation must be judged against the person's own cultural, social and economic milieu, so that survival-driven or subcultural offending, or antisociality confined to a substance-use context, is not scored as trait pathology, and the diagnosis is not read through a single culture's norms. Structured group and mentalisation-based programmes for the disorder are scarcely available outside a few tertiary and forensic centres.

COMMON TRAP

Collapsing psychopathy into antisocial personality disorder and treating the two as one label. The antisocial criteria are behaviour-based and are met by a large, heterogeneous group, most of whom are not psychopathic; psychopathy is the narrower affective-interpersonal construct measured by the PCL-R, and it, not the criminal record, drives the most instrumental and remorseless offending. Writing "psychopath" where the assessment supports only antisocial personality disorder, or vice versa, is a straight error, and in a court report it is a consequential one.

3	15	18	20
OF THE SEVEN CRITERIA TO DIAGNOSE ANTISOCIAL PERSONALITY DISORDER	AGE (YEARS) BEFORE WHICH CONDUCT DISORDER MUST BE EVIDENT	MINIMUM AGE (YEARS) FOR THE ANTISOCIAL DIAGNOSIS	ITEMS ON THE HARE PSYCHOPATHY CHECKLIST-REVISED (PCL-R)

HOLD THIS

Antisocial personality disorder is a pervasive disregard for the rights of others, three or more of the seven criteria (failure to conform to law, deceitfulness, impulsivity, irritability and aggressiveness, reckless disregard for safety, consistent irresponsibility, lack of remorse), gated by conduct disorder before fifteen and an age of at least eighteen; it is not a synonym for psychopathy (the narrower affective-interpersonal PCL-R construct) nor for criminality, and its forensic weight is in the structured assessment of dangerousness and the court report, not in the insanity defence.

8 . Histrionic and narcissistic personality disorders

Why these two share a page. Both sit in **cluster b**, the dramatic, emotional or erratic group, and both are built around a hunger for the regard of others, so the examiner tests them together and rewards the candidate who can separate them cleanly. histrionic personality disorder is a pervasive pattern of excessive emotionality and **attention-seeking** (DSM-5-TR), and narcissistic personality disorder is a pervasive pattern of grandiosity, a **need for admiration** and a lack of empathy (DSM-5-TR). They look alike from a distance, two people who must be regarded, but the object of the wanting differs: the histrionic person needs to be the centre of attention and will take any role to get there, while the narcissistic person needs admiration for a superiority they believe is real.

This fragment frames the pair on one grid, takes each through its essential feature and criterion threshold, then isolates the single modern high-yield point, the split within narcissism between **grandiose narcissism** and **vulnerable narcissism**, the overt entitled presentation and the covert, hypersensitive, shame-prone one. Two cautions carry over and are assumed throughout: the general personality-disorder criteria (an enduring, pervasive, inflexible pattern, deviant from the person's own culture, with onset by adolescence or early adulthood, causing impairment, and not better explained otherwise) must be cleared before either type is named; and ICD-11 has abolished both as categories, so histrionic and narcissistic survive as labels only in DSM-5-TR and in clinical shorthand. The fully taught structured psychotherapies of this chapter and the general technique sit in the Psychotherapies, clinical assessment, MSE and nosology notes; the

borderline neighbour that both are most often confused with is developed elsewhere in this chapter.

8.1 The two on one frame

Both crave regard; the object of the craving divides them. Read the pair as a single question asked two ways. The histrionic patient organises a whole personality around being noticed, with emotion as the currency; the narcissistic patient organises it around being admired as superior, with a fragile self-esteem underneath. Learn the essential feature, the threshold and the one discriminator for each as a block, and most stems fall out of it.

TYPE	ESSENTIAL FEATURE (DSM-5-TR)	THRESHOLD	CORE DISCRIMINATOR
Histrionic	Pervasive and excessive emotionality and attention-seeking; discomfort when not the centre of attention	Five or more of the eight features	**Wants attention itself; will be fragile, seductive or dependent, whatever draws the eye**
Narcissistic	Grandiosity (in fantasy or behaviour), need for admiration, and lack of empathy	Five or more of the nine features	**Wants admiration for a believed superiority; entitlement and empathy failure, over a fragile self-esteem**

The two Cluster B attention-oriented types with their essential features, criterion thresholds and the single dividing discriminator; the accompanying figure sets attention-seeking against need for admiration on one axis.

PEARL

One question separates them at the bedside: *what does the attention buy?* For histrionic personality disorder attention is the goal in itself, and the person will happily be seen as fragile, ill or dependent if that is what turns heads. For narcissistic personality disorder attention must come as admiration of superiority; being pitied or seen as needy is intolerable, because it threatens the grandiose self.

8.2 Histrionic personality disorder

Emotion as performance, staged to be watched. The essential feature of histrionic personality disorder is a pervasive pattern of excessive emotionality and attention-seeking behaviour, beginning by early adulthood and present across contexts, shown by **five or more of the eight** features (DSM-5-TR). The eight are: discomfort in situations where they are not the centre of attention; interaction often marked by inappropriate sexually seductive or provocative behaviour; rapidly shifting and shallow expression of emotions; consistent use of physical appearance to draw attention to the self; a style of speech that is excessively impressionistic and lacking in detail; self-dramatisation, theatricality and exaggerated expression of emotion; suggestibility, being easily influenced by others or by circumstances; and considering relationships to be more intimate than they actually are. The signature is a person who is lively, charming and flirtatious on first meeting but whose emotions seem turned on and off too quickly to be deeply felt, whose strong opinions come with dramatic flair but no supporting detail, and

who becomes uncomfortable or aggrieved the moment the spotlight moves. Impairment tends to be milder than in the other Cluster B types and is chiefly interpersonal, with romantic and same-sex friendships strained by the demand for constant attention and the provocative style.

GOOD TO REMEMBER

- **Histrionic personality disorder:** defining criterion is pervasive excessive emotionality and attention-seeking, five or more of the eight features, from early adulthood, with discomfort when not the centre of attention as the anchoring item. Discriminator from narcissistic: it wants attention as such and will accept a fragile or dependent role to get it, where narcissistic wants admiration for superiority. Discriminator from borderline: no chronic emptiness, identity disturbance, self-destructiveness or angry abandonment ruptures. Discriminator from dependent: the flamboyant, theatrical, exaggerated emotionality that dependent lacks. First step: confirm the general personality-disorder criteria, then that the emotionality and attention-seeking are trait-level and pervasive, not a phase or a state.

8.3 Narcissistic personality disorder

Grandiosity above, fragility below. The essential feature of narcissistic personality disorder is a pervasive pattern of grandiosity in fantasy or behaviour, a need for admiration and a lack of empathy, beginning by early adulthood and present across contexts, shown by **five or more of the nine** features (DSM-5-TR). The nine are: a grandiose sense of self-importance; preoccupation with fantasies of unlimited success, power, brilliance, beauty or ideal love; a belief in being special and unique, understood only by, or fit to associate only with, other special or high-status people or institutions; a requirement for excessive admiration; a sense of entitlement, meaning unreasonable expectations of especially favourable treatment or automatic compliance; interpersonal exploitativeness, taking advantage of others to reach one's own ends; a lack of empathy, an unwillingness to recognise or identify with the feelings and needs of others; envy of others or a belief that others envy oneself; and arrogant, haughty behaviours or attitudes. The clinically important addition, spelled out in the DSM-5-TR text, is that the self-esteem beneath the grandiosity is almost always fragile: criticism or defeat can leave the person feeling ashamed, humiliated, hollow and empty, reacting with disdain, rage, or a withdrawal that masks the grandiosity rather than removing it. Empathy is typically cognitive but not emotional, they can read another's perspective yet do not feel with them.

GOOD TO REMEMBER

- **Narcissistic personality disorder:** defining criterion is grandiosity, a need for admiration and a lack of empathy, five or more of the nine features, from early adulthood. Discriminator from histrionic: admiration must be for a believed superiority, and a needy or fragile role is intolerable. Discriminator from antisocial: narcissistic lacks the impulsivity, aggression, deceit and childhood conduct-disorder history, and exploits to enhance the self rather than for material gain. Discriminator from borderline: relatively stable self-image and far less physical self-destructiveness and abandonment terror. First step: confirm the general criteria, then look past the grandiose surface for the fragile self-esteem that the presentation is defending.

8.4 Grandiose versus vulnerable narcissism

One disorder, two faces. The highest-yield modern point is that narcissism presents along two phenotypes rather than one. grandiose narcissism is the overt, textbook picture: openly entitled,

arrogant, exhibitionistic, admiration-demanding, thick-skinned. vulnerable narcissism is the covert picture: hypersensitive, shame-prone, anxiously self-conscious, socially withdrawn, quietly nursing the same grandiose fantasies but defending them behind apparent humility or complaint. DSM-5-TR anchors both in its own text and in its alternative model: it describes narcissistic self-esteem as "variable and vulnerable," regulated through approval-seeking, with grandiosity that may be "either overt or covert," and it records the more vulnerable presentations by adding negative-affectivity traits such as depressivity and anxiousness. The two are not different disorders but different surfaces over a shared core of fragile self-worth; many patients oscillate between them, showing grandiosity when supplied with admiration and collapsing into the vulnerable state when it is withheld. The examiner's trap is to recognise only the loud, grandiose form and miss the quiet, shame-driven one, which is easily mistaken at face value for depression or social anxiety.

FACET	GRANDIOSE (OVERT)	VULNERABLE (COVERT)
Surface presentation	Entitled, arrogant, exhibitionistic, self-assured	**Hypersensitive, shy, self-effacing, complaining**
Self-esteem	Openly inflated, thick-skinned to criticism	Fragile, shame-prone, easily wounded
Response to a slight	Disdain, rage, counterattack	Withdrawal, humiliation, resentment, rumination
Grandiosity	Displayed openly in behaviour	Kept in private fantasy, masked by humility
Common misread	Simple arrogance or a difficult personality	**Depression or social-anxiety disorder**

Grandiose and vulnerable narcissism as two surfaces over one fragile core; the highlighted cells are the covert features most often missed and the diagnosis they are mistaken for.

WORKED EXAMPLE

A man in his thirties presents with low mood, social withdrawal and a sense of being chronically slighted. On the surface this reads as depression. Listening closer, the withdrawal follows a series of perceived humiliations, each one a failure of the world to recognise a talent he privately believes is exceptional; he is exquisitely sensitive to criticism, envious of colleagues he considers his inferiors, and empty when admiration is not forthcoming. There is no overt boastfulness. This is vulnerable narcissism, the covert face of narcissistic personality disorder, not a primary depressive disorder, and treating only the mood while missing the fragile grandiose core underneath is why the presentation keeps returning.

RULE **Attention itself versus admiration for superiority.** The histrionic person wants to be the centre of attention and will take any role, even a fragile or dependent one, to get it; the narcissistic person wants admiration specifically for a superiority they believe is real, and a needy role is intolerable. That is the dividing line.

TRAP **Seeing only the loud narcissist.** Expecting only the grandiose, arrogant presentation and missing vulnerable narcissism, whose covert shame, hypersensitivity and withdrawal are read at face value as depression or social anxiety, leaves the diagnosis and the fragile grandiose core underneath untouched.

8.5 Telling them apart from their neighbours

The confusions the paper actually sets. Both types share features with their Cluster B neighbours, and the marks are in the discriminators, drawn straight from the DSM-5-TR differential text. Hold the grid below and each boundary is a one-line answer.

BOUNDARY	SHARED FEATURE	DISCRIMINATOR
Histrionic vs narcissistic	Both crave attention from others	**Histrionic wants attention as such and accepts a fragile role; narcissistic wants praise for superiority and emphasises status**
Histrionic vs borderline	Attention-seeking, manipulative behaviour, rapidly shifting emotions	Borderline adds self-destructiveness, angry relationship ruptures, chronic emptiness and identity disturbance
Histrionic vs antisocial	Impulsive, superficial, seductive, manipulative	Histrionic manipulates for nurturance and is more exaggerated in emotion; antisocial manipulates for material gain
Histrionic vs dependent	Reliance on others for reassurance	Dependent lacks the flamboyant, exaggerated, theatrical emotionality of histrionic
Narcissistic vs antisocial	Exploitative, lacking empathy	Narcissistic lacks impulsivity, aggression, deceit and a conduct-disorder history; exploits to enhance the self, not for profit
Narcissistic vs borderline	Anger to minor slights	Narcissistic keeps a relatively stable self-image with little physical self-destructiveness or abandonment terror

The six boundaries most often tested around the two types; the highlighted cell is the single discriminator that decides histrionic from narcissistic. The borderline side is developed elsewhere in this chapter.

8.6 The classification shift: ICD-11 and the alternative model

Both categories are gone, but the vocabulary survives. This is where the day's headline nosology point lands on these two types. ICD-11 abolished the categorical personality-disorder types entirely: there is no ICD-11 code for histrionic or narcissistic personality disorder. A histrionic-like presentation is now captured by rating **severity** first (personality difficulty, then mild, moderate or severe) and adding the trait qualifier of negative affectivity for the dramatic, labile emotionality, with the attention-seeking element falling under dissociality. A narcissistic-like presentation is captured by severity plus dissociality, whose text explicitly names self-

centredness, a sense of entitlement, expectation of others' admiration and attention-seeking to remain the centre of focus, with the vulnerable, shame-prone features added under negative affectivity (ICD-11 CDDR). The DSM-5-TR alternative hybrid model treats the two unequally: narcissistic personality disorder is one of the six specific types it retains, defined by impairment plus the antagonism traits of grandiosity and attention-seeking, whereas histrionic is one of the four categorical types it drops, becoming personality disorder, trait specified when the general criteria are met without a named set.

ICD-10 TO ICD-11: WHAT CHANGED

ICD-10 (F60) kept histrionic personality disorder (F60.4) as a named categorical type, but narcissistic never had its own ICD-10 category at all, sitting only under "other specific personality disorder" (F60.8). ICD-11 then removed every categorical type, rebuilding the diagnosis as a severity level plus trait-domain qualifiers, so both histrionic and narcissistic now exist only as descriptive patterns within that dimensional frame. Exams still test the categorical names because DSM-5-TR retains them in its main text and clinicians still speak in them, so read fluently in both languages.

8.7 Management in outline, and the cultural reading

Psychotherapy is the frame; drugs are for comorbidity only. Neither type has a disorder-specific drug, and neither is a receptor problem to be medicated. The working approach is a structured, long-term psychotherapy, with the transference-focused and schema-based models the ones with the most traction for narcissistic pathology (their mechanism and indication are taught in full in their own topics of this chapter). The narcissistic patient tests the alliance hardest, because the very grandiosity that brings collapse also resists the therapist's help, and the vulnerable, shame-prone presentation must be handled without either colluding with the grandiosity or shaming the fragile self beneath it. Medication is reserved for a comorbid depressive or anxiety disorder, or a short crisis, never for the personality itself, and the deep pharmacology is cross-referenced to the Mood disorders: pharmacotherapy notes and the Schizophrenia: management, antipsychotics and adverse effects notes rather than re-taught here.

INDIA

Three genuine India angles converge here. First, under-recognition: personality disorders are diagnosed far less often in routine Indian practice than Western prevalence would predict, and these two surface through their comorbidities, a mood or anxiety disorder, a relational crisis, rather than as a personality label that clinicians often avoid for fear of stigma. Second, the cultural expression of pathology: the general criteria require deviation from the person's *own* culture, so narcissistic-looking traits inflate in individualistic settings and warrant less clinical weight where they are normative, while a warm, expressive, family-embedded emotional style must not be scored as histrionic through a colder cultural lens, and the historical over-diagnosis of histrionic personality disorder in women along gendered social scripts is a bias to guard against actively. Third, availability: the structured psychotherapies these patients need, transference-focused and schema therapy, are unevenly available and still being culturally adapted for India, concentrated at tertiary and private centres. The medico-legal weight of personality pathology attaches to antisocial personality disorder, handled in the Mental health legislation and forensic psychiatry notes, not to these two.

8.8 The countable skeleton

Two essential features, two thresholds, one split. Everything worth carrying into the hall about these two types hooks onto a handful of counts and one distinction. Anchor the mnemonics and each criterion set unpacks.

MNEMONIC

PRAISE ME · GRANDIOSE

PRAISE ME for the eight histrionic criteria: **P**rovocative or seductive; **R**elationships thought more intimate than they are; **A**ttention (uncomfortable when not its centre); **I**nfluenced easily (suggestible); **S**tyle of speech impressionistic and vague; **E**motions shallow and rapidly shifting; **M**ade-up appearance used to draw the eye; **E**xaggerated, theatrical emotional display.
GRANDIOSE for the nine narcissistic criteria: **G**randiose self-importance; **R**equires excessive admiration; **A**rrogant and haughty; **N**eeds to be seen as special and unique; **D**reams of unlimited success, power, brilliance, beauty or ideal love; **I**nterpersonally exploitative; **O**btuse to others' feelings (lacks empathy); **S**ense of entitlement; **E**nvious of others or believes others envy them.

8	9	4	5
HISTRIONIC CRITERIA; FIVE OR MORE NEEDED	NARCISSISTIC CRITERIA; FIVE OR MORE NEEDED	CLUSTER B DRAMATIC TYPES	ICD-11 TRAIT DOMAINS; BOTH TYPES ABOLISHED

HOLD THIS

Histrionic personality disorder is excessive emotionality and attention-seeking (five or more of the eight, uncomfortable when not the centre of attention); narcissistic personality disorder is grandiosity, a need for admiration and a lack of empathy (five or more of the nine); and grandiose and vulnerable narcissism are one disorder's two faces, the overt entitled and the covert shame-prone, over a shared core of fragile self-esteem.

9 . Cluster C: avoidant, dependent and anankastic

Why the anxious cluster earns its marks. **cluster c** is the **anxious or fearful** group, and it rewards the candidate who can give the one-line essential feature of each type cold and then defend the two boundaries an examiner reaches for first: avoidant personality disorder against a genuine loner and against social anxiety disorder, and anankastic personality disorder against obsessive-compulsive disorder. The three types are avoidant personality disorder (social inhibition, feelings of inadequacy and hypersensitivity to negative evaluation, with avoidance of activities involving interpersonal contact), dependent personality disorder (a pervasive and excessive need to be taken care of leading to submissive and clinging behaviour and fears of separation), and obsessive-compulsive personality disorder, the anankastic type (a preoccupation with orderliness, perfectionism and mental and interpersonal control at the expense of flexibility, openness and efficiency) (DSM-5-TR 2022). The thread that ties them is that fear, not oddness and not drama, is the organising affect: fear of rejection, fear of being left, and fear of losing control.

This fragment frames the cluster on one grid, takes each type through its defining criterion and the discriminator that decides it, then isolates the single highest-yield boundary of the group, the anankastic character against the anxiety disorder that shares its name. Two cautions from the framework topics of this chapter are assumed throughout: the general personality-disorder criteria (an enduring, pervasive, inflexible pattern, from early adulthood, causing impairment and not better explained otherwise) must be cleared before any type is named; and ICD-11 has abolished the categorical types, so "avoidant", "dependent" and "anankastic" survive as labels only in the legacy classifications and in clinical shorthand, with the dimensional model taught on the framework topics. The OCD side sits in the Anxiety, OCD and trauma-related disorders notes and the wider psychotherapy technique in the Psychotherapies, clinical assessment, MSE and nosology notes.

9.1 The cluster on one frame

Three types, one affect, three fears. DSM-5-TR groups the three types whose sufferers "often appear anxious or fearful" (DSM-5-TR 2022). Read the cluster by what each type is afraid of and what it does about the fear: the avoidant person wants closeness but withdraws from it for fear of criticism and rejection; the dependent person clings to a caretaker for fear of being left to cope alone; the anankastic person controls and orders the world for fear of anything going wrong. Learning the three essential features with their exact thresholds as one block is the fastest route to every cluster C question, because the thresholds differ across the three and are a favourite trip-wire.

TYPE	ESSENTIAL FEATURE (DSM-5-TR)	THRESHOLD	CORE DISCRIMINATOR
Avoidant	Social inhibition, feelings of inadequacy and hypersensitivity to negative evaluation, with avoidance of interpersonal contact	Four or more of the seven features	**Wants closeness but fears rejection (vs schizoid, who has no desire)**
Dependent	A pervasive, excessive need to be taken care of, leading to submissive, clinging behaviour and fears of separation	Five or more of the eight features	**Appeasement and a replacement caretaker, not rage (vs borderline)**
Anankastic (obsessive-compulsive)	Preoccupation with orderliness, perfectionism and mental and interpersonal control, at the expense of flexibility, openness and efficiency	Four or more of the eight features	**Ego-syntonic traits; no true obsessions or compulsions (vs OCD)**

The three DSM-5-TR Cluster C types with their essential features, criterion thresholds and core discriminators; the accompanying figure lays the same three on a fear-and-response map (fear of rejection, of separation, of loss of control).

PEARL

Tag each type by the fear that drives it: avoidant fears *rejection*, dependent fears *separation*, anankastic fears *loss of control*. Then hold the three thresholds apart, because they are not the same number: avoidant is **four or more of the seven**, dependent is **five or more of the eight**, and anankastic is **four or more of the eight**. Dependent is the odd one out that needs five.

9.2 Avoidant personality disorder

The person who longs for closeness and flees it. The essential feature of avoidant personality disorder is a pervasive pattern of social inhibition, feelings of inadequacy and hypersensitivity to negative evaluation, beginning by early adulthood and present across contexts, shown by **four or more of the seven** features (DSM-5-TR 2022). The seven are: avoiding occupational activities that involve significant interpersonal contact for fear of criticism, disapproval or rejection; being unwilling to get involved with people unless certain of being liked; showing restraint within intimate relationships for fear of being shamed or ridiculed; being preoccupied with being criticised or rejected in social situations; being inhibited in new interpersonal situations because of feelings of inadequacy; viewing the self as socially inept, unappealing or inferior; and being unusually reluctant to take personal risks or try new activities for fear of embarrassment. The signature is a person who deeply wants relationships and feels the loneliness of their absence, but assumes others are critical until stringently proven otherwise. Two contrasts do most of the work. Against schizoid personality disorder, the single question is whether closeness is wanted at all: the avoidant person wants it and fears rejection, the schizoid person has no desire for it. Against social anxiety disorder, the difference is pervasiveness and self-concept: avoidant personality disorder is a trait-level pattern with an entrenched sense of inferiority, present even without the

anxiety disorder, whereas social anxiety may be more situational, though the two overlap heavily and some regard avoidant personality disorder as a more severe form.

GOOD TO REMEMBER

- **Avoidant personality disorder:** defining criterion is pervasive social inhibition, feelings of inadequacy and hypersensitivity to negative evaluation, four or more of the seven features, from early adulthood. Discriminator from schizoid: closeness is wanted but feared (schizoid does not want it). Discriminator from social anxiety disorder: trait-level and pervasive with an entrenched inferiority, present even without the anxiety disorder. First step: confirm the general personality-disorder criteria, then that the avoidance is pervasive and character-level, not confined to circumscribed performance situations.

9.3 Dependent personality disorder

The excessive need to be cared for. The essential feature of dependent personality disorder is a pervasive and excessive need to be taken care of that leads to submissive and clinging behaviour and fears of separation, from early adulthood, shown by **five or more of the eight** features (DSM-5-TR 2022). The eight are: difficulty making everyday decisions without excessive advice and reassurance; needing others to assume responsibility for most major areas of life; difficulty expressing disagreement for fear of losing support or approval; difficulty initiating projects or doing things alone from a lack of self-confidence; going to excessive lengths to obtain nurturance and support, even volunteering for unpleasant tasks; feeling uncomfortable or helpless when alone from exaggerated fears of being unable to cope; urgently seeking another relationship as a source of care when a close one ends; and being unrealistically preoccupied with fears of being left to care for oneself. The behaviours are designed to elicit caregiving and arise from a self-perception of being unable to function alone. The examiner's favoured contrast is with borderline personality disorder: both fear abandonment, but the person with dependent personality disorder responds with increasing appeasement and submissiveness and urgently seeks a replacement caretaker, whereas the person with borderline personality disorder responds with rage, emptiness and demands, against a background of unstable and intense relationships. From avoidant personality disorder it is separated by direction: the dependent person seeks proximity, the avoidant person avoids it, though both share feelings of inadequacy.

GOOD TO REMEMBER

- **Dependent personality disorder:** defining criterion is a pervasive, excessive need to be taken care of leading to submissive, clinging behaviour and fears of separation, five or more of the eight features (the only cluster C type that needs five), from early adulthood. Discriminator from borderline: appeasement and a replacement caretaker, not rage and emptiness; relationships stable-clinging, not unstable-intense. Discriminator from avoidant: proximity-seeking, not proximity-avoiding. First step: confirm the general criteria, then that the dependence is excessive and unrealistic beyond situational and cultural norms, not normative interdependence.

9.4 Anankastic (obsessive-compulsive) personality disorder

Control at the cost of flexibility. The essential feature of obsessive-compulsive personality disorder, the anankastic type, is a preoccupation with orderliness, perfectionism and mental and interpersonal control, at the expense of flexibility, openness and efficiency, from early adulthood,

shown by **four or more of the eight** features (DSM-5-TR 2022). The eight are: preoccupation with details, rules, lists, order, organisation or schedules to the point that the major purpose is lost; perfectionism that interferes with task completion; excessive devotion to work and productivity to the exclusion of leisure and friendships, not explained by economic necessity; over-conscientiousness, scrupulousness and inflexibility about matters of morality, ethics or values, not explained by culture or religion; inability to discard worn-out or worthless objects even when they have no sentimental value; reluctance to delegate unless others submit to exactly one's own way; a miserly spending style, money hoarded against future catastrophe; and rigidity and stubbornness. The core is control: the perfectionism is so complete that projects are never finished and time is poorly allocated, and the rigidity holds even when compromise would clearly serve the person's own interest. The whole pattern is **ego-syntonic**, experienced as reasonable and correct, which is exactly what sets up the marquee trap of the topic.

GOOD TO REMEMBER

- **Anankastic (obsessive-compulsive) personality disorder:** defining criterion is a pervasive preoccupation with orderliness, perfectionism and mental and interpersonal control at the expense of flexibility, openness and efficiency, four or more of the eight features, from early adulthood. Discriminator from OCD: the traits are ego-syntonic character, with no true obsessions and no compulsions. First step: confirm the general criteria and that the perfectionism and control are a pervasive, ego-syntonic trait, then search for (and either exclude or separately co-diagnose) the true obsessions and compulsions of OCD.

9.5 Anankastic versus OCD: ego-syntonic character against ego-dystonic illness

Similar names, different animals. This is the boundary the topic is built to test. Despite the shared name, obsessive-compulsive personality disorder and obsessive-compulsive disorder are clinically quite different (DSM-5-TR 2022). The anankastic personality is not characterised by intrusive thoughts, images or urges, nor by repetitive behaviours performed in response to them; it is an enduring, pervasive maladaptive pattern of excessive perfectionism and rigid control, and it is **ego-syntonic**, the person sees the traits as sensible and right and is not distressed by them, though the people around them often are. Obsessive-compulsive disorder is defined by true **obsessions** (intrusive, unwanted thoughts, images or urges) and **compulsions** (repetitive acts performed to neutralise the distress), and it is **ego-dystonic**, the symptoms are experienced as alien, unwanted and resisted. The presence or absence of true obsessions and compulsions is the line. The two are not mutually exclusive: when the criteria for both are met, both are diagnosed, and comorbid anankastic personality is found in roughly a quarter to a third of people with OCD in longitudinal cohorts. The obsessive-compulsive disorder side, its phenomenology and its treatment, is developed in the Anxiety, OCD and trauma-related disorders notes.

FEATURE	ANANKASTIC (OBSESSIVE-COMPULSIVE) PERSONALITY DISORDER	OBSESSIVE-COMPULSIVE DISORDER (OCD)
Relation to self	Ego-syntonic: traits seen as reasonable, right and desirable	Ego-dystonic: symptoms alien, unwanted, resisted
Core content	A pervasive character style of perfectionism, orderliness and rigid control	Discrete intrusive symptoms sitting on the background personality
Obsessions and compulsions	**Absent: no true obsessions and no compulsions**	Present and defining
Distress	Little distress about the traits themselves; others carry the frustration	Marked distress and active resistance to the symptoms
If both present	When the criteria for both are met, both diagnoses are recorded	

The anankastic-versus-OCD discrimination; the highlighted cell is the single feature that decides it, the absence of true obsessions and compulsions in the personality disorder. The OCD side is developed in the Anxiety, OCD and trauma-related disorders notes.

RULE **The line is true obsessions and compulsions, and ego-tone.** Anankastic personality is an ego-syntonic character of perfectionism and control with no true obsessions or compulsions; OCD is defined by ego-dystonic, resisted obsessions and compulsions. Their presence or absence, not the shared name, decides the diagnosis.

TRAP **Calling a rigid perfectionist "OCD".** Orderliness, perfectionism, hoarding of worthless items and inability to delegate, experienced by the person as simply being thorough and correct, are anankastic personality, not OCD, unless there are genuine intrusive obsessions and neutralising compulsions the person resists.

WORKED EXAMPLE

An accountant in his forties is referred as "OCD". He is a relentless perfectionist who cannot discard years of worn-out paperwork, refuses to delegate, and misses deadlines because he rechecks his work endlessly; he regards all of this as ordinary diligence and is untroubled by it, though his family and colleagues are worn down. He describes no intrusive unwanted thoughts and performs no rituals to neutralise anxiety. This is obsessive-compulsive personality disorder, the anankastic type, not OCD: the pattern is ego-syntonic character without true obsessions or compulsions. Had he also described intrusive contamination fears and washing rituals he resisted, both diagnoses would stand together.

9.6 How cluster C maps onto the dimensional and legacy systems

The categorical names decoded into traits. The framework topics of this chapter teach the dimensional model in full; three cluster-C-specific facts are worth carrying. First, the ICD-11 anankastia trait domain, a narrow focus on a rigid standard of perfection and on controlling oneself, others and situations to enforce it, is essentially the OCPD phenotype re-cast as a dimension, and it is the domain with no counterpart in the DSM-5 alternative model. Second, the avoidant and dependent phenotypes load mainly on negative affectivity with detachment, the

anxious-fearful traits. Third, and high-yield, the DSM-5-TR alternative model of personality disorders retains only six categorical types, antisocial, avoidant, borderline, narcissistic, obsessive-compulsive and schizotypal: avoidant and obsessive-compulsive survive the cut, but dependent personality disorder is one of the four types dropped. In the legacy ICD-10, the same phenotypes carried different names, anankastic for obsessive-compulsive and anxious for avoidant, with dependent kept as it is; exams still test these categorical names because DSM-5-TR retains them and the literature is written in them.

PEARL

Two cluster C facts examiners like: the ICD-11 fifth domain is *anankastia* (the OCPD phenotype), where the DSM-5 alternative model instead has psychoticism; and the alternative model keeps avoidant and obsessive-compulsive but drops dependent, so "which cluster C type is not in the DSM-5 alternative model?" has a clean answer, dependent.

9.7 Management in outline, and the cultural reading

Psychological therapy leads; drugs treat comorbidity only. Cluster C is managed, not cured, and no drug is disorder-specific for any of the three. The primary mode is structured psychological therapy: graded exposure to the avoided or feared situation with cognitive restructuring of the beliefs of inadequacy for avoidant personality disorder (the technique overlaps with the treatment of social anxiety disorder), assertiveness and autonomy-building for dependent personality disorder, and work on rigidity and control for the anankastic patient. The schema-mode and dialectical approaches, and the deeper psychotherapy technique, are developed on the psychotherapy topics of this chapter and in the Psychotherapies, clinical assessment, MSE and nosology notes. Pharmacotherapy stays narrow: where avoidant personality disorder carries a comorbid social anxiety disorder, a serotonin reuptake inhibitor may help that comorbidity, with the agents, Indian brands and dosing carried in the Anxiety, OCD and trauma-related disorders notes rather than re-taught here.

GOOD TO REMEMBER

- **Structured cognitive-behavioural therapy (Cluster C):** mechanism is graded exposure to avoided or feared situations plus cognitive restructuring of the core beliefs (inadequacy in avoidant, helplessness in dependent, the need for control in anankastic), with assertiveness and autonomy skills; indication is all three cluster C types, and it engages fastest in avoidant and dependent personality disorder, where the anxious behaviour is distressing to the person; signature caution is the alliance and pace, shame drives drop-out in the avoidant patient, the anankastic patient resists surrendering control, and the dependent patient can transfer their dependence onto the therapist. Medication is for a comorbidity only, never disorder-specific.

INDIA

Two genuine India angles meet on cluster C. First, under-recognition: the anankastic patient is ego-syntonic and almost never self-refers, reaching services only through burnout, a comorbid depression or a family complaint, while the avoidant and dependent patient usually presents for a comorbid anxiety or depressive disorder rather than for the personality itself, so the diagnosis is made only when it is actively sought. Second, and the more testable, is the cultural reading of dependent personality disorder. In collectivist Indian family life, interdependence, deference to elders, and decisions made jointly or by the family (about marriage, work or money) are normative, not pathological; scoring them as dependent personality disorder through a single culture's autonomy norms is a straight error, and DSM-5-TR itself requires that dependence be judged excessive relative to the person's own cultural and situational context, weighed with an informant. The same caution applies to over-conscientiousness read as anankastic when it reflects religious or cultural observance. Structured psychotherapy for these disorders is available unevenly and mostly at tertiary and private centres.

9.8 The countable skeleton

One line rebuilds the cluster. Three types, three fears, three thresholds and one marquee boundary are the whole of cluster C worth carrying into the hall. Hook them once and each type unpacks from its fear.

MNEMONIC

FLEE, CLING, CONTROL

The three cluster C types by the fear they answer. **FLEE** is avoidant personality disorder (wants closeness, flees it for fear of rejection, four or more of the seven). **CLING** is dependent personality disorder (needs to be cared for, clings for fear of separation, five or more of the eight). **CONTROL** is anankastic or obsessive-compulsive personality disorder (orders the world for fear of anything going wrong, ego-syntonic, no true obsessions or compulsions, four or more of the eight). Flee from people, cling to a person, control the world.

3	5	6
CLUSTER C TYPES (ANXIOUS OR FEARFUL)	ICD-11 TRAIT DOMAINS (ANANKASTIA IS THE CLUSTER C ONE)	DSM-5 ALTERNATIVE-MODEL TYPES KEPT (DEPENDENT DROPPED)

HOLD THIS

Cluster C is anxious or fearful: avoidant wants closeness but fears rejection (four or more of the seven), dependent needs to be cared for and clings for fear of separation (five or more of the eight), anankastic controls and perfects the world (four or more of the eight); and the marquee line is anankastic personality (ego-syntonic character, no true obsessions or compulsions) against OCD (ego-dystonic, resisted obsessions and compulsions).

10 · Borderline personality disorder versus bipolar II

The discriminator the whole chapter builds toward. Two conditions share a surface, mood that will not hold still and behaviour that runs ahead of judgement, and the examiner exploits the overlap: is this borderline personality disorder or is this bipolar II disorder? Getting **borderline**

versus bipolar right is not a fine academic point but the fork on which the management plan turns, because one answer sends the patient to a structured psychotherapy and the other to a mood stabiliser. This note owns that **discrimination**. The bipolar-II side of the picture, the hypomanic and depressive syndromes and their neurobiology, is developed in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes; here the two are held side by side and pulled apart.

The trick is to resist matching on the shared symptom and instead read **one discriminator** at a time, each of which points reliably to one diagnosis. The **bipolar ii differential** reduces to a small grid of these discriminators, the tempo and trigger of the mood change, the duration of a shift, the presence of an unstable identity and chronic emptiness, the character of the self-harm and impulsivity, the family history, and the response to a mood stabiliser. Read across the grid and the answer usually declares itself. The accompanying figure lays the same discriminators out as a two-column contrast, and it is the single image to carry for this topic.

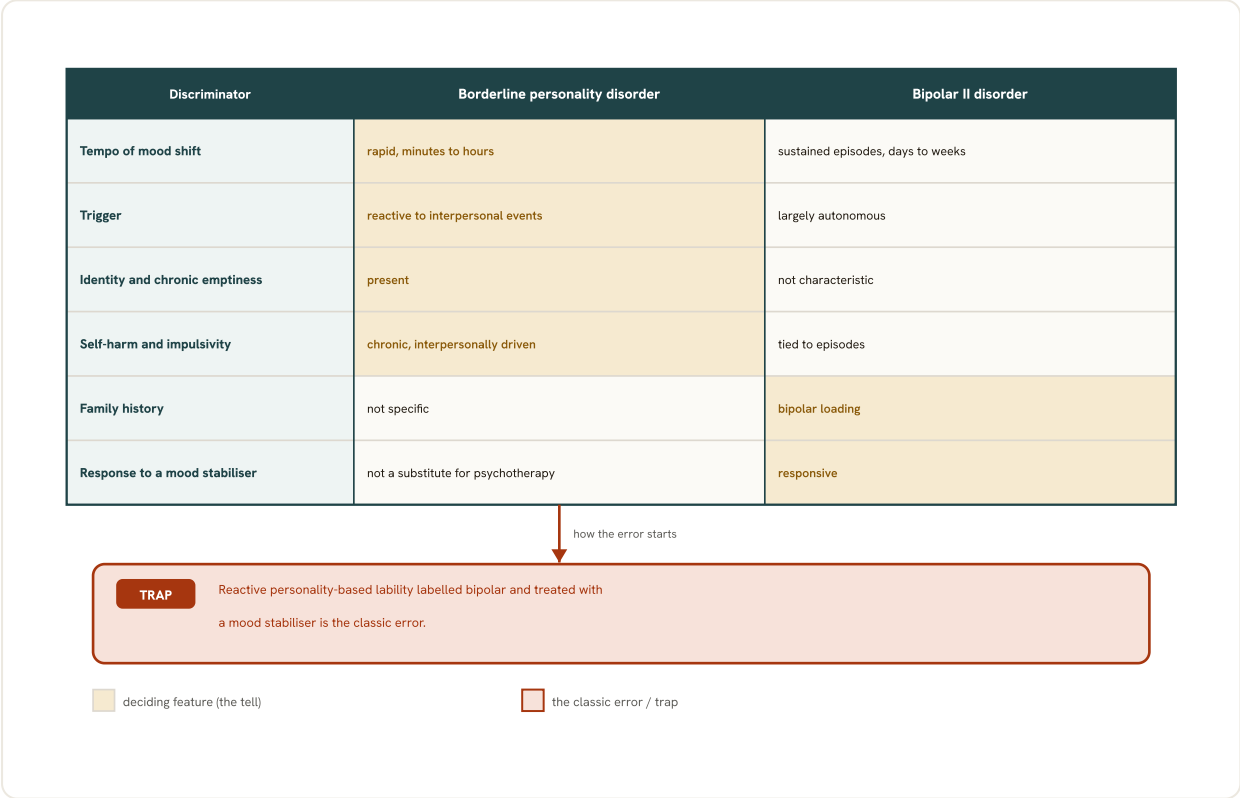


Fig 16.8 Borderline mood instability is rapid and reactive to interpersonal triggers, with identity disturbance and chronic emptiness; bipolar II episodes are sustained and autonomous with a bipolar family history and a mood-stabiliser response. The bipolar syndromes are taught in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes.

10.1 The shared surface, and why the misdiagnosis is easy

Both present with mood lability and impulsivity, so the overlap is real. A patient who describes moods that flip, relationships that combust and impulsive acts they regret can fit either label on first telling, and the temptation is to hear "unstable mood" and reach for bipolar II disorder. The overlap is genuine: affective instability and impulsivity are cardinal in borderline personality disorder and are also the texture of the hypomanic and depressive swings of bipolar II. But the two instabilities have a different *form*, and the discipline of this topic is to describe the

mood change rather than name it, then let its tempo, its trigger and its duration decide. The discrimination fails only when the clinician pattern-matches on the shared word and stops looking.

RULE **Read the mood, do not name it.** Discriminate borderline from bipolar II on the tempo, the trigger and the duration of the affective change: reactive, interpersonally cued shifts over minutes to hours are borderline; autonomous, sustained episodes over days to weeks are bipolar.

10.2 The discriminator grid: one discriminator per row

The object to reproduce cold. Hold the differential as a grid in which each row turns on a single discriminator, and each discriminator points to one side. The highlighted cell in every row is the one that settles that row; read the whole column on either side and the diagnosis emerges as a pattern, not a single sign. This is the same grid drawn in the figure alongside.

DISCRIMINATOR	BORDERLINE PERSONALITY DISORDER	BIPOLAR II DISORDER
Tempo of affective instability	**Rapid shifts over minutes to hours, often several within one day**	Sustained episodes evolving over days to weeks
Trigger of the mood change	**Reactive, cued by an interpersonal event (rejection, criticism, a threat of abandonment)**	Largely autonomous; episodes arise and remit on their own timetable, frequently unprovoked
Duration of a mood shift	Dysphoria, irritability or anxiety usually lasting a few hours and only rarely more than a few days	**Hypomania at least four consecutive days; a depressive episode at least two weeks**
Baseline between shifts	Chronic dysphoria and emptiness; rarely a settled euthymic baseline	**Return to a euthymic baseline between discrete episodes**
Identity and emptiness	**Identity disturbance and chronic emptiness are core and enduring**	Identity is stable; emptiness is not a defining feature
Self-harm and impulsivity	**Self-harm is recurrent and affect-regulating, interpersonally cued; impulsivity is a pervasive lifelong trait**	Risk-taking and impulsivity are state-bound to the hypomanic phase; self-harm clusters in depressive episodes
Family history	Loads toward cluster B traits, trauma, mood and substance problems	**A strong loading for bipolar disorder points toward bipolar**
Response to a mood stabiliser	Modest and symptom-targeted at best; never a substitute for structured psychotherapy	**Often clearly effective; the mainstay of treatment**

The borderline-versus-bipolar-II discriminator grid; each row turns on one discriminator, and the highlighted cell is the one that decides it. No single row is definitive alone; the diagnosis is the whole pattern read across the columns.

5+	4	5
OF NINE BORDERLINE CRITERIA TO DIAGNOSE	DBT SKILLS MODULES (THE THERAPY BORDERLINE RESPONDS TO)	ICD-11 TRAIT DOMAINS (THE DIMENSIONAL CROSS-MAP)

10.3 The affective instability tempo, and the duration of mood shifts

The clock is the first and best discriminator. The **affective instability tempo** in borderline personality disorder is fast: mood swings over minutes to hours, sometimes several times within an afternoon, and it settles as quickly as it flared. The DSM-5-TR criterion says as much, episodic dysphoria, irritability or anxiety usually lasting a few hours and only rarely more than a few days. The **duration of mood shifts** in bipolar II disorder is categorically longer: hypomania requires a distinct period of persistently elevated or irritable mood lasting **at least four consecutive days**, and a major depressive episode lasts **at least two weeks**. Between those episodes the bipolar patient typically returns to a euthymic baseline, whereas the borderline patient rarely does, sitting instead on a floor of chronic dysphoria. So the two questions to ask are: how long does a low or an irritable spell last, and where does the mood return to when it passes.

10.4 The trigger: reactivity to interpersonal triggers versus autonomy

Ask what set the mood off. The second discriminator is the **reactivity to interpersonal triggers**. Borderline affective instability is characteristically reactive: a text left unanswered, a perceived slight, a looming separation, and the mood collapses or the anger flares, then eases when the relationship is repaired. Bipolar mood is largely autonomous; a hypomanic or depressive episode arrives and departs on its own timetable, often with no proportionate external cause, and it does not switch off the moment an interpersonal rupture is mended. This is why the history should chase the antecedent of every mood change: a mood that tracks the state of a relationship minute by minute is borderline reactivity, whereas a mood that runs for a week regardless of what is happening around the person is a bipolar episode. Rejection sensitivity, the exquisite reactivity to perceived abandonment, is the borderline signature that has no bipolar counterpart.

WORKED EXAMPLE

A woman in her twenties is referred as "query bipolar II, mood swings". On history the swings last two to three hours, always follow a fight with her partner or a fear he is pulling away, and lift the moment he reassures her; she describes never knowing who she is and a constant hollow emptiness, and she cuts when the distress peaks. Nothing here is a sustained, autonomous, days-long episode with a euthymic return. Read one discriminator at a time, the hours-long tempo, the interpersonal trigger, the identity disturbance and emptiness, and the picture is borderline personality disorder, not bipolar II. The label matters: it points to a structured psychotherapy, not to a mood stabiliser prescribed for a bipolarity she does not have.

10.5 Identity, chronic emptiness, and the character of self-harm and impulsivity

Look for the features bipolar II simply does not carry. The **identity and self-harm** row is decisive because these features belong to borderline personality disorder and are not part of bipolar II at all. Identity disturbance, a markedly and persistently unstable self-image, and chronic emptiness, a persistent hollowness distinct from depressive sadness, are core borderline criteria

with no bipolar equivalent; a genuinely stable sense of self between episodes argues strongly against borderline. The *character* of the self-harm and impulsivity discriminates too. In borderline personality disorder self-harm is recurrent, interpersonally cued and typically functions to regulate unbearable affect or to end dissociation, and the impulsivity is a pervasive, lifelong trait present between crises. In bipolar II the risk-taking and impulsivity are state-bound, confined to the hypomanic phase and absent when euthymic, and the self-harm clusters within depressive episodes. So the same behaviour, cutting or reckless spending, discriminates by *when* it happens: pervasive and trigger-linked in borderline, phasic and episode-linked in bipolar.

PEARL

Impulsivity that is present *between* episodes is a personality trait; impulsivity that appears only *during* an elevated mood and vanishes when the mood settles is a state. Trait impulsivity, chronic emptiness and an unstable identity together pull hard toward borderline; state-bound impulsivity on a euthymic baseline pulls toward bipolar II. The discriminator is not the behaviour but its timing against the mood.

10.6 Family history, and the response to a mood stabiliser

Two corroborating discriminators, held as support rather than proof. The **family history** is a genuine pointer because bipolar disorder is among the most heritable of psychiatric conditions: a strong, well-documented bipolar loading in first-degree relatives raises the prior for bipolar II, whereas a family picture weighted toward trauma, cluster B traits, mood and substance problems fits borderline better. Treat it as corroboration, not verdict, since both loadings can coexist. The **response to a mood stabiliser** is the other corroborating discriminator, and it is where the error becomes consequential. In bipolar II a mood stabiliser (lithium, valproate, or lamotrigine (Lamitor, Lametec) for the depressive pole) is foundational and often clearly effective; the deep pharmacology sits in the Mood disorders: pharmacotherapy notes. In borderline personality disorder the same drugs have at best a modest, symptom-targeted effect and are never a substitute for structured psychotherapy, which is the primary treatment. A patient whose "mood swings" do not respond to an adequate mood-stabiliser trial was very likely never bipolar; the non-response is itself a discriminator.

GOOD TO REMEMBER

- **Borderline personality disorder:** a pervasive pattern of instability of relationships, self-image and affect with marked impulsivity, five or more of the nine criteria; the affect is rapidly reactive, interpersonally triggered and lasts hours, on a floor of chronic emptiness and an unstable identity. First discriminating step in this differential: read the tempo, the trigger and the baseline of the mood change.
- **Bipolar II disorder:** at least one hypomanic episode (elevated or irritable mood, at least four consecutive days) plus at least one major depressive episode (at least two weeks), with a euthymic baseline between discrete, largely autonomous episodes and no full manic episode. Discriminator: sustained, autonomous, days-to-weeks episodes, not minutes-to-hours interpersonal reactivity.
- **Dialectical behaviour therapy:** the structured psychotherapy the borderline side responds to; it targets emotion dysregulation and self-harm through four skills modules (mindfulness, distress tolerance, emotion regulation, interpersonal effectiveness). Indication is recurrent self-harm and affective instability in borderline personality disorder, not the mood episodes of bipolar II. Caution: it treats the personality pathology, not a coexisting bipolar illness, which still needs its mood stabiliser.

10.7 The classic trap, and holding both diagnoses when they co-occur

The error and its correction. The classic trap is to hear reactive, hours-long, interpersonally driven lability, label it bipolar II, and start a mood stabiliser, medicalising a personality-based instability whose primary treatment is a structured psychotherapy. The drug then chases a misdiagnosis rather than an illness, the patient does not improve, and the failure is read as treatment resistance rather than as the wrong target. The correction is the grid: apply the discriminators before the label. Equally, the two are not mutually exclusive, and a comorbid bipolar II disorder is not rare in patients with borderline personality disorder; when a genuine, sustained, autonomous episode with a euthymic baseline is documented alongside the pervasive reactive pattern, both diagnoses stand and both treatments are needed, the mood stabiliser for the episodes and the structured psychotherapy for the personality pathology. The boundary with complex post-traumatic stress disorder, the other great mimic of borderline instability, is drawn in the Anxiety, OCD and trauma-related disorders notes.

TRAP **Labelling reactive instability "bipolar" and starting a mood stabiliser.** Reading minutes-to-hours, interpersonally cued lability as bipolar II and prescribing a mood stabiliser treats a personality-based instability with the wrong tool and delays the structured psychotherapy that is its actual primary treatment.

COMMON TRAP

Assuming the diagnosis is either-or. A strong bipolar family history or a documented autonomous episode does not exclude borderline personality disorder, and a clear borderline pattern does not exclude a genuine comorbid bipolar II. Diagnose each on its own evidence: the pervasive reactive pattern for borderline, a discrete sustained autonomous episode with a euthymic return for bipolar II. Where both are truly present, treat both.

10.8 The India lens: under-recognition, cultural expression, and access to therapy

The trap is amplified in Indian practice. Borderline personality disorder is markedly under-recognised in India: patients reach services through the overdose or the self-harm, which is coded as the act rather than the pattern, so the reactive lability underneath is repeatedly mislabelled as a mood disorder and medicated as bipolar. Two adaptations matter for this discrimination. First, cultural expression: affective display, transient dissociative or possession-trance presentations, and intense family-embedded reactions are normative idioms of distress in many Indian settings and must be judged against the person's own cultural and social norms before they are read as either borderline reactivity or a bipolar episode; personality pathology must not be read through a single culture's norms. Second, access: the structured psychotherapies the borderline side points to, dialectical behaviour therapy and schema therapy, are being delivered and culturally adapted at Indian tertiary and private centres rather than being widely available, so recognising that a patient needs psychotherapy rather than a mood stabiliser is only the first step, and a realistic plan must reckon with what the local service can actually deliver.

INDIA

Because borderline personality disorder is under-recognised in Indian practice, reactive interpersonal lability is disproportionately mislabelled bipolar and treated with a mood stabiliser, the exact trap of this topic. Judge every mood change against the patient's own cultural norms before scoring it, so that culturally sanctioned emotional expression and dissociative or possession-form idioms are not read as either a borderline criterion or a hypomanic episode. And recognise that catching the borderline diagnosis only helps if dialectical behaviour therapy or schema therapy is reachable; both are available and being adapted in the metros and academic centres but scarce elsewhere, which the plan must accommodate.

MNEMONIC

REACTIVE and RAPID versus AUTONOMOUS and SUSTAINED

The one-line split. Borderline instability is **REACTIVE** (interpersonally triggered) and **RAPID** (minutes to hours, on a floor of emptiness with an unstable identity); bipolar II mood is **AUTONOMOUS** (arises unprovoked) and **SUSTAINED** (days to weeks, with a euthymic baseline). Trigger and tempo first, then the corroborating family history and mood-stabiliser response.

HOLD THIS

Borderline affective instability is reactive, interpersonally triggered and lasts minutes to hours on a floor of chronic emptiness and unstable identity; bipolar II mood is autonomous and sustained over days to weeks (hypomania at least four consecutive days, depression at least two weeks) with a euthymic baseline; the mood stabiliser helps bipolar, while structured psychotherapy is primary for borderline, and mislabelling the first as the second is the classic, consequential error.

Aetiology, assessment and treatment

11 . Aetiology of personality disorders

Ask the question at three levels, then name one model. The **aetiology of personality disorders** is examined the same way every time: at the **genetic** level (what is heritable), the **neurobiological** level (the circuitry and neurochemistry that carry the trait), and the **developmental** level (attachment, trauma, temperament and the environment that shapes the trait into a disorder), all knitted together by a **gene-environment** transaction rather than a single cause. What is inherited is never a diagnostic category; it is a set of continuous personality trait dimensions whose extreme configurations, transacting with a formative environment, become the inflexible patterns the classification then labels.

This fragment walks the three levels in turn, states the integrating gene-environment principle, and then teaches the one disorder-specific aetiological model examiners expect by name, the Marsha Linehan biosocial theory of borderline personality disorder: a biologically heightened **emotional vulnerability** transacting reciprocally, across development, with a pervasively **invalidating environment**. The accompanying figure lays the transaction out schematically. The bipolar-II side of the affective-instability spectrum is cross-referenced to the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes; the complex-PTSD boundary to the Anxiety, OCD and trauma-related disorders notes; the deep serotonergic and mood-stabiliser pharmacology to the Mood disorders: pharmacotherapy notes; and attachment-based technique to the Psychotherapies, clinical assessment, MSE and nosology notes.

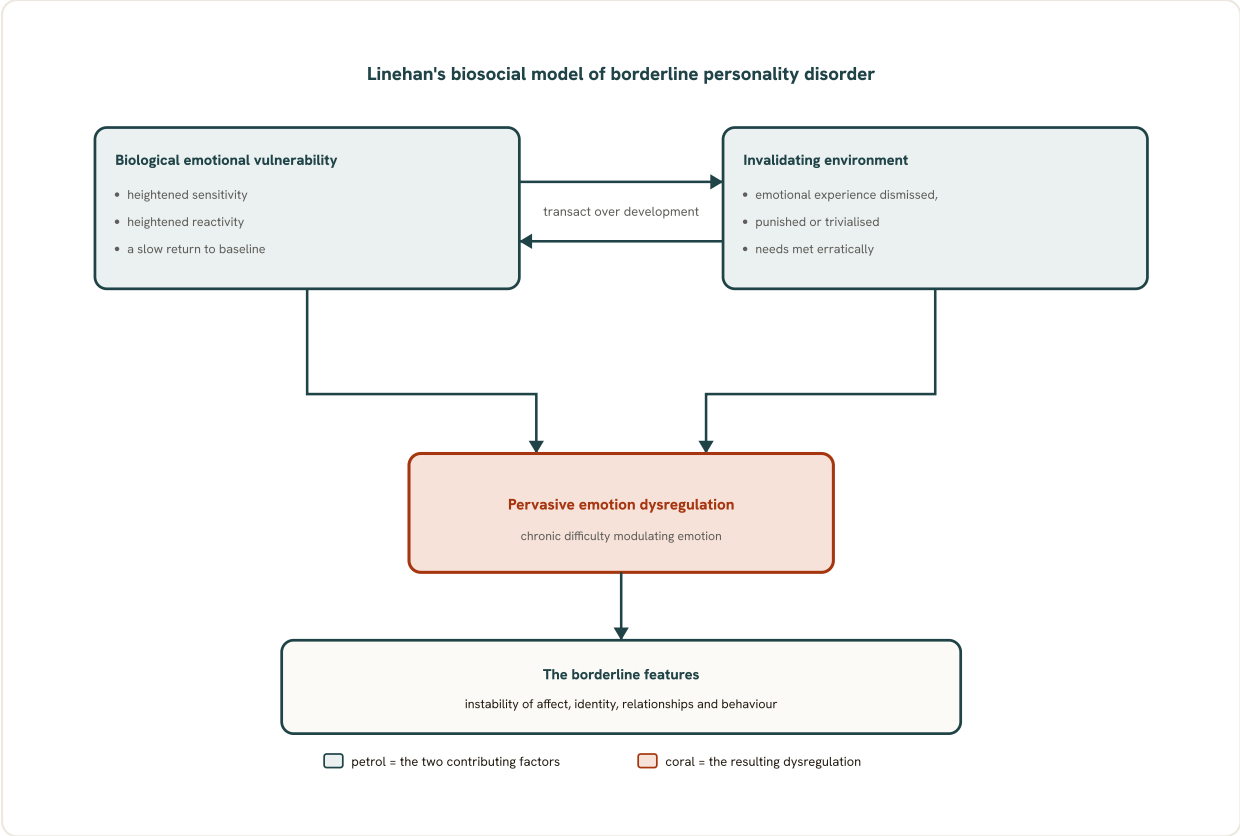


Fig 16.9 Linehan's biosocial model holds that a biological emotional vulnerability (heightened sensitivity and reactivity with a slow return to baseline) transacts reciprocally over development with a pervasively invalidating environment, and the transaction produces the pervasive emotion dysregulation that underlies the borderline features.

11.1 The three-level frame and the diathesis-stress spine

No personality disorder has a single cause. The stable finding across every type is that a heritable trait diathesis is necessary but not sufficient; the disorder emerges only when that diathesis meets a formative environment, and the two do not simply add but transact. Hold the three levels as a scaffold, the **genetic** (heritable trait dimensions), the **neurobiological** (the amygdala-prefrontal emotion circuitry and the serotonergic substrate of impulsive aggression) and the **developmental** (attachment disruption, childhood maltreatment, temperament), and read them not as competing explanations but as three windows on one process. This diathesis-stress spine, sharpened into a reciprocal transaction, is what the Linehan model makes concrete for borderline personality disorder, and it is the frame an examiner is testing when the question simply says "discuss the aetiology".

11.2 The genetic level: heritable dimensions, not heritable categories

Personality disorder is moderately heritable, and inherited as continuous traits. Twin, family and adoption studies agree that liability to personality pathology varies quantitatively and is moderately heritable, with estimates for normal and abnormal personality traits clustering in the roughly 40 to 60 per cent band. Crucially, personality disorders are not transmitted as discrete entities; what is inherited is a spread of trait dimensions, and the disorders are unusual configurations of the same traits that vary across the general population. The heritable loading is shared across spectra rather than tidy per-category packages: an **impulsivity and externalising** spectrum and an **affective-instability** spectrum load onto borderline and antisocial pathology

together, which is why comorbidity among the types is the rule. Most of the heritability sits in complex gene-gene interaction (epistasis) rather than in the average effect of single variants, so that individual common genes explain very little variance even in samples of tens of thousands, the so-called missing-heritability problem; the variants that are found tend to regulate neural development and neuroplasticity.

ENTITY	HERITABILITY ESTIMATE	WHAT IT TELLS YOU
Personality traits (normal + abnormal)	Moderate, roughly 40 to 60 per cent	Inherited as continuous dimensions, not discrete categories; mostly via epistasis (gene-gene interaction)
Any personality disorder	**Broad heritability about 44 per cent (Torgersen twins: MZ concordance 58, DZ 36 per cent)**	The anchor twin figure; DZ correlations well under half of MZ point to gene-environment interaction
Clusters A, B and C	Moderate, 40 to 60 per cent each	Separate heritable influences further differentiate the three clusters
Antisocial personality (symptom count)	The most heritable type, around 38 per cent	Best-studied; adoption and twin data converge; an unstable, hostile home acts synergistically
Paranoid personality (symptom count)	The least, around 28 per cent	Weak-to-moderate range across the ten categorical types

Heritability of personality pathology (Torgersen SCID-II twin data and DSM symptom-count studies). The highlighted any-disorder figure is the number to carry; the message is moderate, dimensional, and gene-environment dependent.

11.3 The neurobiological level: an amygdala-prefrontal imbalance and a serotonergic floor

Emotion dysregulation and impulsive aggression have a shared circuitry. At the **neurobiological** level the recurring finding is an imbalance in the **amygdala-prefrontal** emotion-regulation circuit: a hyperreactive amygdala that responds fast and hard to emotionally salient and socially threatening cues, paired with hypofunction of the prefrontal regions (orbitofrontal cortex and anterior cingulate) that would normally exert top-down inhibitory control. The net effect is intense, poorly braked affect, exactly the reactivity that shows up clinically as affective instability and as anger that outruns its trigger; imaging of individuals with impulsive aggression (Emil Coccaro and colleagues) shows just this exaggerated amygdala and blunted orbitofrontal response to social threat. Beneath the circuit sits a neurochemical dimension: reduced central **serotonergic** function correlates with **impulsive aggression** and with self-directed violence, the endophenotype Larry Siever placed at the centre of the borderline and antisocial impulsive-aggressive spectrum. That serotonergic floor is the rationale, cross-referenced to the Mood disorders: pharmacotherapy notes, for the symptom-targeted use of serotonin reuptake inhibitors against impulsive aggression, and it is a dimensional trait marker, not a disorder-specific lesion.

11.4 The developmental level: attachment, trauma and temperament

Early relationships and adversity shape the trait, but do not simply cause the disorder. Three **developmental** strands recur. First, **attachment disruption**: disorganised early attachment and a caregiving environment that fails to help the child read and regulate internal states leave a fragile capacity to mentalise (to hold minds in mind), which Peter Fonagy places at the heart of the borderline vulnerability. Second, **childhood trauma and maltreatment**: histories of sexual and physical abuse, neglect and pervasive family adversity are over-represented, and childhood sexual abuse is reported by a large minority to a majority of borderline patients (roughly 40 to 70 per cent). Third, **temperament**: early-emerging, procedurally learned dispositions (high negative emotionality, effortful-control deficits, novelty seeking) are the behavioural face of the heritable diathesis and are visible long before a disorder can be diagnosed. The developmental level is the environment that the genetic diathesis meets, and it is where the therapeutic leverage lies; the complex-PTSD-versus-borderline boundary that this trauma strand raises is developed in the Anxiety, OCD and trauma-related disorders notes.

TRAP **Reading childhood abuse as the cause of borderline personality disorder.** Childhood sexual abuse is reported by roughly 40 to 70 per cent of borderline patients, yet the association is only moderate (a meta-analytic effect size of about r = 0.28) and is neither necessary nor sufficient; trauma is a powerful risk factor that transacts with the diathesis, not the single cause.

11.5 The integrating principle: the gene-environment transaction

Diathesis and environment do not add, they transact. The three levels are bound by **gene-environment** interplay operating in both directions. Genes moderate how strongly a child reacts to adversity (gene-environment interaction), and a child's heritable temperament also shapes and selects the very environment it meets: an irritable, emotionally intense infant evokes harsher, more inconsistent caregiving (evocative gene-environment correlation) and later seeks out environments that amplify the trait (active correlation). The consequence is a feedback loop rather than a sum, in which a heritable diathesis and a formative environment escalate one another over years. This is precisely why the same adversity produces a personality disorder in one child and resilience in another, and why heritability estimates that ignore this transaction over-read the genetic share. The transactional reading is the modern successor to plain diathesis-stress, and it is the exact logic the Linehan model applies to borderline personality disorder.

RULE **A heritable trait becomes a disorder only in transaction with development.** Inherited trait dimensions set the diathesis; the disorder emerges through their reciprocal gene-environment transaction with attachment, trauma and the family environment, never from heredity or adversity alone.

11.6 The Linehan biosocial model: the disorder-specific synthesis

Borderline personality disorder is fundamentally a disorder of the emotion-regulation system. The Linehan **biosocial model** is the aetiological theory to name for borderline personality disorder, and it is simply the gene-environment transaction made concrete. In the **Linehan biosocial** account, the pervasive emotion dysregulation that underlies the borderline features results from continuous, reciprocal transactions among three components: a biological

emotional vulnerability, a pervasively **invalidating environment**, and the emotion dysregulation the two of them generate. None of the three is the cause on its own; the causal force is the transaction between them, running back and forth across development, and the figure alongside sets out that reciprocal loop. Because the model locates borderline pathology in emotion regulation rather than in character or manipulation, it is also non-pejorative and directly treatment-guiding, which is why it, and not the older object-relations account alone, is the model expected in an examination answer.

3	3	5	44
COMPONENTS OF THE LINEHAN BIOSOCIAL TRANSACTION	FEATURES OF THE EMOTIONAL VULNERABILITY	ICD-11 DIMENSIONAL TRAIT DOMAINS	BROAD HERITABILITY OF ANY PERSONALITY DISORDER, PER CENT (TORGERSEN TWINS)

11.7 The biological emotional vulnerability

Fast up, hard hit, slow down. The first arm of the model is a biologically mediated **emotional vulnerability**: a predisposition to affective instability arising from genetic, intrauterine and temperamental factors, and defined by three properties. The person is emotionally over-sensitive (a low threshold, so a wide range of ordinary stimuli triggers a response), over-reactive (a high magnitude of physiological arousal once triggered), and slow to return to baseline. The third property is the engine of the disorder: because arousal decays slowly, each subsequent event lands on top of incompletely settled arousal, making extreme responses ever more likely, the emotional equivalent of a burn victim feeling the wind. This vulnerability is the biological diathesis of the transaction, and it is what a treatment such as dialectical behaviour therapy targets with emotion-regulation and distress-tolerance skills.

Heightened sensitivity

A low threshold for emotional response; a wide range of everyday cues sets emotion off.

Heightened reactivity

A high magnitude of physiological arousal once a response is triggered.

Slow return to baseline

Arousal decays slowly, so successive events compound and escalate; the property that drives the instability.

11.8 The pervasively invalidating environment

An environment that teaches the child not to trust its own experience. The second arm is the **invalidating environment**: one that pervasively criticises, minimises, trivialises, punishes or only erratically reinforces the communication of internal experience, and that over-simplifies how easy problems are to solve ("you're not really upset", "you don't know what you want"). Two consequences follow. The child learns that its own thoughts and feelings are wrong, unimportant or shameful, and so comes to rely excessively on the social surround for cues on how to feel, producing the interpersonal hypersensitivity that marks the disorder. And because ordinary emotional displays are dismissed while extreme ones are intermittently attended to, the environment shapes escalation: the child who is ignored until it threatens self-harm, and then receives soothing, is taught that only extreme distress works. Childhood sexual and physical

abuse are the prototypical severe instances, but the invalidation need not be abusive; a well-meaning but poorly matched caregiver of a highly vulnerable child can invalidate inadvertently.

PEARL

The most examinable mechanism inside the invalidating environment is *intermittent reinforcement of extreme emotional displays*. When calm requests are ignored and only crisis behaviour (self-harm, threats) draws a caring response, the environment inadvertently trains the very high-amplitude behaviour it then finds intolerable. Naming this loop explains why borderline self-harm is so resistant to simple reassurance and why dialectical behaviour therapy works to break the contingency rather than to scold the behaviour.

11.9 The transaction, its product, and the treatment it points to

The two arms amplify each other; emotion dysregulation is the product. The force of the model is reciprocal. A highly emotionally vulnerable child is harder to soothe and so makes an environment more invalidating, even when caregivers mean well; and a more invalidating environment, by punishing and confusing emotional learning, further worsens the vulnerability. Round the loop turns, and its cumulative product is a pervasive **emotion dysregulation** that expresses itself across the borderline domains, the unstable relationships, the identity disturbance, the reactive affect, the impulsivity and the self-harm, all of them re-read as failures of emotion regulation rather than as separate symptoms. Because the model names a mechanism, it names a treatment: dialectical behaviour therapy was built directly on it to teach the emotion-regulation skills the transaction never allowed to develop, and schema therapy targets the same developmental deficits through the maladaptive schema modes; both are developed on their own topics in this chapter.

INDIA

Three India-specific points are genuine here. First, under-recognition: personality disorders are markedly under-diagnosed in Indian practice because patients reach services through the self-harm, the overdose or a comorbid depression, which is coded as the event rather than the enduring pattern, so the aetiological formulation is rarely made. Second, cultural expression: judge every trait and every "invalidation" against the person's own cultural and family norms, because collectivist family interdependence must not be misread as pathological dependence or as an invalidating environment, and possession-trance and dissociative idioms are normative in many settings. Third, access and forensic framing: dialectical behaviour therapy and schema therapy are being delivered and culturally adapted at Indian tertiary and private centres rather than being widely available, and antisocial personality disorder in particular carries a medico-legal frame (offender assessment, court reports) developed in the Mental health legislation and forensic psychiatry notes.

GOOD TO REMEMBER

- **Borderline personality disorder (aetiology):** the model to name is the Linehan biosocial theory, a biologically heightened emotional vulnerability (heightened sensitivity, heightened reactivity, slow return to baseline) transacting reciprocally over development with a pervasively invalidating environment, the transaction producing the pervasive emotion dysregulation that underlies the borderline features. Discriminator from a purely genetic or purely trauma account: the cause is the reciprocal transaction, not either arm alone. The diagnosis still rests on five or more of the nine criteria, developed on its own topic; the first aetiological step is to think transaction, not single cause.

GOOD TO REMEMBER

- **Dialectical behaviour therapy (from the model):** mechanism is to correct the emotion dysregulation the biosocial model places at the core, teaching skills across mindfulness, distress tolerance, emotion regulation and interpersonal effectiveness, delivered through its four treatment modes (individual therapy, the skills group, intersession phone coaching, and the therapist consultation team). Indication is borderline personality disorder, especially where reducing recurrent self-harm is the priority (NICE, Indian Psychiatric Society). Signature caution: it is a comprehensive structured programme, not a brief "DBT-informed" add-on, and delivering truncated fragments is not delivering dialectical behaviour therapy.

HOLD THIS

Borderline personality disorder is neither purely inborn temperament nor purely childhood damage: it is the product of a biologically heightened emotional vulnerability transacting reciprocally, across development, with a pervasively invalidating environment, and it is that gene-environment transaction, not either half alone, that generates the pervasive emotion dysregulation underlying the borderline features.

12 · Assessment of personality

Why this matters. The **assessment of personality** is the step that turns a clinical impression into a defensible diagnosis, and it is examined as a set of named instruments plus two governing principles. The instruments split cleanly into two families: clinician-administered **structured interviews** that confirm a diagnosis against the general criteria, and self-report questionnaires that screen for it. The two principles are the ones a stem is built to catch: a self-report screen identifies, an interview confirms, and personality is a trait, not a state, so it must never be diagnosed from the affect of an acute episode. Learn the instruments as their structure, not their item wording, and hold the two principles as the reasoning frame.



Fig 16.10 Personality assessment integrates longitudinal history, clinical interview, collateral information, dimensional trait and severity measures, developmental context and the effects of the current mental state.

This note typesets the working toolkit: the International Personality Disorder Examination (IPDE) and the Structured Clinical Interview for DSM-5 Personality Disorders (SCID-5-PD) as the categorical confirming interviews; the Personality Inventory for DSM-5 (PID-5) as the dimensional self-report of the trait model; the Zanarini Rating Scale for Borderline Personality Disorder (ZAN-BPD) as a symptom-severity and change measure; and the **ICD-11 severity anchors** as the graded frame that a modern, severity-led assessment records first. The general diagnostic criteria that open the chapter are assumed here; this note owns the measurement, the screen-then-confirm logic, and the state-versus-trait caution. The wider technique of clinical assessment and the mental state examination belong to the Psychotherapies, clinical assessment, MSE and nosology notes.

12.1 Two families of instrument: interviews that confirm, questionnaires that screen

Map the toolkit before the details. Every personality instrument is either an interview or a self-report, and either categorical (does the patient meet the criteria of a named type) or dimensional (how severe and along which trait continua). The four workhorses populate the grid: the IPDE

and the SCID-5-PD are clinician interviews that yield categorical diagnoses; the PID-5 is a self-report that yields a dimensional trait profile; the ZAN-BPD is a clinician scale that quantifies borderline severity for tracking change. Sitting over all of them is the ICD-11 severity judgement, which is not a questionnaire at all but a clinical grading of impairment recorded first. Fix that two-by-two picture and each instrument slots into place.

The prior gate still governs. No instrument replaces the general threshold: an enduring, pervasive, inflexible, culturally deviant pattern with onset by adolescence and clinically significant impairment, not better explained by another disorder. The instruments operationalise that judgement; they do not bypass it. A structured interview is, in effect, the general criteria and the type criteria administered as a disciplined, replicable schedule.

12.2 Self-report versus interview: screen wide, confirm narrow

The single most testable design principle. The **self-report versus interview** distinction is the logic that ties the instruments together. Self-report questionnaires (the IPDE screening questionnaire, the SCID-5 Personality Questionnaire, the PID-5) are quick, patient-completed and deliberately over-inclusive: they are sensitive but not specific, so they *screen* and over-identify. The clinician-administered **structured interview** (the IPDE, the SCID-5-PD) then probes only what screened positive and *confirms* the diagnosis, distinguishing a genuine enduring trait from an endorsed item. A positive screen is a prompt to interview, never a diagnosis in itself. This screen-then-confirm architecture is why the interview instruments each ship with a matched self-report front end.

RULE **Screen wide, confirm narrow.** A self-report questionnaire (the IPDE-SQ, the 106-item SCID-5-SPQ, the PID-5) screens and over-identifies; the structured interview (the IPDE, the SCID-5-PD) confirms against the criteria. A screen that is positive earns an interview; it does not earn a label.

PEARL

Read the self-report and interview as a sensitivity-then-specificity pair. The questionnaire is tuned to miss few cases (high sensitivity, low specificity), so its job is to decide which criteria are worth a clinician's time; the interview is tuned to confirm (specificity), so its job is to decide whether the endorsed pattern is real, enduring and impairing. Getting the order wrong, confirming from a questionnaire, is the commonest measurement error in the personality field.

12.3 The instruments, typeset

The object to hold cold. The instruments are learned as their structure and scoring with a citation, not as their items. The table gathers the four workhorse instruments and their matched screeners; the highlighted cells are the structural facts an examiner reaches for.

INSTRUMENT	ADMINISTRATION	STRUCTURE AND COVERAGE	SCORING	SOURCE
IPDE	Clinician semi-structured interview	**Two modules, an ICD-10 and a DSM-IV module, usable alone or together; questions grouped by six life areas (work; self; interpersonal relationships; affects; reality testing; impulse control), not by disorder**	Each relevant criterion rated 0 absent, 1 subthreshold, 2 criterion level; trait present at least the past five years, one criterion before the age of twenty-five; output both dimensional and categorical (definite or probable)	Loranger, Janca, Sartorius; WHO / Cambridge UP (Loranger et al. 1994)
IPDE-SQ	Self-report screener (true or false)	First-pass filter flagging which disorders to probe in the full interview	A positive screen prompts the interview; not diagnostic	IPDE screening questionnaire
SCID-5-PD	Clinician structured interview	Covers the ten DSM-5 (Section II) personality disorders plus other-specified personality disorder; the DSM-5 successor to the SCID-II	**Each criterion rated 1 absent, 2 subthreshold, 3 threshold; the DSM-5 required criterion counts then decide each diagnosis**	First, Williams, Benjamin, Spitzer 2016 (APPI)
SCID-5-SPQ	Self-report screener (yes or no)	A 106-item questionnaire the patient completes first, so the interview probes only criteria that screened positive	Screening only; not itself diagnostic	SCID-5 Personality Questionnaire
PID-5 (and PID-5-BF)	Self-report dimensional trait measure	**Five higher-order trait domains over twenty-five lower-order facets; full form 220 items, Brief Form 25 items (domain level); operationalises the DSM-5 Section III alternative model Criterion B**	Items scored 0 to 3; domain and facet scores as item means (higher is more maladaptive); no single categorical cut-off	Krueger, Derringer, Markon, Watson, Skodol 2012 (APA)

INSTRUMENT	ADMINISTRATION	STRUCTURE AND COVERAGE	SCORING	SOURCE
ZAN-BPD	Clinician-rated severity and change scale	Nine items, one per DSM borderline criterion, spanning the affective, cognitive, impulsive and interpersonal domains; rated over the prior week	**Each item 0 to 4; total on the 0 to 36 scale; higher is greater severity; tracks change, not a diagnostic cut-off**	Zanarini et al. 2003

The four workhorse personality instruments and their matched self-report screeners, typeset as structure and scoring with a citation; the highlighted cells mark the single fact most often tested for each. Item wording is not reproduced.

GOOD TO REMEMBER

- **IPDE:** a WHO semi-structured interview in two modules (ICD-10 and DSM-IV) organised by six life areas, criteria scored 0, 1 or 2, giving both a dimensional and a categorical output, paired with the IPDE-SQ self-report screener.
- **SCID-5-PD:** the DSM-5 structured interview over the ten Section II personality disorders, criteria rated 1, 2 or 3, fronted by the 106-item SCID-5-SPQ self-report screener; the successor to the SCID-II.
- **PID-5:** the self-report dimensional measure of the five trait domains and twenty-five facets (220-item full form, 25-item brief), the alternative-model Criterion B instrument, with no categorical cut-off.
- **ZAN-BPD:** nine clinician-rated items, one per borderline criterion, each 0 to 4 for a total on the 0 to 36 scale; a severity and change measure, not a diagnostic test.
- **ICD-11 severity anchors:** personality difficulty, mild, moderate and severe on a harm gradient; severity is graded first, before any trait qualifier.

12.4 The categorical confirming interviews: IPDE and SCID-5-PD

Two interviews, one job: confirm a named type against the criteria. The IPDE, developed by Armand Loranger out of the earlier Personality Disorder Examination and adopted under the WHO joint programme, is the international standard. Its distinctive move is to organise questions by life area rather than by disorder, walking the patient through work, self, interpersonal relationships, affects, reality testing and impulse control, so the clinician rates the underlying criteria as they surface across the whole life rather than interrogating one type at a time. Each criterion is scored 0, 1 or 2, and the IPDE builds in a temporal guard against late-onset mimics: a criterion counts only if the trait has run for at least the past five years, with at least one criterion satisfied before the age of twenty-five. It returns both a dimensional score per disorder and a categorical verdict (definite, or probable when one criterion short).

The SCID-5-PD is the DSM-native equivalent. The SCID-5-PD covers the ten DSM-5 Section II personality disorders and rates each criterion on the standard SCID convention of 1 (absent), 2 (subthreshold) or 3 (threshold), with the DSM-5 criterion counts then deciding each diagnosis. Its 106-item self-report questionnaire, the SCID-5-SPQ, is completed first so the interview need only probe the criteria that screened positive, the screen-then-confirm logic in a single package.

Both instruments are copyright and are learned as structure and scoring, not as reproduced items.

GOOD TO REMEMBER

- **IPDE (the discriminator):** the interview organised by six life areas, not by disorder; criteria scored 0, 1 or 2 with the five-year and pre-age-twenty-five temporal guard, yielding a dimensional plus categorical result.
- **SCID-5-PD (the discriminator):** the DSM-5 structured interview over the ten Section II types, criteria rated 1, 2 or 3 to the DSM criterion counts, with the 106-item SCID-5-SPQ as its screen.

12.5 The PID-5 and the dimensional trait map

The self-report that measures the trait model directly. The PID-5 is the self-report operationalisation of the DSM-5 Section III alternative model of personality disorders, specifically its Criterion B maladaptive-trait model. It measures five higher-order trait domains, negative affectivity, detachment, antagonism, disinhibition and psychoticism, resolved into twenty-five lower-order facets. The full form is 220 items on a four-point scale from 0 to 3, scored at domain and facet level; the 25-item Brief Form (PID-5-BF), five items per domain, gives a domain-level profile only. Being dimensional, it has no categorical cut-off: an elevated domain or facet mean flags maladaptive trait expression, to be read alongside the Criterion A judgement of how impaired personality functioning is.

The trait domains almost, but not exactly, match ICD-11. The high-yield trap is that the two dimensional systems share four domains and differ on the fifth. Read the table across: the DSM-5 alternative model and ICD-11 both carry negative affectivity, detachment, a callous-antagonistic domain and disinhibition, but ICD-11's fifth domain is anankastia (rigid over-control), whereas the alternative model's fifth is psychoticism (odd, eccentric cognition). ICD-11 also names its antagonistic domain dissociality and adds a borderline pattern qualifier.

TRAIT-DOMAIN THEME	ICD-11 QUALIFIER	DSM-5 ALTERNATIVE MODEL / PID-5 DOMAIN
Negative emotionality	Negative affectivity	Negative affectivity
Social withdrawal	Detachment	Detachment
Callous, antagonistic	Dissociality	Antagonism
Under-control, impulsivity	Disinhibition	Disinhibition
The differing fifth domain	**Anankastia (rigid over-control)**	**Psychoticism (odd, eccentric)**
Optional pattern specifier	Borderline pattern qualifier	A borderline type is reconstructed from the traits

The two dimensional trait systems share four domains; the fifth differs, ICD-11 adding anankastia while the DSM-5 alternative model adds psychoticism. Cross from one to the other by swapping anankastia for psychoticism (and dissociality for antagonism).

MNEMONIC

Three D's, plus N and A

The five ICD-11 trait domains: the three D's, **D**etachment, **D**issociality and **D**isinhibition, plus **N**egative affectivity and **A**nankastia. To convert to the DSM-5 alternative model, keep negative affectivity, detachment and disinhibition, rename dissociality as antagonism, and swap anankastia for psychoticism.

COMMON TRAP

Reading a high PID-5 domain score as a diagnosis. The PID-5 is dimensional and has no categorical cut-off; an elevated negative-affectivity or detachment mean describes trait expression, it does not by itself declare a personality disorder. The diagnosis still needs the level-of-functioning judgement (Criterion A) and the general threshold. A trait score is a profile, not a verdict.

12.6 The ICD-11 severity anchors

Severity is graded first, and it leads the diagnosis. The **ICD-11 severity anchors** are the frame a modern assessment records before anything else: rather than matching a type, the clinician grades how impaired personality functioning is, on a continuum from personality difficulty through mild, moderate and severe. The judgement rests on impairment of the *self* (identity, self-worth, self-direction) and of *interpersonal* functioning (relationships and roles), together with the risk of harm to self or others. There is no numeric cut-off; the harm gradient is the quick discriminator, running from typically none in mild, through sometimes in moderate, to often in severe.

SEVERITY LEVEL (CODE)	SELF AND INTERPERSONAL FUNCTIONING	HARM TO SELF OR OTHERS
Personality difficulty (QE50.7)	Longstanding pronounced traits shown only intermittently (for example under stress) or at low intensity; some but not notable disruption; a health-status factor, not a mental disorder	Minimal
Mild (6D10.0)	Some areas of self-functioning affected, or all areas mildly; problems in many relationships and roles, but some are maintained	Typically none
Moderate (6D10.1)	Multiple areas of self-functioning affected at moderate severity; marked problems in most relationships and most roles compromised; may show mild dissociative or psychotic-like states under stress	**Sometimes**
Severe (6D10.2)	Severe disturbance in the sense of self; virtually all relationships affected and role performance severely compromised or absent; impairment across nearly all of life	**Often**

The ICD-11 severity anchors, graded on self and interpersonal impairment plus harm risk; the harm gradient (minimal, typically none, sometimes, often) is the quick discriminator, and personality difficulty is a health-status factor rather than a disorder. Trait-domain qualifiers may be added at any severity level.

12.7 The ZAN-BPD: a measure of change, not a diagnostic test

Quantify severity, then track it. The ZAN-BPD, derived by Mary Zanarini from the borderline criteria and the revised diagnostic interview for borderlines, is a nine-item clinician-rated scale in which each item maps onto one of the nine DSM borderline criteria, from frantic efforts to avoid abandonment through to transient stress-related paranoia or dissociation. Each item is rated 0 to 4 over the prior week, for a total on the 0 to 36 scale, with higher scores meaning greater severity. Its purpose is to be sensitive to change: it is the instrument used to measure whether borderline symptoms are responding in a treatment trial or over follow-up, not to make the diagnosis. That confirming diagnosis is the job of the general criteria and a structured interview; the ZAN-BPD then meters the severity over time.

GOOD TO REMEMBER

- **ZAN-BPD (the discriminator):** nine clinician-rated items, one per borderline criterion, each 0 to 4 for a 0 to 36 total; a severity and change measure sensitive to treatment response, explicitly not a diagnostic instrument.

12.8 State versus trait: assess personality at baseline, not mid-storm

The caution that governs the whole assessment. The **state versus trait** rule is the reason a personality diagnosis is timed as much as it is measured: a personality disorder is an enduring, pervasive pattern, so it must not be diagnosed from the affect, impulsivity or relational chaos of an acute episode of another disorder. The lability of a mood episode, the disinhibition of intoxication and the reactivity of a fresh crisis all mimic personality pathology while they last. The safeguards are to assess when the patient is at baseline rather than in the acute state, to require that the same pattern predates and outlasts the episode, and to lean on collateral and longitudinal history rather than a single cross-sectional interview. Situational affective lability without the identity disturbance and abandonment fear is not borderline personality; and the reactive, hours-long mood swings of borderline must be separated from the sustained, autonomous episodes drawn out in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes.

TRAP **Diagnosing a personality disorder mid-episode.** Affective instability, impulsivity and stormy relationships during an acute mood episode, an intoxication or a fresh crisis are state, not trait. Diagnose personality at baseline, against a pattern that is enduring, pervasive and pre-existing, or you will pin a lifelong label on a passing storm.

WORKED EXAMPLE

A woman in her twenties is admitted after self-harm during a depressive relapse, floridly labile and rejecting. The temptation is to record borderline personality disorder from the presentation. The disciplined route is the reverse: quantify the acute picture (a ZAN-BPD can meter current borderline symptoms, but does not diagnose), treat the mood episode, and defer the personality assessment. Reassessed at baseline some weeks later with collateral, a structured interview (the SCID-5-PD or the IPDE) then establishes whether an enduring, pervasive pattern truly predated the episode. Screen if useful, confirm by interview, and grade ICD-11 severity, but do it when the storm has passed.

12.9 The India lens and the cultural frame

Under-recognition makes systematic assessment worth more, not less. Personality disorders are substantially under-recognised in routine Indian practice, surfacing through comorbid mood, substance, anxiety or self-harm presentations rather than as a personality diagnosis, and often left uncoded for fear of stigma. A brief self-report screen embedded in a busy clinic is exactly the low-cost step that raises detection of the mixed and subthreshold cases that a purely impressionistic assessment misses, provided a structured interview then confirms. A severity-led ICD-11 reading, which begins with a graded judgement of dysfunction rather than a full type match, suits this reality well.

Read pathology against the patient's own culture, not a single norm. Every instrument still requires deviation from what the person's *own* culture expects, so joint-family interdependence, deference and religiously framed experience must not be scored as dependent, avoidant or odd pathology; personality must not be read through one culture's norms. On the treatment side, the

structured psychotherapies a severity rating points toward, dialectical behaviour therapy and schema therapy, are available and being culturally adapted at Indian tertiary and private centres but scarce elsewhere, so a severe rating can outrun what a service can deliver; the wider technique of these therapies belongs to the Psychotherapies, clinical assessment, MSE and nosology notes. Antisocial personality disorder carries the sharpest medico-legal weight in the Indian context, where the structured assessment feeds offender and court framing, cross-referenced to the Mental health legislation and forensic psychiatry notes.

INDIA

Personality disorders are under-recognised in Indian practice and present through their comorbidities, so a brief self-report screen followed by a confirming structured interview genuinely raises detection of the subthreshold and mixed cases. Judge deviation against the patient's own cultural norms, so collectivist family-embeddedness is not miscoded as dependency and religiously framed experience not as schizotypal oddness. The structured psychotherapies that a severity rating points to, dialectical behaviour therapy and schema therapy, are available and being culturally adapted in the metros and academic centres but unevenly accessible elsewhere; and antisocial personality disorder carries the medico-legal weight, where the assessment feeds the forensic notes.

5	25	0 to 36	4
ICD-11 AND ALTERNATIVE-MODEL TRAIT DOMAINS	PID-5 LOWER-ORDER TRAIT FACETS (220-ITEM FULL FORM)	ZAN-BPD TOTAL SCORE RANGE (NINE ITEMS)	ICD-11 SEVERITY ANCHORS (DIFFICULTY TO SEVERE)

HOLD THIS

Assessment of personality runs screen-then-confirm: self-report questionnaires (the IPDE-SQ, the 106-item SCID-5-SPQ, the PID-5) screen and over-identify, and a structured interview (the IPDE, organised by six life areas; the SCID-5-PD, over the ten DSM-5 types) confirms against the criteria; grade the ICD-11 severity anchors first (difficulty, mild, moderate, severe on a harm gradient), map the five trait domains and twenty-five PID-5 facets, meter borderline change with the ZAN-BPD, and never fix the diagnosis during an acute episode, because personality is a trait, not a state.

13 . Dialectical behaviour therapy for borderline personality disorder

The first treatment that worked, and the template for all the rest. Dialectical behaviour therapy (DBT) is the psychotherapy that changed the outlook for borderline personality disorder: developed by Marsha Linehan out of failed attempts to treat chronically suicidal women with standard behaviour therapy, it was the first treatment of any kind shown in a randomised trial to reduce self-harm in a group that clinicians had come to regard as untreatable. Examiners return to it because it is comprehensive and highly structured, so it can be dismantled into named parts: a theory of the disorder, an organising philosophy, four skills modules, four treatment modes, a hierarchy of what to treat first, and staged goals across the whole arc of recovery. Learn those parts as a scaffold and the topic answers itself.

This fragment builds DBT from its foundations upward. It sets out the **biosocial theory** that DBT rests on, the central **dialectic** of acceptance and change from which the treatment takes its name, the four skills modules with **mindfulness** as their core, the four modes that together make a comprehensive programme, the target hierarchy that decides what is worked on in any given session, the stages of treatment, and the evidence for the reduction in self-harm and hospitalisation that earned DBT its place at the front of the guidelines. The disorder itself is taught on its own topic; here the pharmacology stays deliberately light and adjunctive, and the deep drug detail is cross-referenced to the Mood disorders: pharmacotherapy notes.

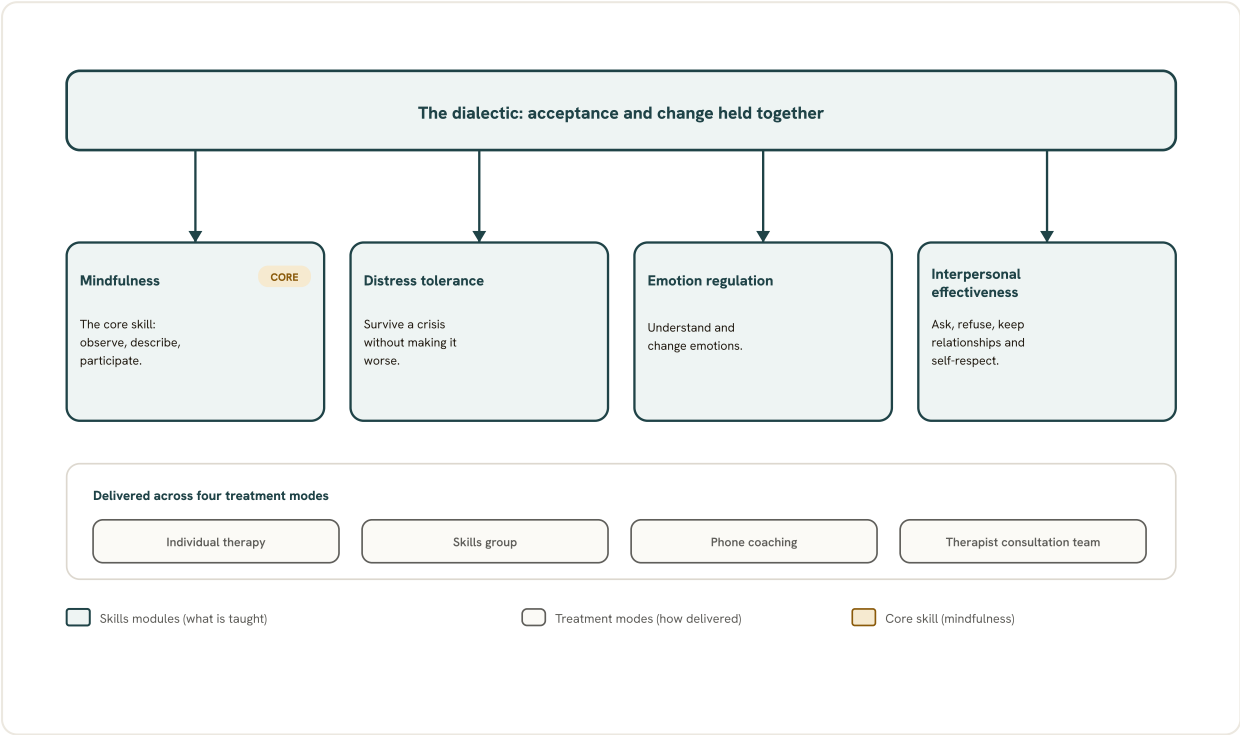


Fig 16.11 Dialectical behaviour therapy holds acceptance and change in dialectic and teaches four skills modules, mindfulness at the core, distress tolerance, emotion regulation and interpersonal effectiveness, delivered across four modes: individual therapy, the skills group, phone coaching and the therapist consultation team.

13.1 Origins and the core proposition

A behaviour therapy rebuilt around emotion dysregulation. Dialectical behaviour therapy grew in the early nineteen-eighties from work on repetitive suicidal and self-harm behaviour. Standard cognitive and behavioural change strategies, applied to chronically suicidal borderline patients, met a wall: pushing for change alone was experienced as invalidating, provoked drop-out and sometimes worsened the very behaviours being targeted. Linehan's solution was to place emotion dysregulation, rather than any single symptom, at the centre of the disorder, and to hold change strategies in constant balance with an equally strong stance of acceptance. The first controlled trial (Linehan and colleagues, published in the Archives of General Psychiatry) tested the new treatment in chronically parasuicidal women and made DBT the first psychotherapy to demonstrate efficacy in borderline personality disorder, opening the era of therapeutic optimism from which schema therapy, mentalisation-based treatment and transference-focused psychotherapy all followed.

4	4	3
SKILLS TRAINING MODULES	TREATMENT MODES IN COMPREHENSIVE DBT	STAGE-ONE TARGET TIERS (LIFE-THREATENING FIRST)

13.2 The biosocial theory of emotion dysregulation

Biology transacting with an invalidating environment. The biosocial theory is DBT's model of how borderline personality disorder arises, and it is the mechanism the whole treatment is built to address. A biological **emotional vulnerability**, meaning heightened sensitivity to emotional stimuli, greater intensity of response, and a slow return to baseline, transacts over development with a pervasively **invalidating environment**, one that dismisses, punishes or responds erratically to the child's inner experience. The transaction is reciprocal: the environment's invalidating responses amplify the biological sensitivity, and the resulting dysregulated behaviour draws further invalidation. The end state is pervasive **emotion dysregulation**, and DBT reads the criterion behaviours of the disorder, self-harm, impulsivity, stormy relationships and identity disturbance, as either the direct consequence of that dysregulation or the person's own attempts to re-regulate an unbearable affective state. Framing self-harm as attempted problem-solving, rather than manipulation, is what makes the theory both compassionate and clinically directive.

PEARL

The biosocial theory is why DBT never treats self-harm as a thing to be simply forbidden. If the behaviour is an attempt to solve the problem of unbearable emotion, then removing it without teaching a replacement skill leaves the person defenceless. Every act on the target list is therefore met with a behavioural chain analysis (what preceded it, what it achieved) and a substitute skill, not merely a safety contract.

13.3 The central dialectic: acceptance and change

Two technologies held in tension. The name of the treatment comes from **dialectics**: the philosophical stance that every position (thesis) calls up its opposite (antithesis) and that truth is found by synthesising the valid kernel of each. The single overarching dialectic in DBT is **acceptance and change**. The therapist must simultaneously accept the patient exactly as they are and relentlessly push for the changes that will build a life worth living, moving fluidly between the two poles rather than settling at either. This resolves the impasse that defeated ordinary behaviour therapy. Practically, DBT fuses two technologies: **behaviourism**, the technology of change (chain analysis, contingency management, skills training, exposure), and mindfulness derived from Zen, the technology of acceptance (validation, and ultimately radical acceptance of reality as it is). The constant motion between accepting and pushing is what gives DBT its characteristic speed and flow, and failures of the treatment are typically dialectical failures, a therapist stuck rigidly at one pole.

RULE **Structured psychotherapy is primary; DBT is the best-evidenced option for self-harm.** In borderline personality disorder the primary treatment is a structured, theory-based psychological therapy, and DBT is the intervention guidelines name first where reducing recurrent self-harm is the priority (NICE 2009, IPS 2023); medication is only adjunctive, symptom-targeted and time-limited.

13.4 The four skills modules, and mindfulness as the core

Four modules, built around a mindfulness centre. DBT teaches concrete behavioural skills in four modules, and Kaplan and Sadock name them exactly: mindfulness, distress tolerance, emotion regulation and interpersonal effectiveness. Mindfulness is the *core*: it is not one module among equals but the foundation, taught first and re-taught recurrently at the start of each of the other three modules. Its skills are the observing, describing and participating "what" skills, and the non-judgmental, one-mindful and effective "how" skills, converging on *wise mind*, the synthesis of emotion mind and reasonable mind. An elegant way to hold the set, shown in the accompanying figure, is that two modules serve *acceptance* (mindfulness and distress tolerance) and two serve *change* (emotion regulation and interpersonal effectiveness), so the four modules themselves mirror the central acceptance-change dialectic. A wrong module is the classic slip; verify the four against this list.

MODULE	POLE	WHAT IT TRAINS	SIGNATURE SKILLS
Mindfulness	**Acceptance (the CORE, re-taught before each module)**	Present-moment, non-judgmental awareness; the ground for all other skills	Observe, describe, participate; non-judgmentally, one-mindfully, effectively; wise mind
Distress tolerance	Acceptance	Surviving a crisis without making it worse; accepting what cannot be changed now	TIP, distraction (ACCEPTS), self-soothe, IMPROVE the moment, radical acceptance
Emotion regulation	Change	Understanding, naming and reducing the intensity of emotions; lowering vulnerability	Check the facts, opposite action, PLEASE (reduce vulnerability), accumulate positives
Interpersonal effectiveness	Change	Asking, refusing and keeping relationships and self-respect intact	DEAR MAN (objectives), GIVE (relationship), FAST (self-respect)

The four DBT skills modules; mindfulness is the core set, taught first and revisited before each of the other three. Two modules serve acceptance, two serve change.

MNEMONIC

DEAR MAN

The interpersonal-effectiveness skill for getting an objective met: **D**escribe the situation, **E**xpress feelings, **A**ssert the ask or the no, **R**einforce (name the benefit to the other), stay **M**indful (broken-record, ignore attacks), **A**ppear confident, **N**egotiate. Its two companions are GIVE (Gentle, Interested, Validate, Easy manner) for keeping the relationship, and FAST (Fair, no Apologies, Stick to values, Truthful) for keeping self-respect.

13.5 Distress tolerance, emotion regulation and interpersonal effectiveness

The three modules that complete the set. **Distress tolerance** is the acceptance-side crisis kit: skills to get through an urge to self-harm or an overwhelming affect without acting on it, from physiological down-regulation (the TIP skills) to distraction, self-soothing and, at its deepest, radical acceptance of a painful reality that cannot be changed in the moment. **Emotion regulation** is the change-side workhorse: it teaches the person to identify and label emotions, to check whether an emotion fits the facts, to act opposite to an unjustified emotion's urge, and to reduce baseline vulnerability by attending to sleep, eating, exercise and mastery. **Interpersonal effectiveness** supplies scripts for asking effectively, refusing without rupture, and preserving both the relationship and self-respect, which directly targets the abandonment sensitivity and the idealisation-devaluation swings of the disorder. The three change-and-tolerance modules are where the biosocial deficits are actively repaired.

TRAP **Calling a stand-alone skills class "DBT".** A weekly skills group on its own is skills training, not comprehensive DBT; the full treatment requires all four modes working together (individual therapy, skills group, phone coaching and a consultation team). Over-relying on distress tolerance while neglecting emotion regulation is the parallel error, since it teaches survival without teaching change.

13.6 The four treatment modes

Four modes, five functions. Comprehensive DBT is delivered through four **modes**, each serving a treatment function. The two that carry the standard trial format are **individual therapy plus skills group**: weekly **individual therapy** (which enhances motivation, uses the diary card and chain analysis, and where the individual therapist bears ultimate responsibility for the target behaviours) and the weekly **skills training group** (which enhances capabilities by teaching the four modules in a psychoeducational, class-like format). Alongside them run between-session phone coaching (which ensures the generalisation of skills into real life, coaching the patient through a crisis in the moment rather than in the next session) and the therapist consultation team (the "therapy for the therapists", which enhances the clinicians' own capability and motivation, guards treatment fidelity, and protects against burnout and dialectical failure). Between them these modes deliver DBT's five functions: enhance capabilities, improve motivation, ensure generalisation, structure the environment, and enhance the therapist. A programme missing any mode is not comprehensive DBT.

MODE	FUNCTION IT SERVES	WHAT HAPPENS IN IT
Individual therapy (weekly)	Improve motivation	One-to-one; diary card review and behavioural chain analysis; the individual therapist holds ultimate responsibility for the targets
Skills training group (weekly)	Enhance capabilities	Class-format teaching of the four modules with homework; a leader and co-leader; opens with a mindfulness exercise
Phone coaching (between sessions)	Ensure generalisation	Brief in-the-moment coaching to apply a skill during a crisis; commonly structured by a rule limiting calls after self-harm
Consultation team	**Enhance the therapist (fidelity and morale)**	Weekly clinician meeting; "therapy for the therapists"; sustains adherence and prevents dialectical failure and burnout

The four modes of comprehensive DBT and the functions they serve. The consultation team, exported into the treatment itself from the trials that use teams to control adherence, is the uniquely DBT mode examiners test.

13.7 The hierarchy of treatment targets

What gets worked on first is fixed, not chosen ad hoc. Because borderline patients typically present with many simultaneous problems, DBT imposes a strict order on what any given individual session addresses. Within the first stage of treatment the targets are ranked: **life-threatening behaviours** first (suicidal and self-harm acts, and credible threats), then **therapy-interfering behaviours** (of the patient or the therapist, such as missing sessions, arriving intoxicated, or a therapist's own drift), and finally **quality-of-life-interfering behaviours** (the substance use, disordered eating, unemployment and relational chaos that seriously destabilise a life). Only once those are in hand does the work turn to increasing behavioural skills. The diary card is scanned against this hierarchy at the top of every session, so a fresh episode of self-harm always pulls the agenda upward regardless of what patient or therapist would rather discuss. This ordering is one of the most reliably examined facts of the topic.

WORKED EXAMPLE

A young woman in comprehensive DBT arrives wanting to talk about a job interview. Her diary card, however, shows a cutting episode three evenings earlier. The target hierarchy decides the agenda: the therapist addresses the life-threatening behaviour first, running a chain analysis of the cutting and rehearsing the distress-tolerance skill that could have replaced it, before any time goes to the interview (a quality-of-life target). The ordering is not coldness; it is the treatment refusing to let the highest-risk behaviour be talked past.

13.8 The DBT stages of treatment

Staged goals across the whole arc of recovery. The **DBT stages** organise the treatment over time, beginning with a distinct pre-treatment phase of orientation and commitment, in which

patient and therapist agree the goals, the mode structure and the working agreements before therapy proper starts. The staged plan then runs from severe behavioural dyscontrol toward a full life, and the target hierarchy above sits inside the first stage.

STAGE	PRESENTING LEVEL	GOAL OF THE STAGE
Pre-treatment	Not yet committed or oriented	Orientation, commitment, agreeing goals, modes and working agreements
Stage one	Severe behavioural dyscontrol	**Behavioural control and stability (the life-threatening, therapy-interfering, quality-of-life target hierarchy)**
Stage two	Quiet desperation; controlled behaviour but emotional suffering	Non-anguished emotional experiencing; processing the past, including trauma and post-traumatic stress
Stage three	Problems in living	Ordinary happiness and unhappiness; self-respect and individual life goals
Stage four	Sense of incompleteness	Capacity for sustained joy, freedom and connection

Pre-treatment plus the four DBT stages. Most suicidal borderline patients enter at stage one, where behavioural control is the priority; trauma processing waits for stage two, after stability is achieved.

13.9 The evidence base: self-harm and hospitalisation

The reductions that earned it the guidelines. The foundational trial (Linehan and colleagues, in chronically parasuicidal women with borderline personality disorder) showed that, compared with treatment as usual, DBT reduced the frequency and medical severity of self-harm, produced fewer psychiatric hospitalisation days, and markedly improved treatment retention by lowering drop-out, even where it did not initially separate on depression or hopelessness. Those two signals, less **self-harm** and less **hospitalisation**, have been the durable core of the DBT evidence base ever since, replicated across later trials and reviews, and DBT remains the most extensively researched and evaluated of all treatments for the disorder (the basis for its Cochrane and guideline standing). Both NICE and the Indian Psychiatric Society recommend DBT specifically to reduce recurrent self-harm and emotion dysregulation, which is exactly the outcome the original trial demonstrated.

13.10 Place among the borderline psychotherapies, and the guideline anchor

One of several structured therapies, first among equals for self-harm. DBT sits alongside schema therapy, mentalisation-based treatment and transference-focused psychotherapy as the evidence-based structured psychotherapies for borderline personality disorder, each with its own mechanism and their own topics in this chapter; DBT is distinguished by its behavioural roots, its skills curriculum, and the strongest evidence base for reducing self-harm. The guideline position is consistent and worth carrying cleanly: structured psychological therapy is the primary treatment, DBT (or an equally comprehensive programme) is offered where recurrent self-harm is

the priority, and pharmacotherapy is not a treatment for the disorder itself but a symptom-targeted, time-limited adjunct for a comorbidity or a crisis. A programme is only DBT if it keeps the biosocial theory, the acceptance-change dialectic, all four modes and the target hierarchy; strip those out and what remains is skills training under a borrowed name. The wider technique of the structured psychotherapies is developed in the Psychotherapies, clinical assessment, MSE and nosology notes.

INDIA

Personality disorders are markedly under-recognised in Indian practice, so the borderline patient usually reaches services coded by the self-harm episode rather than by the pattern, and the structured therapy that would help is rarely offered. Two things temper a realistic plan. First, availability: dialectical behaviour therapy and schema therapy are being delivered and culturally adapted at Indian tertiary and private centres rather than being widely accessible, and few settings can staff a full four-mode programme with a trained consultation team, so pragmatic, skills-focused adaptations are common. Second, cultural fit: the mindfulness and acceptance core of DBT sits naturally with Indian contemplative traditions, an asset when framed in the patient's own idiom, while the interpersonal-effectiveness scripts must be calibrated to family interdependence rather than imported wholesale, since assertiveness norms and the very expression of personality pathology differ by culture and must not be read through a single culture's lens.

GOOD TO REMEMBER

- **Dialectical behaviour therapy (DBT):** core mechanism is the biosocial theory, an emotional vulnerability transacting with an invalidating environment to produce pervasive emotion dysregulation, treated by fusing behavioural change with mindfulness-based acceptance (the acceptance-change dialectic). Structure: four skills modules (mindfulness as the core, plus distress tolerance, emotion regulation and interpersonal effectiveness) delivered through four modes (individual therapy, skills group, phone coaching and consultation team), with a target hierarchy of life-threatening, then therapy-interfering, then quality-of-life-interfering behaviours across staged treatment. Indication: borderline personality disorder with recurrent self-harm, suicidality and chronic emotion dysregulation; it is the first-line structured psychotherapy for self-harm (NICE, IPS). Signature caution: it must be comprehensive and delivered with fidelity, it is resource-intensive, and trauma processing waits for stage two, only after stage-one behavioural control.

HOLD THIS

DBT rests on the biosocial theory of emotion dysregulation and the acceptance-change dialectic, and is delivered as four skills modules (mindfulness at the core, with distress tolerance, emotion regulation and interpersonal effectiveness) through four modes (individual therapy, skills group, phone coaching, consultation team), targeting life-threatening before therapy-interfering before quality-of-life behaviours; its landmark evidence is the reduction in self-harm and hospitalisation.

14 . Schema therapy for personality disorders

The integrative psychotherapy built for the difficult patient. Schema therapy is Jeffrey Young's integrative model, weaving cognitive-behavioural technique together with attachment theory, object relations and the experiential (gestalt) tradition, and designed expressly for the chronic, characterological presentations on which ordinary short-term cognitive-behavioural therapy

stalls. It matters in the examination because it is one of the small handful of structured psychotherapies with a genuine borderline personality disorder evidence base, and because its vocabulary, **early maladaptive schemas**, coping styles, **schema modes** and **limited reparenting**, is asked directly. Learn it as a four-part architecture: the schemas (the enduring self-defeating patterns), the domains that group them, the coping styles that keep them alive, and the modes framework that carries the work with the labile borderline patient.

This fragment teaches the model forward: what a **schema** is and where it comes from, the **five schema domains** holding the **eighteen early maladaptive schemas**, the **three coping styles** (surrender, avoidance, overcompensation), and the mode map that reduces the borderline patient's shifting states to a workable set of parts. It then teaches the two signature techniques, limited reparenting and experiential **mode work**, and closes on the trial evidence and the Indian picture. The wider landscape of psychotherapy models and technique sits in the Psychotherapies, clinical assessment, MSE and nosology notes; the borderline construct itself, and the sibling therapies dialectical behaviour therapy and mentalisation-based treatment, are developed on their own topics in this chapter.

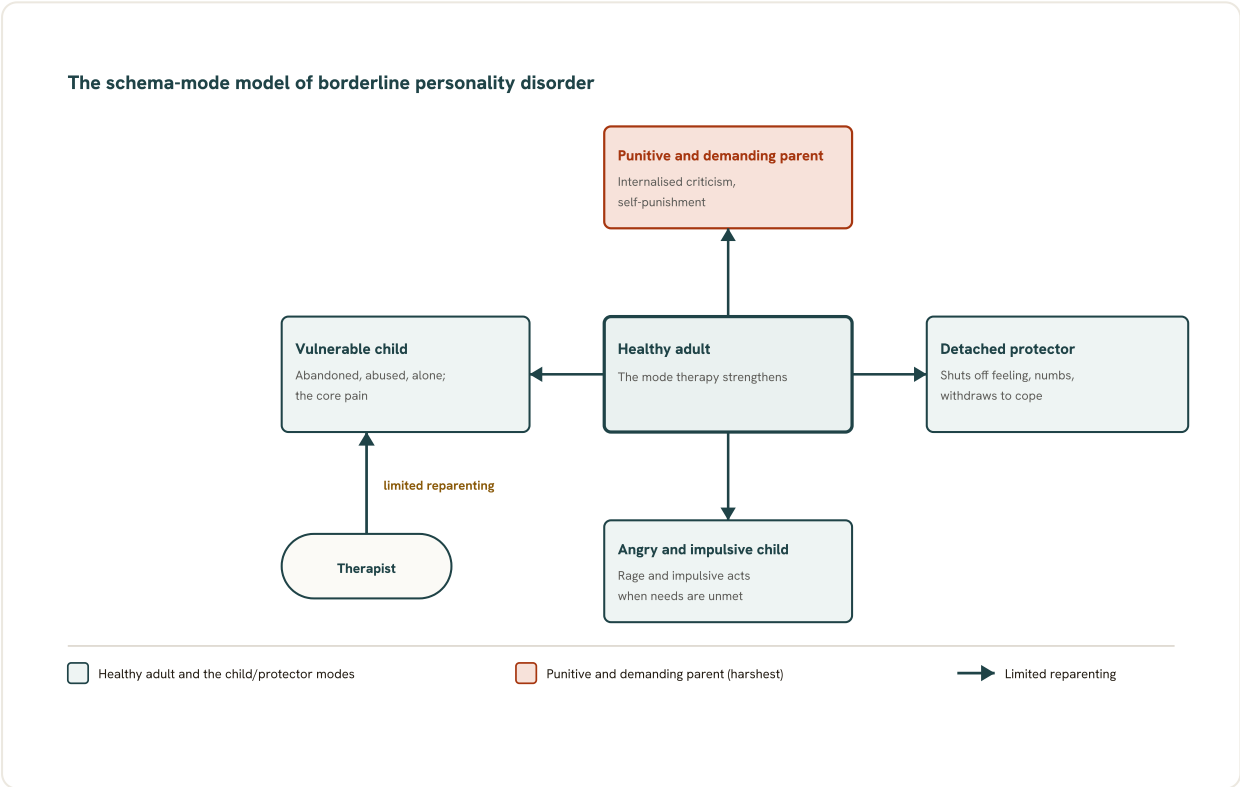


Fig 16.12 Schema therapy formulates borderline personality disorder as shifts between modes, the vulnerable child, the angry and impulsive child, the detached protector and the punitive and demanding parent, and uses limited reparenting to meet the vulnerable child's needs and build up the healthy adult mode.

14.1 What schema therapy is, and who it is for

An integrative model for ego-syntonic, characterological pathology. Standard cognitive-behavioural therapy assumes a patient who forms an alliance quickly, has a stable identity and clear goals, can access and verbalise affect, and can change through logic and homework. The personality-disordered patient breaks every one of those assumptions: the pathology is rigid, ego-syntonic and interpersonal, and it defeats a symptom-focused approach. Schema therapy was

constructed by Young for exactly this population. Its organising idea is that maladaptive personality patterns grow from **unmet core emotional needs** in childhood, five of them, secure attachment, autonomy and competence and a sense of identity, freedom to express valid needs and emotions, spontaneity and play, and realistic limits and self-control. Where these needs go unmet, through aversive experience interacting with temperament, the child lays down self-defeating patterns that harden into personality. The therapy aims to meet those needs, in a bounded therapeutic form, and so to heal the patterns rather than merely manage the symptoms.

14.2 Early maladaptive schemas: the enduring self-defeating pattern

Broad, pervasive, self-perpetuating themes about self and relationships. An early maladaptive schema is a broad, pervasive theme about oneself and one's relationships, comprising memories, emotions, cognitions and bodily sensations, laid down in childhood or adolescence and elaborated across the lifespan, dysfunctional to a significant degree. The examples make it concrete: abandonment, mistrust and abuse, emotional deprivation, defectiveness and shame. A schema begins as a reasonably accurate reading of a harmful early environment and becomes inaccurate as the person grows, yet it fights for survival: the patient assimilates new experience to fit the schema and discounts what would disconfirm it, which is schema perpetuation. This is what makes personality pathology so treatment-resistant, and it is why the schema, not the presenting symptom, is the unit of the work. Schemas are traits: present as a vulnerability, they may or may not be activated at a given moment, and when a schema is triggered the person is flooded with the original affect.

18	5	3	4
EARLY MALADAPTIVE SCHEMAS (YOUNG)	SCHEMA DOMAINS GROUPING THEM	MALADAPTIVE COPING STYLES	DYSFUNCTIONAL BORDERLINE MODES

14.3 The five schema domains and the eighteen schemas

Each domain answers one thwarted childhood need. The **eighteen early maladaptive schemas** are grouped into **five schema domains**, and the domain is the more examinable unit because each maps cleanly onto one of the unmet core emotional needs. Hold the five domains and one or two schemas under each, rather than reciting all eighteen; the domain structure is what the questions test.

DOMAIN	THWARTED CORE NEED	REPRESENTATIVE SCHEMAS WITHIN IT
Disconnection and Rejection	**Secure attachment: safety, stability, nurturance, acceptance**	**Abandonment/Instability; Mistrust/Abuse; Emotional Deprivation; Defectiveness/Shame; Social Isolation**
Impaired Autonomy and Performance	Autonomy, competence, a sense of identity	Dependence/Incompetence; Vulnerability to Harm; Enmeshment/Undeveloped Self; Failure
Impaired Limits	Realistic limits and self-control	Entitlement/Grandiosity; Insufficient Self-Control/Self-Discipline
Other-Directedness	Freedom to express valid needs and emotions	Subjugation; Self-Sacrifice; Approval/Recognition-Seeking
Overvigilance and Inhibition	Spontaneity and play	Negativity/Pessimism; Emotional Inhibition; Unrelenting Standards; Punitiveness

The five schema domains, each anchored to the childhood emotional need it reflects; the highlighted Disconnection and Rejection domain is the one most central to borderline pathology and the main target of limited reparenting.

14.4 The three maladaptive coping styles: surrender, avoidance, overcompensation

How the patient responds when a schema is triggered. A schema is the wound; the coping style is what the person does when it is touched. Young identifies **three coping styles**, and they map onto the innate threat responses. In surrender, the patient yields to the schema, accepts it as true and lives it out, choosing partners and situations that confirm it. In avoidance, the patient arranges life so the schema is never activated, blocking the thoughts and numbing the affect, often through detachment, substance use or workaholism. In overcompensation, the patient fights the schema by acting as though its opposite were true, so a defectiveness schema can drive grandiose perfectionism. All three are adaptive survival responses in childhood that become maladaptive later, because each perpetuates the very schema it was meant to escape.

COPING STYLE	INNATE ANALOGUE	WHAT THE PATIENT DOES
Surrender	Freeze	Yields to the schema, accepts it as true, repeats the schema-driven pattern and confirms it
Avoidance	Flight	Keeps the schema from firing at all: blocks thought and affect, withdraws, self-medicates, disengages from therapy
Overcompensation	**Fight**	**Behaves as though the opposite of the schema were true; counter-attacks, and overshoots into grandiosity or control**

The three maladaptive coping styles and their fight, flight, freeze analogues; a single patient uses different styles with different schemas and at different times.

MNEMONIC

FIGHT, FLIGHT, FREEZE

The three coping styles as the three threat responses: **Fight** is overcompensation (act as if the opposite is true), **Flight** is avoidance (keep the schema from firing), **Freeze** is surrender (yield to it and live it out). Three responses, three coping styles, one schema underneath.

14.5 The schema modes framework: from traits to states

Modes are the workhorse for the labile borderline patient. The original schema model is a trait model, and it fits the more stable personality disorders. It struggles with borderline personality disorder, where patients score high on almost every schema at once and flip between extreme states within minutes, angry, then terrified, then detached, then self-hating. Young answered this with the schema modes concept: a mode is the moment-to-moment state, the cluster of schemas and coping responses that is active right now, in contrast to the schema, which is the enduring trait. Reframing a chaotic patient as a small set of parts that alternate, rather than dozens of simultaneously active schemas, is what makes borderline pathology workable in the room, and it is why the modes framework, not the schema list, is the tool used with these patients. The mode map is shown in the accompanying figure.

RULE **Trait for the stable, state for the labile.** Use the schema (trait) model for the more stable personality disorders and the schema modes (state) model for the borderline patient who shifts between extreme states, because that patient has too many schemas active at once to work with one at a time.

14.6 The borderline modes: the four that shift, and the one that heals

Four dysfunctional modes, alternating around an underdeveloped Healthy Adult. The borderline patient characteristically moves between **four dysfunctional modes**. The **vulnerable child** (the Abandoned Child) carries the raw pain of the schemas, fragile, frightened, alone; the Angry and Impulsive Child erupts in rage or acts out impulsively when needs go unmet; the

detached protector is a coping mode of avoidance, shutting off all feeling and connection to keep the pain out; and the **punitive parent** (the internalised critical, sometimes demanding, parent) attacks the child with self-hatred and punishment, and drives much of the self-harm. Against these stands the fifth mode, the Healthy Adult, which in the borderline patient is weak and which the therapy exists to strengthen: the goal of treatment is to build a Healthy Adult that can nurture the vulnerable child, set limits on the angry child, bypass the detached protector and banish the punitive parent.

WORKED EXAMPLE

A woman in her twenties arrives numb and monosyllabic, saying she feels nothing (the detached protector is in charge). As the therapist gently makes contact, she begins to cry about being unlovable and terrified of being left (the vulnerable child breaks through). Asked about the previous night's cutting, she says flatly that she deserved it and is disgusting (the punitive parent speaks). Minutes later she is furious that the session must end (the angry child). The formulation is not "unstable and manipulative" but a rapid cycling through four modes, each of which is addressed differently: soothe the child, validate but contain the anger, get past the protector, and fight the punitive parent.

14.7 Limited reparenting: the relational engine

The therapist partially meets the unmet childhood needs, within bounds. Limited reparenting is the central relational stance of the therapy and its main active ingredient. Within the ethical and professional limits of the therapeutic frame, the therapist deliberately provides an approximation of the emotional experiences the patient missed in childhood, warmth, stability, containment and, where needed, firm limit-setting, so as to directly address the core emotional needs behind the schemas, above all those in the Disconnection and Rejection domain. It is *limited* precisely because the therapist does not become the parent and does not regress the patient into dependency; the more severe the early deprivation, and the more childlike the borderline patient's needs, the more central this reparenting becomes. It runs alongside empathic confrontation, in which the therapist holds warmth and honest challenge together, confronting the schema-driven behaviour while staying firmly on the patient's side.

PEARL

Limited reparenting is what most sharply distinguishes schema therapy from ordinary cognitive-behavioural therapy, in which the relationship is a vehicle for technique rather than an active ingredient. Here the relationship *is* a treatment: the therapist is a stable, caring figure who models the Healthy Adult the patient will internalise. The word "limited" is load-bearing, and marks the difference between therapeutic reparenting and a boundary violation.

14.8 Experiential mode work: imagery rescripting and chair work

Change is driven at the level of affect, not just cognition. Schema therapy works across four channels, cognitive (testing and reframing the schema), behavioural (pattern-breaking, replacing the coping responses), the therapy relationship (limited reparenting and empathic confrontation), and, most distinctively, the experiential. Experiential **mode work** engages the modes emotionally

rather than by argument. In imagery rescripting, the patient re-enters a painful childhood image; the therapist, and later the patient's own Healthy Adult, enters the scene to protect and comfort the vulnerable child and to confront the offending figure, so the memory is re-scripted with the need met. In chair work, the modes are externalised onto chairs and put into dialogue, so the Healthy Adult can, for instance, be given a voice to answer and expel the punitive parent. These techniques are the engine of schema change, and treating the therapy as cognitive disputation alone forfeits them.

TRAP **Running schema therapy as ordinary CBT.** Reducing it to cognitive disputation and homework, skipping the limited reparenting and the experiential imagery and chair work, strips out its two signature ingredients and leaves the schemas, which are held in affect and memory, untouched.

14.9 The evidence, in borderline and other personality disorders

A real trial base, strongest in borderline personality disorder. The landmark trial is Giesen-Bloo and colleagues' multicentre randomised study in the Netherlands (2006), which ran schema therapy against transference-focused psychotherapy over roughly three years in borderline personality disorder and found schema therapy superior, with a higher recovery rate (about double) and notably lower attrition. Farrell and colleagues (2009) showed a large added benefit from a group form of schema therapy, and Bamelis and colleagues (2014) extended the evidence beyond borderline, with a randomised trial supporting schema therapy across a range of personality disorders (including avoidant, dependent, obsessive-compulsive, paranoid, histrionic and narcissistic types), for which specific mode models have since been mapped. On this base, schema therapy sits, with dialectical behaviour therapy and mentalisation-based treatment, among the structured psychological therapies that are the primary treatment for borderline personality disorder; drug treatment is not first-line, and the deep pharmacology is cross-referenced to the Mood disorders: pharmacotherapy notes.

14.10 Place in management, and the Indian picture

A structured, longer-term psychotherapy delivered by trained, supervised therapists. Schema therapy is a structured, theory-based, longer-term treatment, typically delivered over a couple of years, moving from assessment and schema education, through the experiential and cognitive change work built on the reparenting relationship, to behavioural pattern-breaking and relapse prevention. It is not a brief intervention and, like the other borderline-specific therapies, it should not be delivered outside a supervised, structured service. Where availability is thin, its ideas, the mode formulation and limited reparenting, still usefully inform a general management plan even when the full protocol is out of reach.

INDIA

Personality disorders are markedly under-recognised in Indian practice, so the patients who would benefit from schema therapy are often reached only through a self-harm presentation and never formulated. Access is the second constraint: schema therapy, like dialectical behaviour therapy, is being delivered and adapted at a small number of Indian tertiary and private centres rather than being widely available, and trained, supervised schema therapists are scarce. Cultural calibration matters throughout, both because the schema content is read against family and cultural norms (interdependence and duty to family are not, in themselves, a Subjugation or Self-Sacrifice schema) and because the reparenting relationship must respect local expectations of the therapeutic bond; personality pathology must never be judged through a single culture's norms.

GOOD TO REMEMBER

- **Schema therapy (Young):** mechanism is healing early maladaptive schemas, the enduring self-defeating patterns laid down by unmet core emotional needs, through limited reparenting (the therapist partially and within bounds meets the missed needs) plus experiential mode work (imagery rescripting, chair work) alongside cognitive and behavioural change; the eighteen schemas sit in five domains, the three coping styles are surrender, avoidance and overcompensation, and the borderline patient is worked through the schema modes (vulnerable child, angry and impulsive child, detached protector, punitive parent) toward a strengthened Healthy Adult. Indication is chronic, characterological personality pathology, with the strongest evidence in borderline personality disorder (Giesen-Bloo 2006, superior to transference-focused psychotherapy) and support across other personality disorders (Bamelis 2014). Signature caution: it is a structured, longer-term therapy needing trained, supervised delivery, and stripping out the reparenting and the experiential work turns it into ordinary CBT that leaves the schemas untouched.

HOLD THIS

Schema therapy heals early maladaptive schemas through limited reparenting and experiential mode work; for the borderline patient the workhorse is the schema modes map, four dysfunctional modes (vulnerable child, angry and impulsive child, detached protector, punitive parent) cycling around a Healthy Adult that the therapy exists to strengthen.

15 . Mentalisation-based therapy and transference-focused psychotherapy

Two more borderline-specific therapies, two different engines. Alongside dialectical behaviour therapy and schema therapy, the borderline literature carries two further structured, manualised, evidence-based models, and the examiner wants the *mechanism* of each, not a vague label. Mentalisation-based therapy (**MBT**, also called mentalisation-based treatment, developed by Bateman and Fonagy) reads borderline pathology as a collapse of mentalising, the capacity to understand behaviour in terms of underlying mental states, that occurs under attachment stress; its whole technique is to restore that capacity through a particular therapeutic posture. Transference-focused psychotherapy (**TFP**, developed by Clarkin and Kernberg) reads the same pathology through object relations theory as a set of split, unintegrated internal representations of self and other, and works to integrate them in the live, here-and-now transference.

The high-yield frame is the contrast: both work in the here and now and both use the therapeutic relationship as the instrument, but MBT deliberately does *not* interpret the unconscious (it takes a curious, not-knowing **mentalising stance** to get the patient thinking about minds again), whereas TFP *does* interpret, using the sequence of clarification, confrontation and interpretation to fuse the idealised and persecutory images the patient cannot hold together. This fragment teaches each engine, its indications and its evidence, and closes by placing both alongside dialectical behaviour therapy and schema therapy; those two are taught on their own topics in this chapter, and the wider psychodynamic and general models are cross-referenced to the Psychotherapies, clinical assessment, MSE and nosology notes.

15.1 Mentalising: holding mind in mind

Mentalising is reading behaviour, one's own and others', in terms of mental states.

Mentalising is the social-cognitive ability to make sense of actions, of the self and of other people, in terms of the mental states behind them, thoughts, feelings, wishes, beliefs and desires; in plain language, it is attentiveness to thinking and feeling in oneself and in others. It is an ordinary human capability that underpins everyday interaction, and it runs across four dimensions that can each become unbalanced: automatic versus controlled, self versus other, cognitive versus affective, and internal versus external. In personality disorder these capacities are reduced, and reduced most sharply at moments of interpersonal stress, which is exactly when they are most needed. Bateman and Fonagy argue that many borderline symptoms emerge from this distortion or loss of mentalising: the person loses the felt distinction between their own perspective and external reality, cannot easily coordinate their mind with another's, and is left isolated, since the joining of minds (the so-called we-mode) is the ingredient of ordinary connection that the loss of mentalising obstructs.

15.2 The collapse under attachment stress, and the nonmentalising modes

Rising arousal switches mentalising off, and older, prementalising modes reappear.

Mentalising develops within attachment relationships and is vulnerable within them: high arousal, generated by attachment hyperactivation and disorganised attachment strategies, disrupts the less well-practised, higher cognitive capacity to reflect. As the accompanying figure shows, when interpersonal arousal climbs past a threshold, balanced mentalising drops away and three developmentally earlier, nonmentalising modes take over. The examinable point is that borderline phenomena are not random: each mode is what you get when one dimension of mentalising dominates and the others fail.

NONMENTALISING MODE	EXPERIENCE OF THE MIND	CLINICAL FACE
Psychic equivalence	**Inner states are felt as literally, unquestionably real; thought equals reality, so no alternative perspective is possible ("concreteness of thought")**	Overwhelming certainty ("the therapist hates me", "I am wicked"), the drama and terror that make self-harm feel comprehensible
Teleological	Mental states are believed only if their outcome is physically observable; affection is real only with a touch, care real only with an action	Demands for concrete proof of caring; self-harm or action as the only "real" expression of a state; the automatic pole dominates
Pretend mode	Thoughts and feelings become severed from reality; much is said about mental states with little genuine connection to them	Hypermentalising or pseudo-mentalising, long inconsequential talk about feelings; taken to an extreme, derealisation and dissociation

The three nonmentalising (prementalising) modes that reappear when mentalising collapses under arousal; the highlighted psychic-equivalence cell is the one that makes borderline self-harm and quasi-psychotic certainty intelligible.

MNEMONIC

TOO REAL · ONLY IF SEEN · NOT REAL AT ALL

The three nonmentalising modes in three tags. **Too real** = psychic equivalence (thought is experienced as reality). **Only if seen** = teleological (a state counts only if physically demonstrated). **Not real at all** = pretend mode (talk about feelings cut loose from any real feeling; hypermentalising).

15.3 The mentalising stance: curious, not-knowing, restoring the capacity to think

The stance is the treatment: inquisitive, not-knowing, aimed at reviving mentalising rather than delivering insight. The bedrock clinical principle of MBT is an authentic **mentalising stance**, an inquisitive, "not-knowing" posture that respects the opacity of minds: minds can never be truly known, so the clinician's task is to inquire, to be genuinely curious, and to be willing to be surprised by the patient's answer, with the aim of raising the patient's own awareness of their internal states through a shared process. The work is in the here and now and stays close to preconscious, working-memory experience rather than pursuing unconscious meaning through free association; a session typically settles onto a single focus within the first ten to fifteen minutes and then works around it. Crucially, MBT does not push interpretation while the patient is non-mentalising and highly aroused; the first job is to lower arousal and re-open thinking, because interpreting a mind that has collapsed into psychic equivalence only confirms the concreteness. The secure-base relationship to the therapist is what makes it safe to explore one's own mind and find it reflected in another's.

WORKED EXAMPLE

A patient arrives certain that "you were going to cancel on me, I could tell". A not-knowing MBT response is not a reassurance and not an interpretation of transference; it is a curious inquiry: "I did not know that was in your mind, help me understand what told you that, and what it was like to sit with it." The clinician marks their own not-knowing, slows the moment, and invites the patient back into thinking about the mental states involved, theirs and the clinician's, rather than settling the "fact". The same opening moment in TFP would be handled differently (see below), and that difference is the whole point of the topic.

RULE **Structured, borderline-specific psychotherapy is the treatment; the model is chosen by fit, not by a proven winner.** MBT, TFP, dialectical behaviour therapy and schema therapy are all evidence-based for borderline personality disorder, and head-to-head trials show no single model is reliably superior; choose by patient fit, therapist training and local availability, and deliver it as a structured programme, not as eclectic support.

15.4 MBT: structure, indications and evidence

A structured, time-limited programme of individual plus group work, first proven in a partial-hospitalisation trial. MBT is delivered as a combination of individual and group sessions within a structured, time-limited programme (the original model ran in a day-hospital and partial-hospitalisation setting, with later intensive-outpatient versions), all built around the mentalising stance. Its indications have widened from borderline personality disorder (the primary and best-evidenced target) to antisocial personality disorder (MBT-ASPD), to adolescents with emerging borderline features and self-harm (MBT-A), and to other conditions marked by mentalising failure. The founding evidence is Bateman and Fonagy's randomised trial of partial-hospitalisation MBT against treatment as usual: the MBT group showed significant reductions in depressive symptoms, in suicidal and self-injurious behaviour and in inpatient days, with better social and interpersonal functioning; the gains began to appear after about six months and were maintained after treatment ended, with long-term follow-up showing durable benefit. That "benefit emerges over months, then holds" shape is itself examinable.

PEARL

MBT reframes what a borderline crisis *is*: not primarily a behaviour to be managed but a moment when mentalising has gone offline. This is why the intervention is a stance rather than a technique menu, and why "the therapist not knowing what to say" is treated as useful data, an accurate read of the patient's own collapsed mentalising, rather than a therapist failure.

GOOD TO REMEMBER

- **Mentalisation-based therapy (MBT), Bateman and Fonagy:** mechanism, borderline symptoms arise from a loss of mentalising (understanding behaviour in terms of mental states) under attachment-stress arousal, so the therapy restores mentalising through a curious, not-knowing mentalising stance in the here and now, working close to conscious experience rather than interpreting the unconscious. Indication, borderline personality disorder first-line among structured therapies, extended to antisocial personality disorder and to adolescents; evidence from a partial-hospitalisation RCT versus treatment as usual with gains maintained after termination. Signature caution, do not push interpretation while the patient is non-mentalising and highly aroused, lower arousal and re-open thinking first.

15.5 TFP and the object-relations frame: split, unintegrated representations of self and other

The borderline mind is built of split object dyads that idealise and persecute but never integrate. Transference-focused psychotherapy rests on an ego-psychological and **object relations** framework derived from Melanie Klein and elaborated by Otto Kernberg. Its unit of analysis is the internal *object dyad*: a single mental representation of the self linked to a representation of another person by an affect (for example, a weak, needy self bound to an exploitative but needed other by fear). In health these representations integrate into whole, ambivalent images; in borderline personality organisation (BPO) they do not. Instead the patient relies on splitting, keeping idealised and persecutory representations apart so that the same person is experienced as all-good or all-bad and flips between the two. TFP therefore diagnoses along a *level of personality organisation* axis rather than by categorical criteria, assessing the interrelated domains of identity, object relations, primitive defences, reality testing, aggression and moral values in a structural interview, which the Structured Interview of Personality Organization (STIPO-R) helps to operationalise. The core therapeutic target is **identity diffusion**, the lack of an integrated sense of self, and the goal is identity consolidation.

COMMON TRAP

Reading TFP as "diagnose the DSM type, then treat it". TFP works on borderline personality organisation, a broader structural construct than DSM borderline personality disorder that cuts across many categorical personality diagnoses and also covers narcissistic pathology. Two patients with different DSM labels can share the same borderline-level organisation and the same split object relations, which is exactly what TFP targets; the categorical label is not the treatment axis.

15.6 The TFP technique: integrating the dyads in the here-and-now transference

Contract first, then channel the split into the transference and interpret it into integration. TFP is an individual therapy, tested as a twice-weekly treatment of at least one to two years' duration, and it begins with explicit contracting, goal-setting and limit-setting. The wager is that the patient's split, unintegrated representations of self and other will inevitably be enacted in the relationship with the therapist, the *transference*, where they become available in the room in the here and now rather than only in history. Work follows a priority hierarchy (suicidal and self-destructive behaviour first, then threats to the continuity of the treatment, then the dominant transference theme) and a technical sequence of clarification, then confrontation of contradictions, then interpretation. By naming, for example, that the patient is treating the

therapist as the persecutor of the moment while a needy, idealising self is split off, TFP brings the two poles into contact so they can begin to integrate; as the split dyads fuse into whole-object relations, identity consolidates. Reflective functioning and integration, not symptom management alone, are the intended fruits.

TRAP **Deep transference interpretation into a mind that has already collapsed.** Interpretation only works on a patient who can still mentalise; delivering a Kernberg-style transference interpretation while the patient is in psychic equivalence and high arousal tends to confirm the concreteness and destabilise, which is precisely the failure MBT was built to avoid. Restore mentalising and lower arousal first; interpret when there is a mind available to think with.

3	4	6	2
MBT NONMENTALISING MODES (PSYCHIC EQUIVALENCE, TELEOLOGICAL, PRETEND)	DIMENSIONS OF MENTALISING IN MBT	TFP STRUCTURAL-INTERVIEW DOMAINS OF PERSONALITY ORGANISATION	TFP SESSIONS A WEEK (TWICE WEEKLY, OVER ONE TO TWO YEARS)

15.7 TFP indications and evidence

For borderline and narcissistic pathology in a patient who can tolerate interpretation, with a solid RCT base. TFP is indicated for borderline and narcissistic personality disorders and, more broadly, for patients at a borderline level of organisation who can commit to a long, twice-weekly, interpretation-based treatment and tolerate the affect it raises; the containing contract and limit-setting are what make it usable in a high-risk population. The evidence base is genuinely randomised. Clarkin and colleagues' three-arm trial compared TFP, dialectical behaviour therapy and supportive psychodynamic therapy and found all three efficacious, with TFP producing broad change across domains; Doering and colleagues found TFP superior to treatment by experienced community psychotherapists on borderline symptoms, suicide attempts and dropout; and the Giesen-Bloo multicentre trial comparing schema therapy and TFP showed both producing significant improvement, with schema therapy holding an advantage on recovery and retention. Mechanism-consistent findings (Levy and colleagues) show TFP increasing reflective functioning and shifting attachment toward security, which is the change the object-relations model predicts.

GOOD TO REMEMBER

- **Transference-focused psychotherapy (TFP), Clarkin and Kernberg:** mechanism, an object-relations therapy that treats borderline pathology as split, unintegrated internal representations of self and other (object dyads) held apart by splitting, and integrates them by working the here-and-now transference through clarification, confrontation and interpretation, with identity diffusion as the core target and identity consolidation the goal. Indication, borderline and narcissistic personality disorders (borderline personality organisation) in a patient able to tolerate a long, twice-weekly, interpretive treatment; evidence from several RCTs. Signature caution, it is interpretation-heavy, so it needs a mind that can still mentalise and a firm contract, or the interpretation destabilises.

15.8 Where MBT and TFP sit alongside dialectical behaviour therapy and schema therapy

Four structured models, four different theories of the same disorder. The four borderline-specific psychotherapies are best held as one grid: each names a different core mechanism and a

different signature technique, and no head-to-head trial has crowned one as reliably best, which is why the selection RULE above governs. The two owned on their own topics in this chapter (dialectical behaviour therapy and schema therapy) are set here beside MBT and TFP so the discriminators are visible at a glance.

THERAPY	THEORETICAL MODEL	CORE MECHANISM / TARGET	SIGNATURE TECHNIQUE
Dialectical behaviour therapy (Linehan)	Biosocial: emotional vulnerability plus an invalidating environment	Emotion dysregulation and behavioural dyscontrol	Skills training (mindfulness, distress tolerance, emotion regulation, interpersonal effectiveness) held in dialectic of acceptance and change
Mentalisation-based therapy (Bateman and Fonagy)	Attachment and mentalising deficit	Loss of mentalising under arousal	**Curious, not-knowing mentalising stance that restores thinking about mental states in the here and now**
Transference-focused psychotherapy (Clarkin and Kernberg)	Ego-psychology and object relations (Klein, Kernberg)	Identity diffusion; split, unintegrated self and other representations	**Here-and-now transference interpretation (clarification, confrontation, interpretation) to integrate the split dyads**
Schema therapy (Young)	Early maladaptive schemas and schema modes	Maladaptive schema modes (vulnerable child, detached protector, punitive parent)	Limited reparenting and mode work

The four structured, evidence-based borderline psychotherapies; the two highlighted cells are the discriminator of this topic, MBT restores mentalising through a stance while TFP interprets the transference to integrate split object relations.

INDIA

Personality disorders are markedly under-recognised in Indian practice, and the specialist psychotherapies are scarcer still. Dialectical behaviour therapy has the widest, if uneven, adaptation and delivery at Indian tertiary and private centres; mentalisation-based therapy and transference-focused psychotherapy are far less available, concentrated in a few academic and psychodynamically trained settings, and the binding constraint is the training and supervision pipeline rather than patient demand. Two cautions travel with the models. First, mentalising norms are cultural: the we-mode, joint attention and the expression of affect are read differently across Indian family systems, and interdependence must not be mistaken for a mentalising failure. Second, the object-relations reading of a case must be held against the patient's own cultural idiom, so that a culturally normative deference or a shared family self is not over-interpreted as split or diffuse identity. Judge the mind against its own context, not a single culture's template.

HOLD THIS

MBT (Bateman and Fonagy) restores lost mentalising through a curious, not-knowing stance and does not interpret; TFP (Clarkin and Kernberg) integrates split object-relations dyads by interpreting the here-and-now transference, and does; both work in the present through the therapeutic relationship, and both sit as evidence-based options beside dialectical behaviour therapy and schema therapy.

16 . Pharmacotherapy in personality disorders

The most trapped question on the day: which drug? The examinable truth about **pharmacotherapy in personality disorders** is almost entirely a truth about restraint. There is no medication registered to treat any personality disorder, structured psychological therapy is the primary treatment, and every drug that is used is used **symptom-targeted** and adjunctive, aimed at a defined target symptom or a comorbidity, never at the disorder itself. The single fact worth more than any dose is the NICE position on borderline personality disorder: drug treatment is not first-line, and the candidate who reaches for a mood stabiliser or an antipsychotic as the answer has walked into the classic trap.

This fragment leads with the guideline law, states the NICE rule as both a rule and a trap, then reconciles it with what the wider bodies (the Indian Psychiatric Society CPG and WFSBP) permit at symptom-domain level. It teaches the three psychobiological symptom domains and the agent class attached to each, keeps the pharmacology deliberately light, and cross-references the deep drug detail to the Mood disorders: pharmacotherapy notes and the Schizophrenia: management, antipsychotics and adverse effects notes. The bipolar-II differential that so often triggers a wrong prescription sits in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes, and the forensic frame for antisocial personality disorder in the Mental health legislation and forensic psychiatry notes.

16.1 The governing principle: adjunctive, symptom-targeted, never disorder-specific

No drug licensed. The organising principle of **pharmacotherapy in personality disorders** is that it is never a disorder-specific registered treatment. **No drug licensed** for any personality disorder exists in any major formulary, and every guideline body, however permissive, agrees that psychotherapy is primary and medication is at most an adjunct. What medication can legitimately do is act on a discrete **symptom-targeted** problem, an aggressive outburst, a run of cognitive-perceptual disturbance, a depressive or anxious swing, or a comorbid Axis-I disorder sitting alongside the personality pathology. It follows that a drug is prescribed against a named, measurable target with a defined review point, and is stopped if that target does not move. The diagnosis itself must be secure before any of this begins: an enduring, pervasive, inflexible pattern with onset by adolescence, not a situational state, and for borderline personality disorder that means the full pattern (five or more of the nine criteria), not a single stormy fortnight.

PEARL

Read every personality-disorder drug question as a question about a target symptom, not about the disorder. "What is the drug treatment for borderline personality disorder?" has no correct drug answer, the correct answer is that structured psychological therapy is the treatment and medication is only a time-limited, symptom-targeted adjunct. Reframing the question this way is what protects you from the trap the stem is usually setting.

16.2 The NICE rule: drug not first-line for borderline

The most tested management fact of the day. NICE (2009, CG78) states that drug treatment should not be used specifically for borderline personality disorder or for the individual symptoms and behaviours associated with it (repeated self-harm, marked emotional instability, risk-taking, transient psychotic symptoms). Structured psychological therapy is primary. Medication is legitimate in only two situations: to treat a diagnosed comorbid condition, or short-term during a crisis (a sedative, usually for no longer than one week). NICE guidance is explicit that antipsychotic drugs should not be used for the medium- and long-term treatment of the disorder. This is the highest-yield line of the topic, and a mis-statement of it is a critical error.

RULE **Drug not first-line for borderline.** In borderline personality disorder, structured psychological therapy is primary; any medication is symptom-targeted, adjunctive and time-limited, for a comorbidity or a crisis only, and antipsychotics are not for medium- or long-term use (NICE 2009).

TRAP **Reaching for a drug first.** Starting a mood stabiliser or antipsychotic as the primary treatment for borderline personality disorder, or for its self-harm and lability directly, is the classic error and contradicts NICE outright; there is no licensed disorder-specific drug to reach for.

0	3	1
DRUGS LICENSED FOR BORDERLINE PERSONALITY DISORDER	SYMPTOM-TARGET DOMAINS FOR ADJUNCTIVE DRUGS	WEEK, USUAL MAXIMUM FOR CRISIS SEDATION (NICE)

16.3 Reconciling the guidelines: NICE, the Indian Psychiatric Society, WFSBP

Same primacy of psychotherapy, differing latitude on adjuncts. The bodies agree that psychological therapy is the primary treatment and that no drug is a registered disorder-specific treatment; they differ in how much symptom-targeted prescribing they permit. NICE is the most restrictive (no drug for the disorder or its symptoms; a crisis sedative or comorbidity treatment only). The Indian Psychiatric Society CPG (IPS 2023) makes psychotherapy central but allows that, in some patients, antipsychotics may reduce hostility, suspiciousness, affect dysregulation and cognitive-perceptual distortions, and that mood stabilisers may reduce impulsivity and aggressiveness. WFSBP (2007) supplies the fullest symptom-domain framework for adjunctive agents. Hold NICE as the safe default answer and the domain framework as the "where is there any evidence" detail.

GUIDELINE (YEAR)	POSITION ON DRUG TREATMENT	WHAT IT PERMITS
NICE, CG78 (2009)	**Do NOT use drugs specifically for borderline personality disorder or its symptoms; no antipsychotic for medium- or long-term use**	Treat a comorbidity; a crisis sedative for usually no longer than one week; review and deprescribe
NICE, personality disorders (2015)	No drug for the personality itself; structured clinical assessment to diagnose	Antipsychotic or sedative only for short-term crisis or a comorbid condition; group cognitive-behavioural therapy for antisocial personality disorder
the Indian Psychiatric Society CPG (2023)	Psychotherapy is central; DBT recommended early	Symptom-targeted antipsychotics and mood stabilisers in some patients; avoid benzodiazepines
WFSBP (2007)	Adjunctive, symptom-targeted only, not a registered treatment	Agent chosen by symptom domain; trial for at least three months against defined targets
APA (2024)	Structured psychotherapy primary; medication adjunctive	Time-limited, single measurable target symptom; reconcile and review medications at least every six months

The guideline hierarchy for these notes: NICE leads and is the safest default, the Indian Psychiatric Society and WFSBP add the symptom-domain latitude, APA supplies the core prescribing principles.

16.4 The three symptom domains and the agent attached to each

The Soloff-style psychobiological domains organise all adjunctive prescribing. When medication is used at all, it is targeted at one of three symptom domains rather than at the disorder, a framework running from Soloff's psychobiological model through the APA and WFSBP schemes. The **cognitive-perceptual** domain (suspiciousness, ideas of reference, transient quasi-psychotic or dissociative experiences) attracts a low-dose antipsychotic; the **impulsive-behavioural dyscontrol** domain (impulsive aggression, self-damaging impulsivity, anger) attracts a mood stabiliser, with a low-dose antipsychotic as an alternative where aggression dominates; and the **affective instability domain** (affective dysregulation, depressive mood swings, anxiety) attracts an SSRI. The mapping is the examinable core, shown in the accompanying figure.

SYMPTOM DOMAIN	TARGET FEATURES	AGENT CLASS WITH ADJUNCTIVE EVIDENCE
Cognitive-perceptual	Suspiciousness, ideas of reference, transient quasi-psychotic and dissociative symptoms	**Low-dose antipsychotic (second-generation)**
Impulsive-behavioural dyscontrol	Impulsive aggression, self-damaging impulsivity, anger and behavioural discontrol	**Mood stabiliser (a low-dose antipsychotic where aggression dominates)**
Affective instability and anxiety	Affective dysregulation, depressive mood swings, rejection sensitivity, anxiety	**SSRI**

The three psychobiological symptom domains and the drug class attached to each; this is the framework the wider guidelines use, always as an adjunct to primary psychotherapy, never as a treatment for the disorder.

16.5 Low-dose antipsychotics: cognitive-perceptual and impulsive domains

Low, short, and for a named target only. A **low-dose antipsychotic**, a second-generation agent such as quetiapine (Qutipin, Seroquel), olanzapine (Oleanz, Zyprexa) or aripiprazole (Arip, Abilify), carries moderate adjunctive evidence in the **cognitive-perceptual** domain and, where impulsivity and aggression dominate, in **impulsive-behavioural dyscontrol** (WFSBP 2007; IPS 2023). The doses used are low and the course is meant to be short and target-defined; the deep pharmacology, receptor profiles and adverse effects belong to the Schizophrenia: management, antipsychotics and adverse effects notes and are not re-taught here. The overriding constraint is the NICE one: an antipsychotic is legitimate short-term, but must not be continued for the medium- and long-term treatment of borderline personality disorder, so a crisis prescription is reviewed and stopped once the crisis resolves.

16.6 Mood stabilisers: impulsive aggression

For impulsive aggression, not for a personality-based "mood swing". A **mood stabiliser**, valproate or divalproex (Valprol, Encorate), lamotrigine (Lamitor, Lametec) or topiramate, has adjunctive evidence for reducing impulsivity and impulsive aggression that antipsychotics have not settled (IPS 2023; WFSBP 2007). The trap this sets is the borderline-versus-bipolar-II confusion: the rapid, reactive affective instability of borderline personality disorder, minutes to hours and triggered by interpersonal events, is not the sustained syndromic mood episode of bipolar II, and starting a mood stabiliser for personality-based lability, mislabelled as bipolarity, is a common and consequential error. That differential is developed in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes, and the deep drug detail in the Mood disorders: pharmacotherapy notes; here the mood stabiliser stays a targeted adjunct for impulsive aggression.

TRAP **Treating borderline lability as bipolar II.** Rapid, reactive, interpersonally cued affective instability is a borderline feature, not a bipolar mood episode; reflexively starting a mood stabiliser for it medicalises a personality target and misses the primary psychotherapy.

16.7 SSRIs: the affective instability and anxiety domain

Best-shown class for affective dysregulation and anxiety, still adjunctive. Of the drug classes, the SSRI has the clearest evidence for the **affective instability domain**, the depressive mood, mood swings and anxiety of the disorder (WFSBP 2007), and an SSRI such as fluoxetine (Fludac, Prozac) or sertraline (Serlift, Zoloft) is a reasonable adjunct where that domain predominates or where a comorbid depressive or anxiety disorder is present. It also carries the practical advantage of relative safety in overdose, which matters in a population with recurrent self-harm. As always, this is symptom-targeted and adjunctive to psychotherapy, and where an SSRI is used for a comorbidity it is that comorbidity, not the personality disorder, that is being treated; the deep detail sits in the Mood disorders: pharmacotherapy notes.

16.8 The cautions: avoid polypharmacy, deprescribe, and what never to use

The prohibitions are as examinable as the indications. Several cautions run across the guidelines. Avoid benzodiazepines: the Indian Psychiatric Society CPG advises against them in borderline personality disorder because of dependence risk and disinhibition that can worsen impulsive behaviour. Avoid drugs dangerous in overdose: WFSBP counsels against irreversible MAOIs and lithium despite some efficacy, precisely because these patients need agents safe in parasuicidal acts. Above all, **avoid polypharmacy** and long-term prescribing without a clear indication: NICE guidance is to review repeat prescriptions regularly, to discourage polypharmacy, and to withdraw drugs started in a crisis once it resolves, aiming to reduce and stop unnecessary treatment. The maintenance rule that antipsychotics are not for medium- or long-term use in borderline personality disorder belongs here too.

> **COMMON TRAP**
>
> A borderline patient accumulates a low-dose antipsychotic, a mood stabiliser, an SSRI and a "when required" benzodiazepine over successive crises, none reviewed. This is exactly the polypharmacy NICE tells you to unwind: benzodiazepines should be off entirely, the crisis-era drugs deprescribed once the crisis has passed, and the whole regimen reconciled against a single measurable target. Deprescribing is an active clinical act, not neglect.

16.9 Crisis, comorbidity, and antisocial personality disorder

Where a drug is genuinely indicated, and where none is. Two legitimate windows remain. In a crisis, short-term cautious sedation (an antihistamine such as promethazine, or a low-dose antipsychotic) may be considered as part of an overall plan, usually for no longer than one week, alongside risk assessment and a collaborative crisis plan (NICE 2009). For a diagnosed comorbid depression, post-traumatic stress or anxiety disorder, that comorbidity is treated on its own terms within the structured programme. Antisocial personality disorder is the instructive contrast: there is no drug treatment for the antisocial personality itself, the mainstay is a group cognitive-behavioural intervention (often in criminal-justice or health settings), and pharmacotherapy is reserved strictly for a comorbid mental disorder (NICE 2015). The offender-assessment and court-report frame is cross-referenced to the Mental health legislation and forensic psychiatry notes.

WORKED EXAMPLE

A woman in her twenties with borderline personality disorder presents in crisis after an argument, with rising urges to self-harm and transient paranoid ideas. The correct plan is not to "start" a drug for the disorder: assess risk, enhance coping and reflective capacity, agree a crisis plan, and, if sedation is needed, offer it cautiously and briefly (usually no longer than one week), reviewing to stop it as the crisis settles. The definitive treatment is referral to a structured psychological therapy such as dialectical behaviour therapy; any antipsychotic used for the cognitive-perceptual symptoms is short-term and target-defined, never a maintenance prescription.

16.10 Place in the plan, and the Indian picture

Medication sits inside a psychotherapy-led, stepped plan. The management spine holds: outpatient care by default with admission avoided and, when unavoidable, brief and purposeful; short-term focus on crisis and safety, mid-term on the core features through structured psychological therapy, long-term on function and relationships. Within that, pharmacotherapy is a symptom-targeted, time-limited adjunct, layered onto (never in place of) dialectical behaviour therapy, schema therapy, mentalisation-based treatment or transference-focused psychotherapy by availability and fit. The candidate who leads with a drug has inverted the plan.

INDIA

Personality disorders are markedly under-recognised in Indian practice, so many patients reach services only through a self-harm or crisis presentation and are prescribed a symptom drug without ever being formulated or offered the structured therapy that is the actual treatment. Two realities shape a sensible plan. Access: dialectical behaviour therapy and schema therapy are being delivered and culturally adapted at a small number of Indian tertiary and private centres rather than being widely available, so the psychotherapy-first rule can be hard to enact and makes disciplined, minimal prescribing (and active deprescribing) all the more important. Culture: personality pathology must never be read through a single culture's norms, its expression, and the antisocial and medico-legal framing in particular, differs by setting, and the forensic use of an antisocial diagnosis carries weight that belongs with the forensic notes, not with a prescription pad.

GOOD TO REMEMBER

- **Pharmacotherapy overall:** mechanism is symptom-targeted and adjunctive (never disorder-specific; no drug licensed); indication is a defined target symptom, a comorbidity, or short-term crisis sedation; signature caution is that it is not first-line for borderline personality disorder, psychotherapy is primary, and antipsychotics are not for medium- or long-term use (NICE 2009).
- **Low-dose antipsychotic:** targets the cognitive-perceptual domain (and impulsive aggression where it dominates); short-term and low-dose; caution is no medium- or long-term use in borderline personality disorder.
- **Mood stabiliser:** targets impulsive-behavioural dyscontrol and impulsive aggression; caution is not to mistake reactive borderline lability for bipolar II and medicalise a personality target.
- **SSRI:** targets the affective instability and anxiety domain and any comorbid depression or anxiety; advantage is relative safety in overdose; caution is it treats the symptom or comorbidity, not the disorder.
- **Never:** avoid benzodiazepines (dependence, disinhibition), avoid drugs dangerous in overdose (irreversible MAOIs, lithium), and avoid polypharmacy; review and deprescribe.

HOLD THIS

No drug is licensed for a personality disorder; structured psychological therapy is primary and NICE says drug treatment is not first-line for borderline personality disorder, so all pharmacotherapy is symptom-targeted and adjunctive, a low-dose antipsychotic for the cognitive-perceptual domain, a mood stabiliser for impulsive-behavioural dyscontrol, an SSRI for the affective instability and anxiety domain, for a comorbidity or a crisis only, while you avoid benzodiazepines, avoid polypharmacy, and deprescribe.

17 . The integrated management of borderline personality disorder

The treatment block, assembled into one plan. The separate topics teach the disorder and each therapy on its own; this one is the synthesis, the single algorithm an examiner wants when the question is simply "how would you manage this patient". The integrated management of borderline personality disorder is *integrated* in two senses: it braids the strands of care (crisis work, structured psychotherapy, selective medication, care planning and psychoeducation) into one coherent plan, and it reconciles the guideline bodies (NICE, the Indian Psychiatric Society and WFSBP) into one defensible line. The plan is built on a three-part spine, **LOCUS** (where care happens), **FOCUS** (what is targeted, and when) and **MODUS** (by what means), and it is anchored, above everything, on one rule that examiners test relentlessly: a drug is not the first-line treatment for this disorder.

This fragment walks the spine end to end. It fixes the **locus** of care as outpatient and community by default, sets the **focus** by phase from short-term crisis and risk through the mid-term core-feature work to long-term function and remission, and lays out the **modus**, with structured psychological therapy as the primary mode and medication kept symptom-targeted, time-limited and adjunctive. Throughout, the guideline order is NICE first (CG78), then the Indian Psychiatric Society CPG and WFSBP, and the pharmacology stays deliberately light, with the deep drug detail cross-referenced to the Mood disorders: pharmacotherapy notes and the Schizophrenia: management, antipsychotics and adverse effects notes. The integrated algorithm is drawn in the accompanying figure.

4	0	1 wk
STRUCTURED PSYCHOTHERAPIES FOR THE DISORDER (DBT, SCHEMA, MBT, TFP)	DRUGS LICENSED FOR BORDERLINE PERSONALITY DISORDER (NICE)	USUAL CEILING FOR A CRISIS SEDATIVE (NICE)

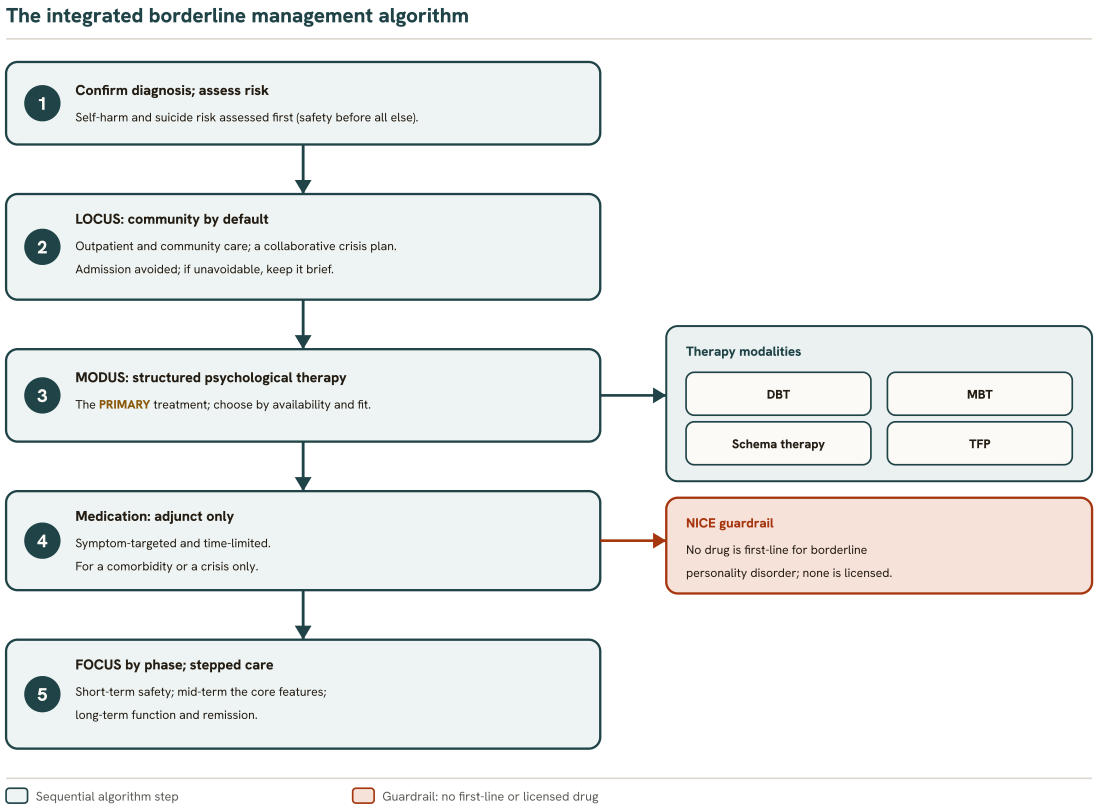


Fig 16.13 The integrated plan treats borderline personality disorder mostly in the community with a crisis plan, makes structured psychological therapy (dialectical behaviour therapy, mentalisation-based therapy, schema therapy or transference-focused psychotherapy) the primary treatment, and uses medication only, symptom-targeted and time-limited, for a comorbidity or a crisis, because no drug is first-line or licensed for the disorder.

17.1 The integrated frame, and the one rule that governs it

One plan, one governing rule. Before the spine, fix the principle that shapes every branch of it. NICE (2009, CG78) states that drug treatment should not be used specifically for borderline personality disorder or for its individual symptoms (repeated self-harm, marked emotional instability, risk-taking, transient psychotic symptoms), that no drug is licensed for the disorder, and that structured psychological therapy is the primary treatment; medication is reserved for a comorbid condition or short-term use in a crisis. The Indian Psychiatric Society (IPS 2023) agrees, making psychotherapeutic methods the central treatment and permitting only symptom-targeted adjuncts; WFSBP (2007) frames any drug as adjunctive and symptom-domain-targeted rather than disorder-specific. The three bodies differ only in how much room they leave for adjunctive medication, NICE the most restrictive, IPS and WFSBP allowing symptom-targeted agents, and they are unanimous that psychotherapy is primary. The whole integrated plan is therefore a psychotherapy-led plan into which crisis care, selective medication and care planning are fitted.

RULE **Structured psychological therapy is primary; any medication is adjunctive.** In borderline personality disorder the first-line treatment is a comprehensive, structured, theory-based psychotherapy delivered by trained supervised practitioners; medication is only ever symptom-targeted, time-limited and reserved for a comorbidity or a crisis (NICE 2009, IPS 2023, WFSBP 2007).

TRAP **Reaching for a drug first-line for the disorder itself.** Starting an antipsychotic or a mood stabiliser as the primary treatment for borderline instability, or continuing antipsychotics for medium- and long-term management, runs directly against NICE (which recommends no drug for the disorder and no antipsychotic for its longer-term treatment). A wrong first-line for borderline personality disorder is a critical error.

17.2 LOCUS, where the care happens

Outpatient and community by default; admission avoided, and when unavoidable, brief and purposeful. The **locus** of care is the community. Borderline personality disorder is managed in outpatient and community settings within a stepped care framework, matching intensity to need and stepping up only as required. Inpatient admission is actively avoided, because prolonged admission tends to entrench regression, reinforce crisis behaviour and disrupt the very relationships and roles that recovery depends on; NICE is explicit that admission should be avoided unless there is a serious risk to self or others that cannot be managed any other way, and that when it does happen it should be brief and for an agreed, specific purpose (typically the containment of acute risk), not open-ended asylum. The **service frame** matters as much as the setting: people with the disorder must not be excluded from any health or social care service because of the diagnosis or because they have self-harmed, and any planned change or withdrawal of a service is agreed with the person through a structured, phased plan rather than an abrupt discharge. Community continuity, not the ward, is the therapeutic base.

COMMON TRAP

Admitting the recurrently self-harming borderline patient to a general ward for safety, and keeping them. Beyond the brief, purposeful containment of an unmanageable acute risk, prolonged admission is not protective; it interrupts the outpatient therapy that actually reduces self-harm, models the crisis as the route to care, and is where iatrogenic regression sets in. The default is to manage the crisis in the community and return the person to their structured programme.

17.3 FOCUS, the target shifts by phase

Three phases, three different jobs. The **focus** of the work is not static; it moves as the patient stabilises. In the *short term* the target is safety, the job is crisis management and **risk** (containing self-harm and suicidality, and building a collaboratively agreed crisis plan). In the *mid term* the target is the core disorder itself, the emotion dysregulation, identity disturbance, abandonment sensitivity and unstable relationships, addressed through a sustained course of structured psychological therapy. In the *long term* the target is life beyond symptoms, function, relationships, work or study, and consolidated remission, which for many patients is a realistic goal given that borderline personality disorder has a substantially remitting long-term course. Sequencing

matters: trauma processing and deep character work wait until behavioural safety is established, so a plan that opens with intensive trauma exposure while the patient is still cutting weekly has the phases in the wrong order.

PHASE	PRIMARY TARGET (THE FOCUS)	THE MAIN WORK
Short-term	**Safety, risk and the acute crisis**	Risk assessment, crisis management, a collaboratively agreed crisis plan with identified triggers; brief, purposeful containment only if risk is otherwise unmanageable
Mid-term	The core disorder features	A sustained course of structured psychological therapy (the emotion dysregulation, identity, abandonment and relational instability)
Long-term	Function, relationships and remission	Rehabilitation into role and relationship, relapse prevention, and consolidation of gains toward remission

The focus of the integrated plan shifts by phase; safety is secured before core-feature therapy, and function follows.

17.4 The short-term focus, crisis management, risk and self-harm

Assess the risk, hold the person, agree a plan, avoid the ward. When a patient presents in crisis, the sequence is concrete. Assess the current **risk** to self and others; ask what has happened before and what helped then; help the person manage the surge of anxiety by enhancing coping and reflective capacity rather than simply removing them from their life; and avoid hospital admission unless there is a serious risk that cannot be managed otherwise (NICE 2009). The durable output of a crisis contact is a crisis plan, agreed collaboratively and documented, that names the person's individual triggers, the early-warning signs, the self-management steps and skills to use first, and exactly whom to contact and how, so that the next crisis has a rehearsed pathway that is not the emergency department by default (IPS 2023 makes the collaboratively agreed crisis plan central to reducing hospitalisation in acutely suicidal patients). Self-harm is managed within, not outside, this frame: it is understood, taught and responded to inside the structured therapy, and the person is never excluded from care because of it. Where a sedative is genuinely needed to get through an acute crisis, its use is short-term and time-limited (see the medication topic below), and benzodiazepines are avoided.

WORKED EXAMPLE

A woman known to the community team presents at night after superficial cutting following a relationship rupture, distressed but not acutely suicidal on assessment. The integrated response is not admission. The clinician assesses current risk, reviews what helped in previous episodes, helps her down-regulate the immediate arousal, and works with her on the crisis plan, updating the trigger list, rehearsing the distress-tolerance skill to use first, and confirming the daytime contact route back into her structured therapy. If night-time distress is extreme, a short-term sedative for a few days may be considered as part of the plan, not a new standing prescription, and she returns to her outpatient programme rather than to a ward.

17.5 MODUS, structured psychological therapy as the primary mode

The primary means is a structured, theory-based psychotherapy, delivered whole. The **modus** of the plan is led by structured psychological therapy. The question is rarely whether to offer psychotherapy but *which structured psychotherapy*, chosen by availability, patient fit and the dominant problem: dialectical behaviour therapy (DBT, Marsha Linehan), the best-evidenced option where reducing recurrent self-harm is the priority; schema therapy (Jeffrey Young), where enduring maladaptive patterns and identity are central; mentalisation-based treatment (MBT, Bateman and Fonagy), where the loss of mentalising under attachment stress dominates; and transference-focused psychotherapy (TFP, Clarkin and Kernberg), an object-relations treatment for the patient who can tolerate a long interpretive therapy. What matters more than the brand is that whichever is chosen is comprehensive, theory-based, of adequate duration and delivered by trained, supervised practitioners; NICE warns specifically against brief psychological interventions of less than three months offered outside a structured, supervised service. Each modality has its own topic; the wider models and technique are developed in the Psychotherapies, clinical assessment, MSE and nosology notes.

STRUCTURED THERAPY	CORE MECHANISM (WHAT IT TARGETS)	BEST-FIT INDICATION
Dialectical behaviour therapy (DBT)	**Emotion dysregulation from a biosocial deficit; skills plus acceptance-change balance**	Recurrent self-harm and suicidality the priority (the first-line, best-evidenced choice for self-harm)
Schema therapy	Early maladaptive schemas and schema modes; limited reparenting	Pervasive lifelong patterns and identity work; where relational-pattern change is central
Mentalisation-based treatment (MBT)	Restoring mentalising that collapses under attachment-stress arousal	Marked mentalising failures and attachment-driven relational storms
Transference-focused psychotherapy (TFP)	Integrating split self-other representations through the here-and-now transference	Identity diffusion in a patient able to tolerate a long, interpretive treatment

The four structured psychotherapies of the modus; the choice is by availability and fit, and all four have randomised support. Delivery must be comprehensive and of adequate duration.

MNEMONIC

LOCUS, FOCUS, MODUS

The integrated plan on one spine. **LOCUS**, where: outpatient and community, stepped care, admission avoided (and brief and purposeful if unavoidable). **FOCUS**, what and when: short-term safety and risk, mid-term the core disorder via structured therapy, long-term function and remission. **MODUS**, by what means: structured psychological therapy primary, medication symptom-targeted and time-limited, plus multidisciplinary care planning and psychoeducation. The three read as a single sentence, care in the community, targeted by phase, delivered chiefly by psychotherapy.

17.6 Schema therapy done properly, the mode framework

The therapy that reads the disorder as shifting modes, and reparents them. Because it is the lens many Indian trainees will use, schema therapy deserves its structure stated cleanly. It understands borderline personality disorder not as one steady state but as rapid flips between *schema modes*, moment-to-moment states each schema activates. In the borderline patient the recurring modes are the **vulnerable child** (the abandoned, abused, frightened core the whole treatment aims to protect and heal), the **angry and impulsive child** (raw rage and impulsive self-harm when needs go unmet), the **detached protector** (the numbing, dissociative, disconnected withdrawal that shields the child from feeling), the **punitive and demanding parent** (the internalised critical voice that attacks the self and drives self-harm and guilt), and the **healthy adult** (the mode the therapy builds up to meet needs adaptively). The signature mechanism is *limited reparenting*: within professional bounds the therapist provides, in a corrective form, the safety, validation and limits the patient's developmental environment failed to supply, and through mode work (including chair work) weakens the maladaptive modes and strengthens the healthy adult. It is delivered as a longer-term treatment, and its randomised evidence in borderline personality disorder is a genuine strength.

GOOD TO REMEMBER

- **Structured psychological therapy (the primary mode):** mechanism, whichever of DBT (biosocial emotion dysregulation, skills plus the acceptance-change dialectic), schema therapy (schema modes healed by limited reparenting), MBT (restoring mentalising under attachment stress) or TFP (integrating split object representations in the transference) fits; all four are comprehensive, theory-based and of adequate duration. Indication, borderline personality disorder as the first-line treatment; the choice is by availability and fit, with DBT the best-evidenced where recurrent self-harm is the priority. Signature caution, a brief or fragmentary intervention of less than three months outside a structured supervised service is not adequate treatment, and behavioural safety precedes deep trauma or character work.

17.7 MODUS, the place of medication, symptom-targeted and time-limited

Not for the disorder; for a comorbidity or a crisis, by symptom domain. Medication is the adjunctive, not the primary, arm of the modus, and its rules follow the guideline order. NICE (2009) is the most restrictive: no drug for the disorder or its symptoms, no antipsychotics for medium- and long-term treatment, and any drug started in a crisis reviewed and stopped once

the crisis resolves, with regular review of repeat prescriptions and active discouragement of polypharmacy. Two legitimate windows remain. The first is **medication for comorbidity**: a co-occurring depressive, anxiety, post-traumatic or other disorder is treated on its own merits, within the structured borderline programme. The second is the short-term crisis: a sedative (for example a sedating antihistamine, or a low-dose antipsychotic) may be used cautiously as part of the plan, usually for no longer than one week. Where IPS and WFSBP permit symptom-targeted adjuncts, they are matched to the dominant symptom domain, and Indian brand names are given first with the pharmacology kept light and cross-referenced. Two agents to avoid: benzodiazepines (dependence and disinhibition, IPS), and drugs unsafe in overdose such as irreversible MAOIs and lithium as a first choice (WFSBP), because these patients must be given drugs safe in parasuicidal acts.

SYMPTOM DOMAIN	ADJUNCTIVE CLASS (INDIAN BRAND FIRST; LIGHT)	GUIDELINE NOTE
Cognitive-perceptual (suspiciousness, transient quasi-psychotic symptoms)	**Low-dose atypical antipsychotic, quetiapine (Qutipin) or olanzapine (Oleanz)**	WFSBP first among drugs here; NICE forbids medium- and long-term antipsychotic use, so short, targeted only
Affective dysregulation (depressed mood, anxiety, mood swings)	SSRI, sertraline (Serlift) or fluoxetine (Fludac)	WFSBP best-shown class for this domain; treat true comorbid depression or anxiety on its merits
Impulsive-behavioural dyscontrol and aggression	Low-dose atypical antipsychotic; mood stabiliser, valproate or divalproex (Valprol, Encorate), if antipsychotic insufficient	IPS and WFSBP symptom-targeted option; not a disorder-specific treatment
Acute crisis (short-term only)	A sedative, a sedating antihistamine or low-dose antipsychotic	NICE, cautious, part of the plan, usually no longer than one week; review and stop

Adjunctive medication is symptom-domain-matched, time-limited and reserved for a comorbidity or a crisis; the deep dosing sits in the pharmacotherapy notes. Doses are not re-taught here.

PEARL

The most useful prescribing question in a borderline patient already on three or four psychotropics is not "what to add" but "what to stop". NICE asks you to review people prescribed drugs without a diagnosed comorbidity, aim to reduce and discontinue treatments started in past crises, and discourage polypharmacy. A careful deprescribing review is often the single most guideline-concordant medication act you can perform, and it protects a group who are, by the nature of the disorder, at high overdose risk.

17.8 Multidisciplinary care planning, psychoeducation and the service frame

The connective tissue that holds the plan together. Around the therapy and the selective medication sit the elements that make the plan durable. A comprehensive **multidisciplinary care plan** is developed with the person (and carers where appropriate), documenting the agreed goals, the roles of each team member, the crisis plan with its identified triggers, and the long-term aims for education and employment; it names who does what and is the reference point every

team member works from, which is also how a patient prone to splitting is held by a consistent, communicating team rather than played between its members. **Psychoeducation** is therapeutic in its own right: a collaborative, de-stigmatising explanation of the condition, its typically remitting long-term course, and the rationale for a psychotherapy-led plan improves engagement and reduces the hopelessness the diagnosis can carry. The **service frame** closes the loop, no exclusion from services because of the diagnosis or self-harm, agreed supervision for the staff who do this demanding work, and a structured, phased handover whenever care is transferred, so that the person never falls through the gap between services.

17.9 The guideline synthesis, NICE then IPS and WFSBP reconciled

One line the three bodies will all sign. The examiner-safe synthesis is easy to hold once the hierarchy is clear. All three agree that structured psychotherapy is primary and that no drug is a registered treatment for the disorder; they differ only in how much adjunctive medication they permit. NICE (CG78, 2009) leads and is the most restrictive, no drug for the disorder, no long-term antipsychotic, drugs only for a comorbidity or briefly in a crisis. The Indian Psychiatric Society (IPS 2023) makes psychotherapy central, names DBT for the early reduction of emotion dysregulation and self-harm, builds the plan around a collaboratively agreed crisis plan, and permits symptom-targeted antipsychotics or mood stabilisers in some patients while forbidding benzodiazepines. WFSBP (2007) supplies the symptom-domain map for those adjuncts and insists any drug be trialled against clear targets for at least three months and stopped if it does not help. Read together (the guideline stack, nice ips wfsbp), the message is one: lead with structured psychological therapy, use medication sparingly and by symptom, and review it to stop.

GUIDELINE	POSITION ON PSYCHOTHERAPY	POSITION ON MEDICATION
NICE 2009 (CG78), the home guideline	**Structured, theory-based psychotherapy is primary; DBT or MBT where self-harm reduction is the priority**	No drug for the disorder; no medium- or long-term antipsychotic; only for a comorbidity or short-term in a crisis (a sedative, usually up to one week)
Indian Psychiatric Society 2023	Psychotherapy central; DBT early for emotion dysregulation and self-harm; a collaboratively agreed crisis plan	Symptom-targeted antipsychotics or mood stabilisers in some patients; benzodiazepines avoided
WFSBP 2007	Psychotherapy primary; pharmacotherapy adjunctive only	Symptom-domain-matched (antipsychotic for cognitive-perceptual and impulsive, SSRI for affective); avoid MAOIs and lithium first; trial at least three months

The three guideline bodies reconciled; they converge on psychotherapy-primary and diverge only on the room left for symptom-targeted adjuncts, NICE most restrictive.

17.10 The integrated plan in Indian practice

Where the algorithm meets the ground here. The integrated plan is drawn as an algorithm in the accompanying figure; four India realities shape how it runs. First, *under-recognition*,

personality disorders are markedly under-recognised in routine Indian practice, and borderline patients often reach services labelled only by their crises, self-harm, an overdose, a mood or substance comorbidity, so the disorder is captured, and the psychotherapy-led plan started, only when it is actively looked for. Second, *availability and cultural adaptation*, the structured psychotherapies the plan depends on are concentrated in a few tertiary and metropolitan centres; DBT and schema therapy are being trained and culturally adapted in India (attending to family involvement, idioms of distress and the collectivist framing of autonomy and relationship), but access is uneven, and a realistic plan often blends available structured elements with skilled generic clinical management rather than assuming a full programme. Third, the *medico-legal frame*, most forcefully around antisocial rather than borderline personality disorder, is where the diagnosis carries legal weight, and offender assessment, court reports and the prediction of dangerousness are developed in the Mental health legislation and forensic psychiatry notes. Fourth, the *cultural expression of personality pathology*, deviation is judged against the person's own cultural, social and economic milieu, so that culturally sanctioned dependence, help-seeking idioms or situational distress are not misread as trait pathology, and the disorder is not read through a single culture's norms.

INDIA

A pragmatic Indian version of the integrated plan holds the spine and adapts the resourcing. The locus stays outpatient (admission is even less desirable where beds are scarce and asylum-style regression easy to induce), and the crisis plan is built around the family and, for many patients, WhatsApp-reachable daytime contact rather than a formal crisis line. The modus leads with whatever structured therapy is genuinely available, DBT-informed skills work most often, with schema therapy where a trained therapist exists, delivered with cultural adaptation; medication stays symptom-targeted and minimal, with Indian brands (quetiapine as Qutipin, sertraline as Serlift) named first but kept light and, crucially, reviewed to stop. The single most common local error is the mirror image of the guideline: a borderline patient carried for years on rotating polypharmacy with no structured psychotherapy ever started. Distinguishing borderline instability from bipolar II before reaching for a mood stabiliser is developed in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes, and the complex-PTSD boundary in the Anxiety, OCD and trauma-related disorders notes.

GOOD TO REMEMBER

- **Borderline personality disorder (the disorder being managed):** defining criterion set, a pervasive pattern of instability of affect, self-image and relationships with marked impulsivity, diagnosed on five or more of the nine DSM-5-TR criteria (and captured as the borderline pattern qualifier on the ICD-11 dimensional model). First management step, establish safety and a collaboratively agreed crisis plan, then start structured psychological therapy as the primary treatment. The discriminator that changes management, it is an enduring, pervasive, inflexible pattern with onset by adolescence, not a situational affective lability and not bipolar II, so the answer is a psychotherapy-led plan, not a mood stabiliser started first-line.

HOLD THIS

Borderline personality disorder is managed community-first on the LOCUS, FOCUS, MODUS spine, with structured psychological therapy as the primary treatment and medication only symptom-targeted, time-limited and for a comorbidity or a crisis: NICE says no drug is first-line for the disorder, and starting one is the trap.

Apply and consolidate

18 . Worked cases

The arc closer, where the chapter is put to work. A personality-disorders question is rarely won on the criteria list alone; it is won on the **formulation**, the reasoning that carries a presentation through the general criteria, to a named diagnosis, past its mimics, into a model of why the person is the way they are, and out to a defensible first-line plan. Long cases and vivas test exactly this movement, so this fragment reasons four worked cases end to end rather than restating the facts the earlier topics have already fixed. Each case is a **worked example** in the strict sense: the presentation is given, and then the discriminators, the model and the management are argued out loud.

The four are chosen to exercise the four highest-yield skills of the chapter. The first is a borderline personality disorder case formulated on both the Linehan biosocial and the schema-modes models and treated with structured psychotherapy, with medication kept symptom-targeted; the second works the borderline-versus-bipolar-II discrimination through the discriminator grid to the correct diagnosis and the correct first-line treatment; the third is an antisocial forensic vignette, with its conduct-disorder history, its structured risk assessment and its medico-legal frame; and the fourth is a cluster-C (anankastic) case. Read across them and one spine repeats, laid out in the figure alongside: clear the general criteria, count and type, discriminate from the mimic, formulate, and treat with psychotherapy first.

3	5	9	4
DSM-5 CLUSTERS (A, B AND C)	ICD-11 TRAIT DOMAINS	BORDERLINE CRITERIA, THRESHOLD FIVE	DBT SKILLS MODULES

18.1 Working a personality-disorder case: the shared spine

Every case runs the same five-step spine. Before any single case, hold the sequence that all four share, because a case answer that jumps straight to a label has skipped the marks. First, clear the **general personality-disorder criteria**: an enduring, pervasive, inflexible and maladaptive pattern of inner experience and behaviour, deviating from the person's cultural expectation, stable and of long duration with onset traceable to adolescence or early adulthood, causing distress or impairment, and not better explained by another mental disorder, a substance or a medical condition. Second, **count and type** against the criteria of the suspected disorder. Third, **discriminate** from the presentations that mimic it, above all the borderline-versus-bipolar-II line. Fourth, **formulate**, on a disorder-specific model where one exists. Fifth, **treat**, with structured psychotherapy primary and any drug symptom-targeted, adjunctive and time-limited.

The spine is the same whether the type survives as a DSM-5-TR category or is re-expressed as an ICD-11 severity level with trait qualifiers; the categorical name is a shorthand for a point on that dimensional map.

RULE **Formulate before you medicate.** Clear the general criteria, count and type, discriminate from the mimic, build the formulation, and only then treat, with structured psychotherapy primary and any drug symptom-targeted, adjunctive and time-limited; the label is the start of the reasoning, not the end of it.

18.2 case: the borderline patient, presentation and the general criteria

case: A woman in her early twenties is referred after an overdose that followed a break-up. On history she describes a terror of being left that predates this relationship, a lifelong pattern of relationships that swing from "he is perfect" to "he is cruel" within a single afternoon, a persistent sense of never knowing who she really is, recurrent cutting between crises, moods that flip within a couple of hours when a text goes unanswered, a background hollow emptiness, and disproportionate anger she cannot hold down. The presentation is dramatic, but the discipline is to work the spine, not to pattern-match. The general criteria are cleared first: this is an enduring, pervasive pattern present across relationships and settings, traceable to her adolescence, ego-syntonic and inflexible, not confined to the current crisis, and not better explained by a primary mood disorder or a substance. Only now is the count taken, and it is comfortably met: abandonment fear, unstable idealising-devaluing relationships, identity disturbance, recurrent self-harm, reactive affective instability, chronic emptiness and inappropriate anger give **five or more of the nine criteria** with room to spare. The diagnosis is defensible because the criteria can be named and shown to be trait, not a fresh state.

18.3 case: the borderline patient, the dual formulation

Two models, read together, not as rivals. The formulation borrows from both disorder-specific frameworks, because each answers a different question. Marsha Linehan's biosocial model answers *why*: a constitutional **emotional vulnerability**, heightened sensitivity, intense responses and a slow return to baseline, has transacted over her development with a pervasively **invalidating environment** that dismissed or punished her inner experience, and the two have amplified one another into a pervasive **emotion dysregulation**; her overdose and her cutting are read as attempts to solve the problem of unbearable affect, not as manipulation. Jeffrey Young's schema therapy answers *what is in the room*: because she scores high on almost every early maladaptive schema at once and flips between extreme states within minutes, she is formulated not as a list of schemas but through the **schema modes**, the small set of parts that alternate, cycling through the vulnerable (abandoned) child, the angry and impulsive child, the detached protector and the punitive parent, around a Healthy Adult that is weak and must be strengthened. The dual formulation is drawn in the accompanying figure, the biosocial pathway feeding the mode map.

PEARL

The two models are complementary, not competing. The Linehan biosocial theory gives the *mechanism* (emotion dysregulation) and the technology of change (concrete skills); the schema-modes map gives the *parts* (which mode is speaking now) and the relational and experiential engine (limited reparenting, chair work). A single clinician can formulate one patient on both, which is exactly why dialectical behaviour therapy and schema therapy are best held as siblings in one evidence-based family rather than as a forced choice.

WORKED EXAMPLE

Re-expressing the same patient in the ICD-11 dimensional system, forward-taught on the framework topics, gives a formulation of the form "moderate personality disorder, with prominent negative affectivity and disinhibition and some dissociality, plus the borderline pattern qualifier": the severity level is rated first and leads, the trait domains qualify it, and the borderline pattern is appended last. The categorical name "borderline personality disorder" and this dimensional string describe the same woman; the ICD-11 borderline pattern qualifier was retained precisely to flag the patients who respond to the borderline-specific psychotherapies, which is what makes both worth carrying.

18.4 case: the borderline patient, the structured-therapy plan

Structured psychotherapy is primary; the drug is a time-limited adjunct. The plan follows the formulation and the guidelines exactly. Structured psychological therapy is the primary treatment (NICE 2009, IPS 2023): where reducing recurrent self-harm is the priority, comprehensive dialectical behaviour therapy is the option named first, delivering its **four skills modules** (mindfulness at the core, with distress tolerance, emotion regulation and interpersonal effectiveness) through its four modes, with the target hierarchy putting the life-threatening behaviours ahead of everything else. The schema layer runs alongside or in sequence: limited reparenting and experiential mode work address the parts the skills alone do not reach, and the two layers map neatly onto her modes, as below. Medication stays symptom-targeted, adjunctive and time-limited: no drug is licensed for the disorder, so a short course of a sedative or a low-dose antipsychotic such as quetiapine (Qutipin, Seroquel) may be considered cautiously in a crisis, usually for no longer than a week, and a serotonin reuptake inhibitor such as fluoxetine (Fludac, Prozac) is added only if a comorbid depressive disorder is present, with the dosing carried in the Mood disorders: pharmacotherapy notes rather than re-taught here. The complex-PTSD boundary, which her trauma history raises, is drawn in the Anxiety, OCD and trauma-related disorders notes.

BORDERLINE MODE	HOW IT PRESENTS IN THE ROOM	THE MATCHED MOVE (DBT AND SCHEMA)
Vulnerable (abandoned) child	Raw terror of being left; fragile, frightened, alone	**Limited reparenting and validation; soothe and meet the need within bounds**
Angry and impulsive child	Rage or impulsive acting-out when a need goes unmet	Validate the feeling and contain the behaviour; distress-tolerance and emotion-regulation skills
Detached protector	Numbness, "I feel nothing", connection shut off	Gently bypass it to reach the child; empathic confrontation of the avoidance
Punitive parent	Self-hatred, "I deserved it", driving the self-harm	Fight and expel it through chair work; build the Healthy Adult and self-compassion

The four borderline schema modes matched to the therapeutic move, showing how the DBT skills (distress tolerance, emotion regulation) and the schema-therapy engines (limited reparenting, chair work) act on different modes of the same patient.

GOOD TO REMEMBER

- **Borderline personality disorder:** defining requirement is a pervasive pattern of instability of relationships, self-image and affect with marked impulsivity, meeting five or more of the nine criteria, on a base already cleared against the general personality-disorder criteria. First diagnostic step in the case: clear the general criteria, then count the nine; the affect is rapidly reactive and interpersonally cued and lasts hours, which is what separates it from bipolar II.
- **Dialectical behaviour therapy:** mechanism is the biosocial theory (emotional vulnerability transacting with an invalidating environment to give emotion dysregulation), treated by fusing behavioural change with mindfulness-based acceptance across four skills modules and four modes with a life-threatening-first target hierarchy; indication is borderline personality disorder with recurrent self-harm, the first-line structured therapy for self-harm (NICE, IPS); caution is that it must be comprehensive and delivered with fidelity, and trauma work waits for stage two.
- **Schema therapy:** mechanism is healing early maladaptive schemas through limited reparenting plus experiential mode work (imagery rescripting, chair work), with the labile borderline patient worked through the schema modes toward a strengthened Healthy Adult; indication is chronic characterological pathology, strongest-evidenced in borderline personality disorder; caution is that stripping out the reparenting and the experiential work leaves it as ordinary CBT that never touches the schemas.

18.5 case: borderline versus bipolar II, working the grid to the diagnosis and the treatment

case: A woman in her mid-twenties is referred as "query bipolar II disorder, mood swings, please start a mood stabiliser". The temptation is to hear "unstable mood" and reach for the drug, so the whole task is to read the mood rather than name it, working one discriminator at a time. On history the swings last two to three hours, always follow a fight with her partner or a fear that he is pulling away, and lift the moment he reassures her; between them she sits not on a settled euthymic baseline but on a floor of chronic emptiness; she describes never knowing who she is; and she cuts when the distress peaks. Read across the discriminator grid, the tempo is minutes to hours rather than the sustained days-to-weeks of a bipolar episode; the trigger is reactive and interpersonal rather than autonomous; the baseline is chronic dysphoria rather than a euthymic

return; and identity disturbance, chronic emptiness and affect-regulating self-harm are present, none of which belongs to bipolar II. Nothing here is a distinct hypomanic period of **at least four consecutive days** or a major depressive episode of **at least two weeks**. The diagnosis is borderline personality disorder, not bipolar II, and the first-line treatment follows the diagnosis: a structured psychotherapy, not a mood stabiliser prescribed for a bipolarity she does not have. The bipolar-II syndromes themselves are developed in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes.

TRAP **Reaching for a drug first, on a pattern-matched label.** Reading reactive, hours-long, interpersonally cued lability as bipolar II and starting a mood stabiliser first-line, or drugging borderline personality disorder itself against NICE, treats a personality-based instability with the wrong tool and delays the structured psychotherapy that is its actual primary treatment.

GOOD TO REMEMBER

- **Bipolar II disorder:** defining requirement is at least one hypomanic episode (elevated or irritable mood lasting at least four consecutive days, with change in sleep, energy and goal-directed activity) plus at least one major depressive episode (at least two weeks), with a euthymic baseline between discrete, largely autonomous episodes and no full manic episode. Discriminator from borderline: the mood runs sustained, autonomous and days-to-weeks long, not the minutes-to-hours interpersonal reactivity of the personality disorder; the mood stabiliser is foundational here, whereas in borderline it is at best a symptom-targeted adjunct. When a genuine autonomous episode is documented alongside the pervasive reactive pattern, both diagnoses stand and both treatments are needed.

18.6 case: the antisocial forensic vignette, the history and the risk assessment

case: A man in his thirties is remanded after a violent robbery and referred for a court report with a request to "diagnose psychopathy". The vignette turns on the developmental gate and on the structure of the risk estimate. Collateral and documentary sources, which the manual insists on because deceit is central and the account cannot be taken on his word, show truanting, cruelty to animals and theft from well before the age of twelve, expulsions, a chaotic work record, unpaid debts, repeated adult convictions, and a flat indifference to the people he has hurt. The conduct disorder before fifteen and the age of at least eighteen are both satisfied, and he meets **three or more of the seven** adult criteria comfortably, so the diagnosis is antisocial personality disorder. The demand for a "diagnosis of psychopathy" is answered carefully: psychopathy is the narrower affective-interpersonal construct measured on the Hare Psychopathy Checklist-Revised, and it is not asserted without a rated instrument. The risk of future violence is then estimated by **structured professional judgement**, not by clinical impression and not by a raw checklist total: empirically derived factors are rated systematically, for instance on the HCR-20 across its historical, clinical and risk-management scales, and then weighed for this individual to a reasoned low, moderate or high rating.

RULE **No conduct disorder before fifteen, no antisocial personality disorder; and structure the risk estimate, do not total it.** The antisocial diagnosis is developmental and needs a documented childhood conduct disorder, and dangerousness is judged by structured professional judgement, factors rated systematically and then weighed for the case, never by the raw count on a checklist.

18.7 case: the antisocial forensic vignette, the medico-legal frame and the mainstay

The report claims only what it can defend, and the treatment is psychological. The medico-legal frame is where the diagnosis carries its weight, and its central caution is that antisocial personality disorder is a matter of disposal, not of exculpation. The insanity defence turns on an unsoundness of mind such that the accused did not know the nature of the act or that it was wrong, and a stable trait pattern rarely meets that legal test; the report therefore states three things and no more, that the diagnosis is antisocial personality disorder (not, on this assessment, formally psychopathy, which would need the rated instrument), that the disorder does not amount to the unsoundness of mind that founds an insanity defence and so does not reduce his responsibility, and that his risk of future violence, structured and then judged, is high and should guide disposal. The value of the report lies as much in what it declines to claim as in what it asserts, and the statutes, the fitness assessment and the disposal pathways sit in the Mental health legislation and forensic psychiatry notes. Management is modest and psychological-first: NICE recommends group-based cognitive and behavioural interventions, with the person sharing the choice of duration and intensity (NICE 2015), delivered where relevant in criminal-justice settings; no drug treats the personality, and where impulsive aggression is a target it is addressed adjunctively and off-licence, for example with divalproex (Valprol, Encorate), the detail cross-referenced to the Mood disorders: pharmacotherapy notes. Mentalisation-based treatment adapted for the disorder is an emerging structured option under trial.

GOOD TO REMEMBER

- **Antisocial personality disorder:** defining requirement is a pervasive pattern of disregard for and violation of the rights of others since fifteen, three or more of the seven criteria, gated by documented conduct disorder before fifteen and an age of at least eighteen, and not confined to schizophrenia or a bipolar illness. Discriminator: it is a trait pattern with a childhood conduct-disorder precursor, not a synonym for a criminal record or for the narrower affective-interpersonal construct of psychopathy; its forensic weight is in the structured assessment of dangerousness and the court report, not in the insanity defence.
- **Group cognitive-behavioural therapy (for antisocial personality disorder):** mechanism is a structured, skills-based group intervention targeting the cognitions and behaviours that drive offending, delivered with firm limits and shared choice of intensity; indication is antisocial personality disorder, especially with an offending history, and it is the NICE-recommended mainstay (NICE 2015); signature caution is that no drug is recommended for the personality itself (medication only for a comorbidity or, adjunctively and off-licence, for impulsive aggression) and that poor engagement and manipulation of the therapeutic frame are the rule, since the condition is ego-syntonic.

18.8 case: the cluster-C (anankastic) patient, formulation and management

case: An accountant in his forties is referred as "OCD, please treat". He is a relentless perfectionist who cannot discard years of worn-out paperwork, refuses to delegate unless colleagues submit to

exactly his method, and misses deadlines because he re-checks his work endlessly; he regards all of this as ordinary diligence and is untroubled by it, though his family and his team are worn down. Crucially, he describes no intrusive unwanted thoughts and performs no rituals to neutralise anxiety. The spine settles the diagnosis: the general criteria are cleared (an enduring, pervasive, ego-syntonic pattern from early adulthood, causing impairment and not better explained otherwise), and he meets **four or more of the eight** features of obsessive-compulsive personality disorder, the anankastic type, a preoccupation with orderliness, perfectionism and mental and interpersonal control at the expense of flexibility, openness and efficiency. The single discriminator that decides the case is the absence of true obsessions and compulsions and the ego-syntonic tone: this is character, not the ego-dystonic, resisted symptom pattern of obsessive-compulsive disorder, whose side is developed in the Anxiety, OCD and trauma-related disorders notes. In the ICD-11 dimensional system the phenotype is captured by prominent **anankastia**, the fifth trait domain. Management is psychological-first: structured cognitive-behavioural therapy working on the rigidity and the need for control, with the schema-mode formulation informing the work where a full protocol is out of reach; medication is reserved for a comorbidity only, never for the personality, and had he also described genuine resisted obsessions and washing rituals, both diagnoses would stand together.

GOOD TO REMEMBER

- **Obsessive-compulsive (anankastic) personality disorder:** defining requirement is a pervasive, ego-syntonic preoccupation with orderliness, perfectionism and mental and interpersonal control at the expense of flexibility, openness and efficiency, four or more of the eight features, from early adulthood. First diagnostic step in the case: clear the general criteria, confirm the perfectionism and control are ego-syntonic trait, then search for true obsessions and compulsions; their absence, not the shared name, discriminates it from obsessive-compulsive disorder.
- **Cognitive-behavioural therapy (for cluster C):** mechanism is graded exposure to the avoided or feared situation plus cognitive restructuring of the core belief (the need for control in anankastic, inadequacy in avoidant, helplessness in dependent), with work on rigidity, assertiveness and autonomy; indication is all three cluster-C types, engaging fastest where the anxious behaviour distresses the person; signature caution is the alliance and pace (the anankastic patient resists surrendering control), and medication is for a comorbidity only, never disorder-specific.

18.9 The thread through the four cases, and the India lens

One method, four applications. Laid side by side, the four cases show the same reasoning applied to different pathology, and the grid below is the object to carry into the hall: in every row the diagnosis is reached by clearing the general criteria and then discriminating from a mimic, and in every row the first-line treatment is a structured psychotherapy, with medication either symptom-targeted and time-limited, reserved for a comorbidity, or absent altogether. The synthesis map alongside arranges the same four against the decision points of the chapter. The wider technique of the psychotherapies, beyond the disorder-specific models owned here, sits in the Psychotherapies, clinical assessment, MSE and nosology notes; the schizotypal-versus-schizophrenia boundary that a cluster-A case would raise is in the Schizophrenia: aetiology, phenomenology, classification and course notes.

WORKED CASE	THE DECISIVE FEATURE(S)	DIAGNOSIS	FIRST-LINE TREATMENT	MEDICATION
The self-harming young woman	Five or more of the nine; reactive hours-long affect on a floor of emptiness and unstable identity	**Borderline personality disorder**	Structured psychotherapy (DBT skills plus schema mode work)	Symptom-targeted, time-limited, adjunctive
"Query bipolar II, mood swings"	Hours-long, interpersonally cued lability; no autonomous days-long episode; identity disturbance and emptiness	**Borderline personality disorder (not bipolar II)**	Structured psychotherapy, not a mood stabiliser	Only for a genuine comorbidity
The remanded violent offender	Three or more of the seven; conduct disorder before fifteen; remorseless	**Antisocial personality disorder**	Group cognitive-behavioural therapy; structured risk assessment	None for the personality; adjunct for impulsive aggression only
The perfectionist "referred as OCD"	Ego-syntonic perfectionism and control; no true obsessions or compulsions	**Obsessive-compulsive (anankastic) personality disorder**	Structured CBT on rigidity and control	For a comorbidity only

The four worked cases mapped to their decisive feature, diagnosis, first-line treatment and medication role; the shared conclusion is that structured psychotherapy is primary across all four and the drug is never the treatment for the personality itself.

INDIA

Four genuine India angles converge on these cases. First, under-recognition: personality disorders are markedly under-recognised in Indian practice, so all four patients typically reach services through something else, the overdose, the "mood swings" referral, the legal remand, the burnout, and the underlying pattern is captured only when a corroborated developmental history is deliberately taken. Second, access: the structured psychotherapies the borderline and cluster-C cases need, dialectical behaviour therapy and schema therapy, are being delivered and culturally adapted at Indian tertiary and private centres rather than being widely available, so recognising that a patient needs psychotherapy rather than a mood stabiliser is only the first step; the mindfulness core of DBT sits naturally with Indian contemplative traditions, while its interpersonal-effectiveness scripts must be calibrated to family interdependence rather than imported wholesale. Third, the medico-legal frame of the antisocial case: the insanity defence rests on the unsoundness-of-mind test carried into the Indian Penal Code, which antisocial personality disorder rarely satisfies, and the dedicated forensic infrastructure to support the risk assessment is thin. Fourth, cultural expression: every criterion is judged against the person's own cultural, social and economic milieu, so that normative family interdependence is not scored as dependence, culturally sanctioned emotional or dissociative-trance display is not over-read as borderline reactivity, and survival-driven or subcultural offending is not read as trait antisociality; personality pathology must never be read through a single culture's norms.

HOLD THIS

Every personality-disorder case runs one spine: clear the general criteria, count and type, discriminate from the mimic (above all borderline from bipolar II), formulate on the biosocial and schema-mode models, and treat with structured psychotherapy first, the drug being only ever a symptom-targeted, time-limited adjunct for a comorbidity or a crisis, and never the first-line treatment for the personality itself.

19 · Consolidation

The last step is not new material, it is retrieval. This closing topic turns a chapter you have *read* into one you can *reproduce* under exam pressure. The single most examinable idea of the personality-disorders chapter, that the **general criteria** are a gate and that ICD-11 rates **severity first** before any trait, is learned not by rereading it but by forcing it out of memory. The evidence is one-directional: testing yourself on half-learned material, **retrieval practice**, fixes it far more durably than reading it again, and the efficient way to study is to **cover the answer** and pull each fact out before checking it. Everything below is built for that, a **mnemonic** that reassembles the whole chapter from one line, answer-free **retrieval prompt** lists, two answer vaults to check against, and a whole-chapter **synthesis map** to reproduce.

Use it actively, not by rereading. Say the master mnemonic once, then close the notes and work the retrieval prompts with the vaults covered; only then uncover the Good-to-remember vaults and mark what you missed. Finish by reproducing the synthesis map on a blank sheet. Do those three things and the chapter is consolidated, and the gaps you find are exactly where to go back. The wider technique of **active recall** and spaced retrieval sits alongside the clinical material, and

the general models and technique of the psychological therapies are developed in the Psychotherapies, clinical assessment, MSE and nosology notes.

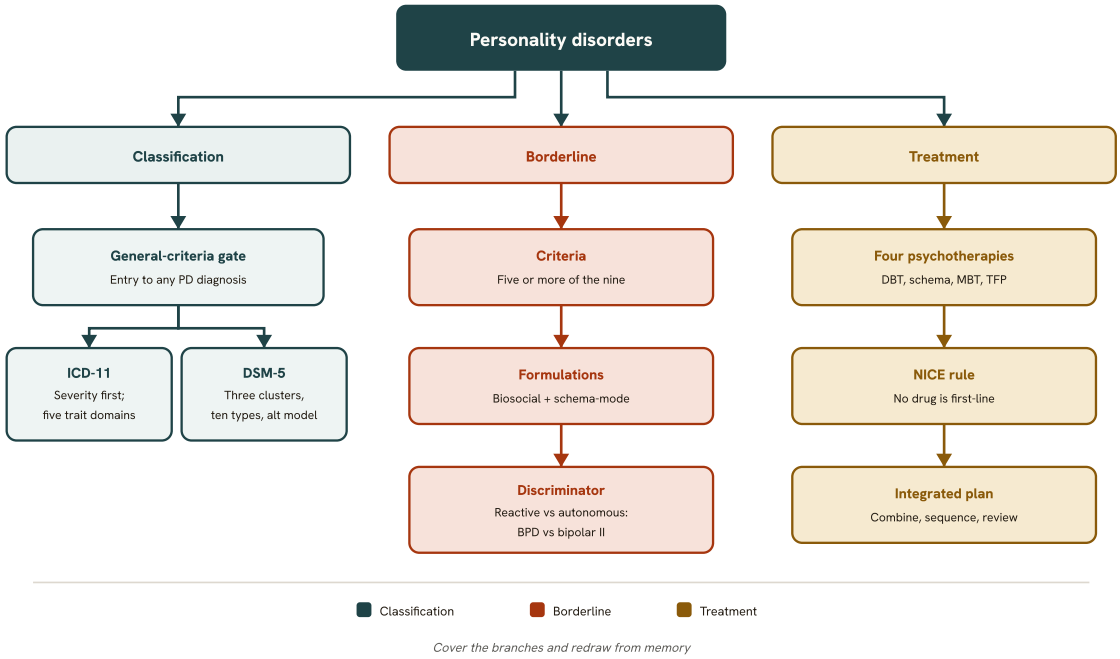


Fig 16.14 The chapter in one map: the general-criteria gate opening onto the ICD-11 dimensional and DSM-5 categorical classifications; borderline personality disorder with its criteria, its biosocial and schema-mode formulations and the bipolar-II discriminator; and the treatment branch of four structured psychotherapies with the rule that no drug is first-line. Cover the branches and redraw from memory.

19.1 The master mnemonic, paid off

One line rebuilds the whole chapter. The chapter opened by seeding a single **mnemonic**, and this is where it is redeemed. Its four beats are the four countable skeletons of the day, the clusters and types, the ICD-11 trait domains, the borderline criterion count, and the core skills therapy, and saying the line should make the branches beneath each beat unfold. If the line is solid, the whole family, however you later classify it, is recoverable from it.

MNEMONIC

MAD BAD SAD, FIVE DOMAINS, NINE-FOR-FIVE, FOUR TO COPE

MAD BAD SAD are the three DSM-5-TR clusters holding the ten categorical types: *mad* is Cluster A, odd or eccentric (Paranoid, Schizoid, Schizotypal); *bad* is Cluster B, dramatic or erratic (Antisocial, Borderline, Histrionic, Narcissistic); *sad* is Cluster C, anxious or fearful (Avoidant, Dependent, Anankastic). **FIVE DOMAINS** are the ICD-11 trait qualifiers, hooked as *New Dogs Do Dig Antiques*: Negative affectivity, Detachment, Dissociality, Disinhibition, Anankastia, plus the optional borderline pattern qualifier that sits apart. **NINE-FOR-FIVE** is borderline personality disorder, defined by **five or more of the nine** criteria. **FOUR TO COPE** is dialectical behaviour therapy and its four skills modules (mindfulness at the core, plus distress tolerance, emotion regulation and interpersonal effectiveness). Four numbers, and the chapter rebuilds from one line.

3	10	5	4
DSM-5-TR CLUSTERS	CATEGORICAL PERSONALITY TYPES	ICD-11 TRAIT DOMAINS	DBT SKILLS MODULES

19.2 How to run the recall

Cover, retrieve, check, redraw. The mechanics of **active recall** for this chapter are fixed and worth stating so the rest of the topic is usable. First, **cover the answer**, keeping the two Good-to-remember vaults below hidden. Second, work each **retrieval prompt** out loud or on paper from memory. Third, uncover the vault and mark every miss. Fourth, close on the **synthesis map** and **redraw from memory** on a blank sheet. The order matters, because the effortful pull of retrieval is what lays down the memory, so a prompt you struggle with and then check is worth more than a paragraph reread. That is why the prompt lists below are deliberately answer-free.

RULE **Two anchors hold the chapter.** The general criteria are a gate that must clear before any type is named, and ICD-11 rates severity *first* (personality difficulty, then mild, moderate, severe) before adding the five trait domains; and in borderline personality disorder structured psychotherapy is primary while a drug is never a first-line treatment for the disorder. Recover those and the detail hangs off them.

19.3 Retrieval prompts: the general criteria, the clusters and the ICD-11 model

Cover the vaults below and answer from memory. Each prompt targets the single point the examiner tests, not a general description. Work them as **retrieval practice**, then check against the criterion vault.

1. State the six-part general personality-disorder gate (Criteria A to F), and why no specific type is named until every part is cleared.
2. Which two or more of the four channels (cognition, affectivity, interpersonal functioning, impulse control) must Criterion A involve, and what age of onset does Criterion D require?
3. What separates a personality *disorder* from a personality *style*, and how does ICD-11 code the style that falls short of the threshold?
4. Name the three DSM-5-TR clusters and the ten categorical types under them, and give each cluster's descriptor.
5. What did ICD-11 abolish, what did it put in its place, and in what order are the three moves made?
6. Name the five ICD-11 trait domains, and say which one is ICD-11-only and which AMPD domain has no ICD-11 counterpart.
7. Where does the borderline pattern qualifier sit in the ICD-11 model, and why was it the one pattern retained?
8. What did ICD-10 keep that ICD-11 removed, and why do the categorical names still get tested?

19.4 Retrieval prompts: the borderline criteria and the bipolar-II discriminator

Still covered. This is the highest-yield discrimination of the chapter, so retrieve it cleanly and check against the criterion vault.

1. Reproduce the nine DSM-5-TR borderline criteria and state the threshold; which four strands do they unpack into?
2. Which single criterion (its reactivity clause) is the pivot of the bipolar-II discrimination, and what does it specify about duration?
3. Read the borderline-versus-bipolar-II differential on tempo, trigger and baseline: which pattern points to each side?
4. Which features belong to borderline personality disorder and have no bipolar-II equivalent at all?
5. How long must a hypomanic episode and a major depressive episode last, and where does the bipolar mood return to between episodes?
6. When do borderline personality disorder and bipolar II both stand, and what does each then need?

GOOD TO REMEMBER

- **Personality disorder (general):** an enduring pattern of inner experience and behaviour, pervasive and inflexible, deviating markedly from cultural expectation in two or more of cognition, affectivity, interpersonal functioning and impulse control, with onset by adolescence, causing impairment or distress, and not better explained by another disorder, a substance or a medical condition. Discriminator from a personality *style*: the impairment or distress (Criterion C); ICD-11 codes the style short of this as personality difficulty. First step: clear all the general criteria before naming any type.
- **ICD-11 dimensional classification:** no types; rate severity *first* (personality difficulty, then mild, moderate, severe by self-and-interpersonal dysfunction and risk of harm), then add any of the five trait domains (negative affectivity, detachment, dissociality, disinhibition, anankastia), then the borderline pattern qualifier if present. Discriminator from DSM-5-TR: DSM keeps the categorical clusters in its main text (with the Section III AMPD hybrid alongside), so read fluently in both.
- **Borderline personality disorder:** a pervasive pattern of instability of relationships, self-image and affect with marked impulsivity, meeting **five or more of the nine** criteria. Discriminator: the affect is rapidly reactive, interpersonally triggered and lasts hours, versus the sustained autonomous episodes of bipolar II. First step: clear the general criteria, then count the nine. ICD-11 keeps the construct as the optional borderline pattern qualifier.
- **Bipolar II disorder (the discriminator):** at least one hypomanic episode (elevated or irritable mood, at least four consecutive days) plus at least one major depressive episode (at least two weeks), with a euthymic baseline between discrete, largely autonomous episodes. Discriminator: sustained, autonomous, days-to-weeks episodes, not minutes-to-hours interpersonal reactivity; the mood stabiliser helps here, not in personality-based instability.
- **The three classic boundary traps:** schizotypal is placed on the schizophrenia spectrum but is a personality disorder marked by enduring cognitive-perceptual oddness without sustained psychosis (the schizophrenia boundary sits in the aetiology-and-phenomenology notes); anankastic personality is an ego-syntonic *trait* of rigid perfectionism, not the ego-dystonic obsessions and compulsions of OCD; and antisocial personality disorder, never diagnosed before adulthood, carries the medico-legal weight of the chapter and is worked in the forensic notes.

19.5 Retrieval prompts: the psychotherapies and their mechanisms

Cover the therapy vault below. Each prompt asks for the *mechanism* and the signature technique, which is what the examiner rewards, not a bare name.

1. State the biosocial theory and the acceptance-change dialectic of dialectical behaviour therapy, and name its four skills modules and four treatment modes.
2. Which behaviours does the DBT target hierarchy address first, second and third within its first stage?
3. Define an early maladaptive schema and name the four borderline schema modes; what is limited reparenting?
4. How does mentalisation-based therapy read borderline pathology, and what is the mentalising stance it uses instead of interpretation?
5. How does transference-focused psychotherapy read the disorder, and by what sequence does it integrate the split object dyads?
6. Which of the four structured therapies is best-evidenced where recurrent self-harm is the priority, and does any head-to-head trial crown one overall?

19.6 Retrieval prompts: the NICE rule and the integrated plan

Still covered. These are the single most examinable management statements of the material; retrieve them and check against the therapy vault.

1. State the NICE (2009, CG78) rule on drug treatment in borderline personality disorder: is any drug licensed, and what are the only two windows for medication?
2. What does NICE say specifically about antipsychotics for the medium- and long-term treatment of the disorder?
3. Lay out the LOCUS, FOCUS, MODUS spine: where care happens, how the target shifts by phase, and by what primary means.
4. Where NICE, the Indian Psychiatric Society and WFSBP differ, what is the one line all three will sign, and which is most restrictive?
5. Which two agents do the guidelines steer away from, and why (dependence, and safety in overdose)?

GOOD TO REMEMBER

- **Dialectical behaviour therapy (Marsha Linehan):** mechanism is the biosocial theory (emotional vulnerability transacting with an invalidating environment to produce pervasive emotion dysregulation), treated by fusing behavioural change with mindfulness-based acceptance; four skills modules (mindfulness as the core, distress tolerance, emotion regulation, interpersonal effectiveness) through four modes (individual therapy, skills group, phone coaching, consultation team) on a target hierarchy of life-threatening, then therapy-interfering, then quality-of-life behaviours. Indication: borderline personality disorder with recurrent self-harm; the best-evidenced structured therapy for self-harm. Caution: must be comprehensive and delivered with fidelity, and trauma work waits for stage two.
- **Schema therapy (Jeffrey Young):** mechanism is healing early maladaptive schemas (self-defeating patterns from unmet childhood needs) through limited reparenting plus experiential mode work (imagery rescripting, chair work); the borderline patient is worked through four modes (vulnerable child, angry and impulsive child, detached protector, punitive parent) toward a strengthened Healthy Adult. Indication: chronic characterological pathology, strongest evidence in borderline personality disorder (superior to TFP in Giesen-Bloo 2006). Caution: strip out the reparenting and the experiential work and it collapses into ordinary CBT that leaves the schemas untouched.
- **Mentalisation-based therapy (Bateman and Fonagy):** mechanism is that borderline symptoms arise from a loss of mentalising under attachment-stress arousal, so the therapy restores it through a curious, not-knowing mentalising stance in the here and now, working close to conscious experience rather than interpreting the unconscious. Indication: borderline personality disorder (extended to antisocial and to adolescents). Caution: do *not* push interpretation while the patient is non-mentalising and highly aroused; lower arousal and re-open thinking first.
- **Transference-focused psychotherapy (Clarkin and Kernberg):** mechanism is an object-relations treatment reading the disorder as split, unintegrated self-and-other representations (object dyads) held apart by splitting, integrated by working the here-and-now transference through clarification, confrontation and interpretation, with identity diffusion the target and identity consolidation the goal. Indication: borderline and narcissistic organisation in a patient able to tolerate a long, interpretive treatment. Caution: interpretation needs a mind that can still mentalise, or it destabilises.

19.7 The whole-chapter synthesis map

Cover the branches and redraw from memory. The final and highest-value exercise is to reproduce the chapter as one picture. The accompanying figure sets out the **synthesis map** as a single tree, a trunk labelled by the master mnemonic and three primary branches: a *classification* branch (the general-criteria gate splitting into the DSM-5-TR categorical clusters and the ICD-11 severity-first dimensional model with its five trait domains), a *borderline* branch (the five-of-nine criterion set and the reactive-versus-autonomous bipolar-II discriminator), and a *treatment* branch (the four structured psychotherapies with their mechanisms, and the NICE psychotherapy-primary, no-drug-first-line rule). Study it once, then cover every branch and **redraw from memory** on blank paper, writing the discriminator or the mechanism at each leaf. A branch you cannot regrow is a branch to reread. This cover-the-branches redraw is the most compact single test of whether the chapter is genuinely consolidated.

INDIA

Four Indian threads run the length of this chapter and belong on the synthesis map. First, *under-recognition*: personality disorders are diagnosed far less often in Indian practice than Western prevalence would predict, because the ego-syntonic pattern surfaces only when it is actively sought behind the self-harm, overdose or comorbidity that brings the patient in. Second, *availability and cultural adaptation*: dialectical behaviour therapy and schema therapy are being delivered and culturally adapted at Indian tertiary and metropolitan centres rather than being widely accessible, so a realistic plan blends what is available with skilled general management. Third, the *medico-legal frame*, sharpest around antisocial personality disorder, is where the diagnosis carries legal weight in offender assessment and court reports (the forensic notes). Fourth, the *cultural expression of pathology*: deviation is judged against the person's own cultural, social and economic milieu, so collectivist family-embeddedness, deference and religiously framed idioms are never read as dependent, avoidant or dissociative pathology; personality is not read through a single culture's norms.

TRAP **The chapter's recurring errors, in one line.** Diagnosing a type without first clearing the general criteria of an enduring, pervasive, inflexible pattern with onset by adolescence; calling reactive, hours-long affective lability bipolar II and starting a mood stabiliser; reaching for a drug first-line for borderline personality disorder against NICE; mislabelling schizotypal as schizophrenia; confusing anankastic personality with OCD; and reading personality pathology through one culture's norms.

HOLD THIS

If you can say *MAD BAD SAD, FIVE DOMAINS, NINE-FOR-FIVE, FOUR TO COPE* and, from it, regrow the general-criteria gate, the ICD-11 severity-first dimensional model with its five trait domains, the five-or-more-of-nine borderline count, the reactive-versus-autonomous bipolar-II split, and the psychotherapy-primary, no-drug-first-line NICE rule, the chapter is consolidated; wherever you cannot, that gap is the reread.

For the deep pharmacology of the mood stabilisers, low-dose antipsychotics and serotonin reuptake inhibitors that appear only as symptom-targeted adjuncts here see the Mood disorders: pharmacotherapy notes and the Schizophrenia: management, antipsychotics and adverse effects notes; for the bipolar-II side of the differential the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes; for the forensic implications of antisocial personality disorder the Mental health legislation and forensic psychiatry notes; for the complex-PTSD-versus-borderline boundary the Anxiety, OCD and trauma-related disorders notes; for the schizotypal-versus-schizophrenia boundary the Schizophrenia: aetiology, phenomenology, classification and course notes; and for the wider psychotherapy models and technique the Psychotherapies, clinical assessment, MSE and nosology notes.

Previously asked

This territory is examined at two levels at once: the disorder (its clinical features, its differential diagnosis, its aetiology and its course) and the treatment (which structured psychotherapy, the

integrated borderline plan, and the place of symptom-targeted medication). The reliable pattern is that borderline personality disorder carries far the most weight, asked at every length and from every angle, that the classification and the clinical assessment of personality recur as standalone notes and essays, and that a single therapy such as dialectical behaviour therapy or a single type such as avoidant personality disorder can be asked as a note in its own right. Every long essay ends in a management plan, so the rule that structured psychological therapy is primary and that a drug is not the first-line treatment for borderline personality disorder must be exam-ready. The genuine questions on record are grouped by band below. The deep pharmacology of the agents used in symptom-targeted treatment is developed in the Mood disorders: pharmacotherapy notes and the Schizophrenia: management, antipsychotics and adverse effects notes; the bipolar side of the differential in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes; the forensic frame of antisocial personality disorder in the Mental health legislation and forensic psychiatry notes; and the wider psychotherapy models in the Psychotherapies, clinical assessment, MSE and nosology notes, while dialectical behaviour therapy, schema therapy, mentalisation-based therapy and transference-focused psychotherapy are owned here.

HOW THIS TERRITORY IS ACTUALLY TESTED

- **Borderline personality disorder, the dominant essay and note.** This is by far the most heavily examined topic in the section. "Describe Kernberg's test of personality organisation. Discuss clinical features and management of Borderline Personality Disorder" and "Discuss aetiology and presentation of Borderline Personality Disorder" have both come as full 25-mark essays, while "Borderline personality disorder", "Borderline personality disorder, clinical features and differential diagnosis" and "Discuss clinical features and psychopharmacological management of Borderline Personality Disorder" recur as 10-mark notes across several sittings. Prepare borderline personality disorder end to end: the criteria and the threshold, the course and complications, the borderline-versus-bipolar-II differential, the Linehan biosocial and the schema-mode formulations, the integrated management plan, and the point that medication is symptom-targeted and adjunctive only. essay and short note, recurring

- **The classification and the clinical assessment of personality.** "Classification of Personality Disorders" has come as a 10-mark note and "Discuss the clinical assessment of personality" as a 25-mark essay, with the assessment of personality also examined on the psychology side. Prepare the general criteria that gate every diagnosis, the ICD-11 dimensional model against the DSM-5 categorical clusters and the alternative model, the categorical-versus-dimensional debate, and the structured instruments and interviews with the state-versus-trait caution. essay and short note, recurring

- **The approach to management and the named psychotherapies.** "Discuss approaches to personality disorders management" has come as a 25-mark essay and "Dialectical Behaviour Therapy (DBT)" as a standalone 10-mark note, and Kernberg's object-relations frame is drawn into the borderline essay. Prepare the guideline-anchored, structured-psychotherapy-first approach, dialectical behaviour therapy with its four skills modules and four modes, schema therapy on the modes framework, mentalisation-based and transference-focused psychotherapy, and the symptom-targeted pharmacotherapy with the not-first-line rule. essay and short note, recurring

- **The individual types as standalone notes.** "Avoidant personality disorder" has come as a 10-mark note, and any single type can be asked this way. Prepare each cluster A, B and C type by its one defining feature

and its discriminator from its neighbours, so a type can be written up cleanly on its own. **short note, recurring**

Prepare this material to be diagnosed and treated, not just recited: the general criteria and the classification shift, the borderline criteria and the borderline-versus-bipolar-II discriminator, the criterion-anchored good-to-remember boxes, the psychotherapy frameworks and the integrated borderline plan in these notes are built to the way the block is examined. The deep pharmacology of the mood stabilisers, low-dose antipsychotics and serotonin reuptake inhibitors used in symptom-targeted treatment lives in the Mood disorders: pharmacotherapy notes and the Schizophrenia: management, antipsychotics and adverse effects notes; the forensic frame of antisocial personality disorder in the Mental health legislation and forensic psychiatry notes; and the wider psychotherapy models in the Psychotherapies, clinical assessment, MSE and nosology notes.

Quick review

THE FRAMEWORK: THE GENERAL CRITERIA AND THE CLASSIFICATION SHIFT	
THE GATE BEFORE ANY TYPE	No type is named until the **general criteria** hold: an **enduring**, **pervasive** and **inflexible** pattern across cognition, affectivity, interpersonal functioning and impulse control, **deviating from cultural expectation**, with **onset by adolescence or early adulthood**, causing distress or impairment, and not better explained by another disorder.
ICD-11 (THE HEADLINE SHIFT)	ICD-11 **abolished the categorical types.** Rate **severity first** (personality difficulty, then mild, moderate, severe), then the **five trait domains** (negative affectivity, detachment, dissociality, disinhibition, anankastia) and the **borderline pattern** qualifier. Severity leads because it predicts outcome and need better than type.
DSM-5-TR (CATEGORICAL) AND THE ALTERNATIVE MODEL	Ten types in three clusters: **A** odd or eccentric, **B** dramatic or erratic, **C** anxious or fearful. Section III **alternative model** = the level-of-personality-functioning scale plus five pathological trait domains (negative affectivity, detachment, antagonism, disinhibition, psychoticism) and six retained types. **ICD-10 kept** the categorical types, which is why exams still test them.
CATEGORICAL VERSUS DIMENSIONAL	Categorical is familiar and communicable but gives excessive comorbidity, arbitrary thresholds and a large not-otherwise-specified group; dimensional has better validity and covers the subthreshold majority. The field moved dimensional (ICD-11 and the DSM-5 alternative model).
THE DISORDERS BY CLUSTER	
CLUSTER A (ODD OR ECCENTRIC)	**Paranoid** (pervasive distrust and suspiciousness), **schizoid** (detachment and restricted affect), **schizotypal** (cognitive and perceptual distortions and eccentricity). Schizotypal sits on the **schizophrenia spectrum** (ICD-11 6A22, outside the personality disorders); the discriminator from schizophrenia is that the signs are attenuated and never become sustained frank psychosis.
BORDERLINE (THE HIGHEST-YIELD TYPE)	Abandonment fears, unstable intense relationships, identity disturbance, impulsivity, recurrent self-harm and suicidality, affective instability, chronic emptiness, inappropriate anger, transient stress-related paranoia or dissociation: **five or more of the nine criteria**. Course trends to **symptomatic remission** over years; sustained functional recovery is harder.

THE DISORDERS BY CLUSTER	
ANTISOCIAL	Pervasive disregard for the rights of others (deceit, impulsivity, aggression, recklessness, irresponsibility, lack of remorse); requires **conduct disorder before age fifteen** and is diagnosed **from age eighteen**. **Psychopathy** (the affective-interpersonal core, PCL-R) is a narrower construct nested within it. The forensic frame is cross-referenced.
HISTRIONIC AND NARCISSISTIC	Histrionic: excessive emotionality and **attention-seeking**. Narcissistic: grandiosity, need for admiration, lack of empathy, split into **grandiose** (overt, entitled) and **vulnerable** (covert, shame-prone) presentations over a shared fragile self-esteem.
CLUSTER C (ANXIOUS OR FEARFUL)	**Avoidant** (social inhibition, feels inadequate, wants closeness but withdraws), **dependent** (needs to be taken care of, submissive, fears separation), **anankastic / obsessive-compulsive** (order, perfectionism, control). Anankastic is **ego-syntonic** traits with **no true obsessions or compulsions**, which is the line from OCD.
THE HIGH-YIELD DISCRIMINATORS	
BORDERLINE VERSUS BIPOLAR II	Borderline mood shifts are **rapid (minutes to hours) and reactive** to interpersonal triggers, with identity disturbance and chronic emptiness; bipolar II episodes are **sustained (days to weeks) and autonomous**, with a bipolar family history and a response to a mood stabiliser. The trap is calling reactive personality-based lability bipolar and starting a mood stabiliser.
COMPLEX PTSD VERSUS BORDERLINE	Complex PTSD carries the PTSD triad plus disturbances in self-organisation with a **stable** negative self-view and relationships of avoidance, after prolonged trauma; borderline shows unstable identity and frantic abandonment fears. Missing complex PTSD behind a personality-disorder label is the classic error.
ANANKASTIC PERSONALITY VERSUS OCD	Anankastic personality is the ego-syntonic character of perfectionism and control with no discrete obsessions or compulsions; OCD is ego-dystonic intrusive obsessions and resisted compulsions.
DO NOT DIAGNOSE IN AN ACUTE STATE	The pattern must be enduring and pervasive. Do not diagnose a personality disorder during an acute episode of another disorder (the state-versus-trait caution); use a structured instrument (IPDE, SCID-5-PD) and corroborating history.
THE TREATMENT BLOCK, THE GUIDELINE SPINE AND THE HARD RULES	
THE GUIDELINE ORDER	Guidelines-first on the where-to-treat, target-by-phase, modes-of-treatment spine: **NICE leads** (the borderline and the antisocial guidelines), then the **Indian Psychiatric Society** and **WFSBP**. Structured psychological therapy is primary throughout.

THE TREATMENT BLOCK, THE GUIDELINE SPINE AND THE HARD RULES	
THE PSYCHOTHERAPIES	**Dialectical behaviour therapy**: four skills modules (mindfulness, distress tolerance, emotion regulation, interpersonal effectiveness) across four modes (individual, skills group, phone coaching, consultation team). **Schema therapy**: work the modes (vulnerable child, angry child, detached protector, punitive parent, healthy adult) by limited reparenting. **Mentalisation-based therapy**: restore the mentalising stance. **Transference-focused psychotherapy**: integrate split object relations in the here-and-now transference.
PHARMACOTHERAPY (THE KEY RULE)	**No drug is first-line for borderline personality disorder** and none is licensed (NICE); no drug reduces total borderline severity (Cochrane). Medication is **symptom-targeted and adjunctive**: a low-dose antipsychotic for cognitive-perceptual and impulsive-behavioural dyscontrol, a mood stabiliser for impulsive aggression, an SSRI for the affective and anxiety domain, only for a comorbidity or a crisis. **Avoid benzodiazepines** and **avoid polypharmacy**; review and deprescribe.
THE INTEGRATED BORDERLINE PLAN	LOCUS: outpatient and community by default, admission avoided and brief. FOCUS: short-term safety and crisis, mid-term the core features via structured therapy, long-term function and remission. MODUS: structured psychotherapy primary, symptom-targeted time-limited medication only, multidisciplinary care planning and a crisis plan.
THE FIVE TRAPS	Diagnosing a type without the general criteria; calling reactive affective lability bipolar and starting a mood stabiliser; giving a drug first-line for borderline personality disorder; reading schizotypal as schizophrenia; and confusing ego-syntonic anankastic personality with ego-dystonic OCD.

References

The personality-disorder content is grounded in the standard psychiatry sources (the source hierarchy below), with Kaplan and Sadock and the New Oxford Textbook as the depth bar for the phenomenology, the classification and the course, the ICD-11 Clinical Descriptions and Diagnostic Requirements and the DSM-5-TR for the criteria and the two classification systems, and the primary psychotherapy literature for dialectical behaviour therapy, schema therapy, mentalisation-based therapy and transference-focused psychotherapy. The management is guideline-first, led by NICE (the borderline and the antisocial guidelines), with the Indian Psychiatric Society, WFSBP and the American Psychiatric Association. Every criterion, trait domain, cluster mapping, severity anchor and guideline rule was checked against these sources and the adversarial content pass; anything that could not be confirmed was omitted and flagged rather than guessed, so several prevalence and effect-size figures are stated by direction rather than by a specific number. Each journal PMID below was verified against PubMed this build and

matched on title, first author and year. Books, manuals and guideline documents are cited by author, title and year without a PMID.

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PART X

X

Eating and Sleep-Wake Disorders

Disordered eating and disordered sleep: the eating disorders and the sleep-wake disorders in full.

01 Eating disorders

02 Sleep-wake disorders

03 Apply and consolidate

PAPER II

Eating and sleep-wake disorders

Two sections . one complete notes document

This material gathers the eating disorders and the sleep-wake disorders into one document, by syndrome and by treatment. The first band is **the eating disorders**: anorexia nervosa and its medical complications, the refeeding syndrome that endangers recovery, the guideline-anchored management, bulimia nervosa and binge eating disorder, avoidant/restrictive food intake disorder, the aetiology and neurobiology, the feeding disorders, and the atypical and non-fat-phobic presentations. The second band is **the sleep-wake disorders**: normal sleep physiology and architecture as the foundation, insomnia and the first-line place of cognitive behaviour therapy for insomnia, narcolepsy and its tetrad, obstructive sleep apnoea, the NREM and REM parasomnias including REM sleep behaviour disorder, the circadian rhythm disorders, and restless legs. The examinable skill is the safe, guideline-anchored diagnosis and treatment of each disorder: which eating disorder behind which weight and behaviour, how to refeed without killing the patient, which drug is licensed for which eating disorder, how a normal night is built, why CBT-I comes before a hypnotic, and how to recognise narcolepsy, sleep apnoea and REM sleep behaviour disorder behind their common disguises.

HOW TO USE THESE NOTES

Read the two bands as one continuous account of how the eating and the sleep-wake disorders are diagnosed and treated. The **eating disorders** band builds the frame: the individual disorders discriminated one from another, the medical complications of starvation, the refeeding syndrome and how to prevent it, and the guideline-anchored management (no drug is first-line for anorexia; cognitive behaviour therapy for eating disorders and family-based treatment carry the weight; fluoxetine is the licensed drug for bulimia). The **sleep-wake disorders** band opens with normal sleep physiology and the hypnogram as the foundation, then teaches insomnia and the first-line place of cognitive behaviour therapy for insomnia, narcolepsy and its orexin loss, obstructive sleep apnoea, the parasomnias including REM sleep behaviour disorder as a prodrome of a synucleinopathy, and the circadian disorders. Every management recommendation is guideline-anchored, led by NICE and MARSIPAN in the eating half and by the BAP guidelines with the Indian Psychiatric Society, NICE and the sleep-medicine consensus in the sleep half, on the where-to-treat, target-by-phase, modes-of-treatment spine; every named syndrome ends with a **Good to remember** box giving the criterion, the discriminator and the first step, and every named management step ends with one giving the principle and the one value or first-line to hold. Figures declare one axis and code it in colour: **petrol** marks structure and the neutral case, **coral** marks the trap or the danger, and **marigold** highlights the number to hold; the rating scales are reproduced as the actual instruments where the licence permits, credited to their sources, or typeset from their structure where it does not. Several boundaries are stated up front: the deep hypnotic pharmacology (melatonin, ramelteon, the dual orexin receptor antagonists, the z-drugs and the benzodiazepines) is taught in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes and cross-referenced here; the deep antidepressant pharmacology in the Mood disorders: pharmacotherapy notes; the sleep neurochemistry and the ascending-arousal anatomy in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and the Functional Neuroanatomy and Neurophysiology notes; the anorexia neuroendocrine axes in the Neurochemistry notes; and the wider cognitive behaviour therapy technique in the Psychotherapies, clinical assessment, MSE and nosology notes. Cognitive behaviour therapy for insomnia, the eating-disorder cognitive behaviour therapy and family-based treatment, and the sleep architecture, the hypnogram and polysomnography are owned and fully taught here. This is doctor-facing revision, so the full technical vocabulary is used, brand names lead with the Indian brand, and every refeeding value, drug dose and scale cut-off is verified against a source or omitted and flagged.

Eating disorders

1 · Anorexia nervosa

The disorder to know cold. **Anorexia nervosa** is the eating disorder of self-imposed starvation: a **restriction of energy intake** that drives the body to a **significantly low weight**, held there by an **intense fear of weight gain** (or a persistent behaviour that blocks it) and a **disturbance in how body weight and shape are experienced**. It carries the highest mortality of any psychiatric illness, so the examiner treats it as a safety topic as much as a phenomenology one. This note owns the diagnosis: the three core features, the ICD-11 and DSM-5-TR criteria and the

amenorrhoea criterion that DSM-5 dropped, the **restricting subtype** and **binge-purge subtype**, the epidemiology and course, and the **medical complications** mapped body system by body system.

The chapter's master mnemonic for the starvation complications, **STARVED**, is seeded here and paid off at consolidation. The neuroendocrine axes that fail in anorexia (the hypothalamic-pituitary-gonadal, thyroid and adrenal changes) are derived in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and are given here only in applied clinical form. The dangerous physiology of re-nourishing a starved patient sits in the refeeding-syndrome topic in these notes, and the guideline-anchored treatment in the anorexia-management account here; what follows is how to recognise and stage the disorder and read its body. First described clinically by Sir William Gull and Charles Lasègue in the 1870s, its most quoted teaching point is that *the fear need not be spoken to be present*.

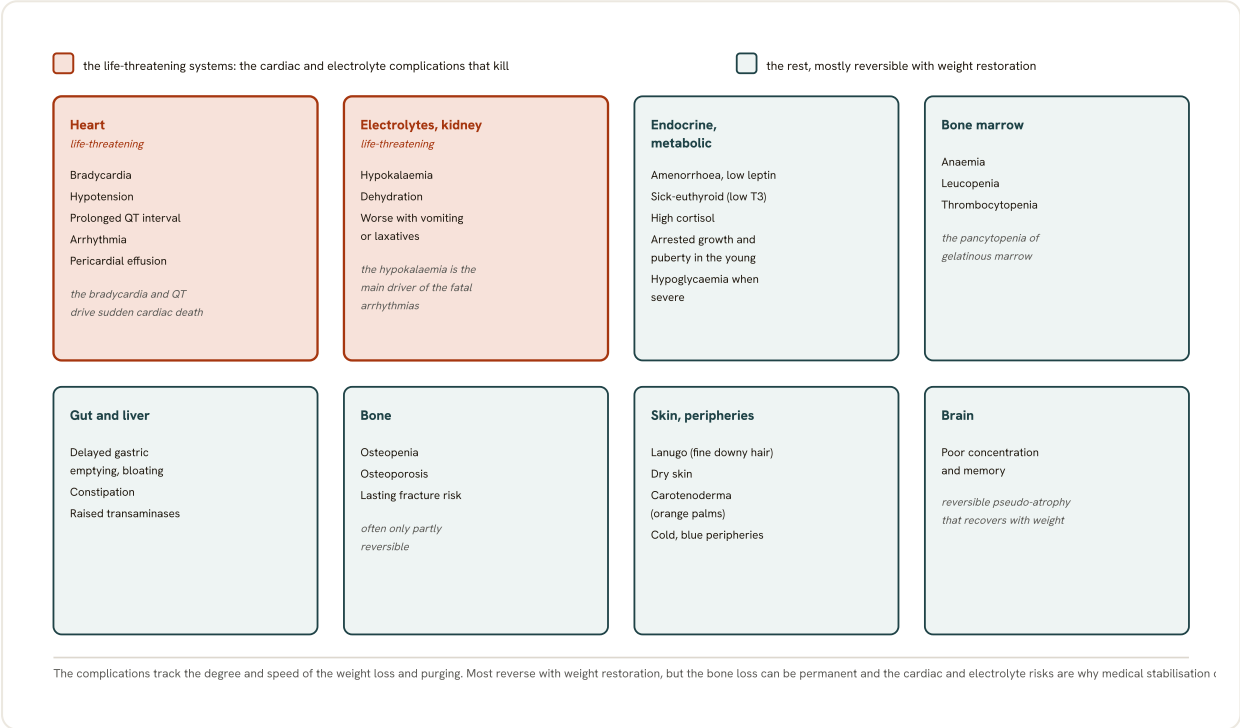


Fig 17.1 The medical complications of anorexia nervosa by body system. Starvation touches every organ. The cardiac and electrolyte complications (coral) are the ones that kill: bradycardia, hypotension, a prolonged QT interval and arrhythmia, and the hypokalaemia and dehydration made worse by vomiting or laxative misuse. The endocrine picture is the low-oestrogen amenorrhoea, a low-leptin and sick-euthyroid state with a raised cortisol, and, in a young patient, arrested growth and puberty; the marrow shows a pancytopenia; the gut is slow, with delayed emptying and constipation; the bone loses density with a fracture risk that may not fully recover; and the skin grows fine lanugo hair with carotenoderma and cold peripheries. Most reverse with weight restoration, but the bone loss can be permanent and the cardiac and electrolyte risks are why medical stabilisation, not psychotherapy, comes first.

SCOFF, THE 5-ITEM SCREEN (REPRODUCED)	SCORE ONE POINT FOR EACH "YES"
S ick	Do you make yourself **Sick** because you feel uncomfortably full?
C ontrol	Do you worry you have lost **Control** over how much you eat?
O ne stone	Have you recently lost more than **One** stone (about 6.35 kg) in a three-month period?
F at	Do you believe yourself to be **Fat** when others say you are too thin?
F ood	Would you say that **Food** dominates your life?
Cut-off	**Two or more "yes" answers is a positive screen for a probable eating disorder and prompts a full assessment**

SCOFF: reproduced from Morgan JF, Reid F, Lacey JH. The SCOFF questionnaire. BMJ. 1999;319:1467-1468. A freely used screening tool; for the free, non-commercial resident edition only.

EAT-26 (TYPESET STRUCTURE)	WHAT TO HOLD
Instrument	The Eating Attitudes Test, a 26-item self-report screen of eating attitudes and behaviours (Garner et al., 1982), across three subscales: dieting, bulimia and food preoccupation, and oral control
Cut-off	**A total score of 20 or more indicates a need for a full assessment; it is a screen, not a diagnosis**

EAT-26: structure and cut-off typeset (Garner DM, Olmsted MP, Bohr Y, Garfinkel PE. Psychol Med. 1982;12:871-878); free for non-commercial use with acknowledgement. For the free, non-commercial resident edition only.

Fig 17.2 The eating-disorder screening scales. SCOFF is a five-item screen whose name is its mnemonic (Sick, Control, One stone, Fat, Food); two or more positive answers is a positive screen and prompts a full assessment. The EAT-26 is a longer 26-item self-report across dieting, bulimia and food preoccupation, and oral control subscales, with a total of 20 or more flagging the need for assessment. Both are screens, not diagnoses: a positive screen leads to a clinical interview against the ICD-11 or DSM-5-TR criteria, and in India a non-fat-phobic presentation can screen negative on the shape-and-weight items yet still be anorexia, so a negative screen does not exclude an eating disorder.

1.1 The three core features

One engine, three faces. Every framework builds anorexia nervosa from the same triad. First, a persistent *restriction of energy intake* relative to requirements that produces a body weight below what is minimally normal for age, sex, developmental trajectory and physical health (in a growing child, this may be a failure to make expected weight gain rather than frank loss). Second, an *intense fear of becoming fat* or a persistent behaviour that interferes with weight gain, present even as the weight falls. Third, a *disturbance in the experience of weight or shape*: undue influence of shape on self-evaluation, or a persistent failure to recognise the medical seriousness of the low weight.

Restriction is the non-negotiable one. The fear and the body-image distortion can be inferred from behaviour; the significantly low weight driven by restriction cannot be worked around. This is why a patient who denies any wish to be thin but relentlessly starves still meets the diagnosis.

GOOD TO REMEMBER

- **Anorexia nervosa (the syndrome):** three essential features, (1) restriction of intake leading to a significantly low weight, (2) intense fear of weight gain *or* persistent behaviour that interferes with weight gain, and (3) disturbed experience of weight/shape or non-recognition of the danger; the defining criterion is the low body weight from restriction, and the fear does not have to be verbalised.

1.2 DSM-5-TR criteria and the severity bands

The three criteria to state. DSM-5-TR criterion A is restriction of energy intake leading to a significantly low body weight in the context of age, sex, developmental trajectory and physical health; B is intense fear of gaining weight or of becoming fat, or persistent behaviour that interferes with weight gain, even at a significantly low weight; and C is a disturbance in the way weight or shape is experienced, undue influence of weight/shape on self-evaluation, or persistent lack of recognition of the seriousness of the low weight (DSM-5-TR 2022). DSM-5 deliberately removed the old numeric anchor (the DSM-IV example of "85% of ideal body weight") so that no single figure is read as the definition.

Severity is scored on current BMI. For adults the severity is graded from the current body mass index, and this is the number set examiners like. The severity may be stepped up for clinical symptoms, functional disability or the need for supervision.

DSM-5-TR SEVERITY (ADULT)	BMI (KG PER M SQUARED)
Mild	≥ 17
Moderate	16 to 16.99
Severe	**15 to 15.99**
Extreme	**< 15**

DSM-5-TR severity grading for anorexia nervosa from current adult BMI (WHO thinness categories); for children and adolescents the corresponding BMI-for-age percentiles are used (DSM-5-TR 2022).

RULE **Significantly low weight from restriction is the anchor.** Diagnosis turns on a restriction-driven, significantly low body weight; the fear of fatness can be shown by persistent weight-defeating behaviour and need not be voiced, and there is no single BMI that defines "low" in either system.

1.3 ICD-11 criteria and the underweight specifiers

Where ICD-11 puts a number on it. ICD-11 requires a significantly low body weight for the individual's height, age and developmental stage, with a commonly used adult threshold of BMI below **18.5 kg per m squared** (or below the 5th percentile for age in children). A distinctive ICD-11 provision: *rapid weight loss of more than **20% of total body weight within 6 months*** can substitute for the low-weight requirement when the other features are met. The presentation

must be a persistent pattern of restrictive eating (or purging or over-exercise) aimed at abnormally low weight, not better explained by another condition or by lack of food (ICD-11 CDDR).

The two underweight grades. ICD-11 stages the danger directly: *anorexia nervosa with significantly low body weight* (BMI 18.5 down to 14.0) and *anorexia nervosa with dangerously low body weight* (BMI below 14.0), the latter flagging the high-complication, high-mortality patient. Fear of weight gain is explicitly *not* an absolute requirement in ICD-11.

FRAMEWORK	WEIGHT THRESHOLD TO DIAGNOSE (BMI IN KG PER M SQUARED)	GRADING OF SEVERITY
DSM-5-TR	No fixed cut-off; adult BMI under 17.0 usually "low", 17.0 to 18.5 possible on clinical grounds	Mild ≥ 17 / Moderate 16 to 16.99 / Severe 15 to 15.99 / Extreme < 15
ICD-11	**Commonly < 18.5, *or* rapid loss > 20% of body weight within 6 months**	Significantly low (18.5 to 14.0); dangerously low (< 14.0)
ICD-10 (historical)	BMI < 17.5 *plus* amenorrhoea in women	Self-induced weight loss with a "dread of fatness"

The weight thresholds compared; the number to quote is ICD-11's BMI under 18.5 (or a greater-than-20% loss in 6 months), against DSM-5-TR's deliberately non-numeric definition.

1.4 The amenorrhoea criterion, dropped in DSM-5

A favourite discriminator. DSM-IV required *amenorrhoea* (absence of at least three consecutive menstrual cycles) as a criterion for anorexia nervosa. DSM-5 removed it, because women who met every other criterion but continued to menstruate did not differ in course, prognosis or severity, and because the criterion could not apply to men, pre-menarcheal girls, post-menopausal women or those on oral contraception (Kaplan and Sadock 2024). ICD-10's F50.0 likewise leaned on a widespread endocrine disorder manifesting as amenorrhoea; ICD-11 has moved the same way, folding amenorrhoea in as a clinical *feature* and consequence of starvation rather than a required criterion.

The take-home. Amenorrhoea is no longer needed to diagnose anorexia nervosa in either modern system, but it remains one of the most reliable clinical *signs* of the hypothalamic-pituitary-gonadal suppression that starvation produces, so it stays in the complications, not the criteria.

GOOD TO REMEMBER

- **Amenorrhoea criterion:** a DSM-IV requirement that DSM-5 abolished (and ICD-11 does not require); it discriminated poorly, excluded men and non-menstruating women, and is now treated as a clinical sign of hypothalamic-pituitary-gonadal suppression rather than a diagnostic criterion.

1.5 The subtypes: restricting versus binge-purge

Defined by the last three months. The restricting subtype (DSM: restricting type) describes weight loss achieved through dieting, fasting or excessive exercise, with *no* recurrent binge-eating

or purging in the last three months. The binge-purge subtype (DSM: binge-eating/purging type) applies when, over the same recent window, the person has engaged in recurrent binge-eating or purging (self-induced vomiting, or misuse of laxatives, diuretics or enemas); some in this group do not binge but regularly purge after small amounts of food. ICD-11 uses the parallel "restricting pattern" and "binge-purge pattern" specifiers.

Crossover is common. Movement between the subtypes over the illness course is frequent, so the label describes *current* symptoms, not the lifetime picture. Clinically it matters because the binge-purge subtype carries more electrolyte derangement and cardiac risk, and it is the group whose bloods most often reveal **hypokalaemia** and metabolic alkalosis.

GOOD TO REMEMBER

- **Restricting subtype:** low weight by dieting, fasting or over-exercise with no binge-eating or purging in the last three months; the classic "pure restrictor".
- **Binge-purge subtype:** recurrent binge-eating or purging (vomiting, laxatives, diuretics, enemas) in the last three months, at a still significantly low weight; carries the higher electrolyte and cardiac risk, and crossover between subtypes is common.

1.6 Epidemiology, onset and course

The numbers. Lifetime prevalence of DSM-5 anorexia nervosa is roughly **1.4% in women** and **0.2% in men**, with a female-to-male ratio near **10 to 1**, though the male share is under-recognised (men present with a drive for muscularity and leanness and may be missed) (Kaplan and Sadock 2024). Point prevalence in girls and women is about 0.5% to 1%, and incidence is rising fastest in the high-risk **15 to 19**-year-old female band. Onset is typically adolescence or early adulthood (ages 10 to 24), often after a stressor and a diet that "works" and becomes self-reinforcing.

Course and lethality. On follow-up, roughly **30% to 50%** achieve full recovery, **10% to 20%** remain chronically ill, and the rest improve but retain some disordered behaviour. The mortality is the headline: individuals are up to **six times** more likely to die than the general population, most deaths from the medical consequences of starvation and about **one in five** from suicide. Shorter illness duration and full weight restoration predict better outcome, which is the whole argument for early detection.

PEARL

Anorexia nervosa has the highest mortality rate of any psychiatric disorder. Hold two numbers: a roughly six-fold excess mortality, and about one death in five by suicide rather than by starvation. This is why "she is just dieting" is never a safe formulation, and why weight, orthostatic vitals, potassium and the ECG QTc are checked at every review.

1.7 Medical complications, mapped by body system

Starvation writes on every organ. The **medical complications** follow from starvation, from the weight-control methods (vomiting, laxatives, over-exercise), and, dangerously, from re-nourishment. The figure alongside maps them onto the body; the table below is the system-by-

system checklist. Two of them are the ones that kill and must be sought at every visit: a prolonged QTc on the ECG and marked **hypokalaemia**.

SYSTEM	SIGNS AND ABNORMALITIES	MECHANISM / NOTE
Cardiovascular	**Bradycardia, hypotension, orthostasis, prolonged QTc, arrhythmia, peripheral oedema**	Commonest fatal pathway; QTc prolongation may occur even without electrolyte derangement
Endocrine / reproductive	Amenorrhoea, low LH/FSH and oestrogen or testosterone, sick-euthyroid pattern, hypercortisolaemia, low leptin	Energy-conserving; most reverse with refeeding
Skeletal / bone	Osteopenia and osteoporosis, fracture risk	Low oestrogen, high cortisol and malnutrition; bone may not fully recover
Haematological	Pancytopenia (leukopenia, anaemia, thrombocytopenia)	Gelatinous marrow transformation of starvation
Renal / electrolyte	**Hypokalaemia, hyponatraemia, hypochloraemia, metabolic alkalosis, dehydration**	Worse in the binge-purge subtype; hypokalaemia is the dangerous one
Gastrointestinal	Delayed gastric emptying, constipation, raised liver enzymes	Hypomotility of starvation
Dermatological	Lanugo, dry skin, hair thinning, carotenaemia (yellow skin)	Visible signs of the starved state
Refeeding (metabolic)	**Hypophosphataemia, hypomagnesaemia, thiamine deficiency, glucose intolerance**	The refeeding-syndrome cluster; detailed in the refeeding-syndrome topic in these notes

Medical complications of anorexia nervosa by body system; the two urgent findings are a prolonged QTc and marked hypokalaemia, and the refeeding cluster is led by hypophosphataemia (Kaplan and Sadock 2024).

MNEMONIC

STARVED

The chapter's master complication mnemonic, seeded here and paid off at consolidation. **S**kin (lanugo, dry skin, carotenaemia); **T**hyroid sick-euthyroid pattern and low Temperature (hypothermia); **A**menorrhoea and the hypothalamic-pituitary-gonadal or leptin axis; **R**ate and rhythm (bradycardia, hypotension, prolonged QTc, arrhythmia); **V**alues, the electrolytes (hypokalaemia, hyponatraemia, dehydration); **E**rythron and marrow (pancytopenia); **D**igestive and Density (delayed gastric emptying and constipation, plus low bone mineral density).

1.8 The neuroendocrine picture, in applied form

Every axis is set to conserve energy. The full endocrinology lives in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the clinical residues are these. The hypothalamic-pituitary-gonadal axis is virtually always suppressed, low LH, FSH and oestrogen or testosterone, mediated in part by low serum leptin that tracks the loss of fat

mass, giving the amenorrhoea and loss of libido. The thyroid shows a euthyroid sick syndrome (low total T3 and T4 with low or normal TSH and a raised reverse T3), an adaptive down-shift, not primary thyroid disease. The adrenal axis runs high, with hypercortisolaemia.

Two safety points. First, the sick-euthyroid pattern is *not* treated with thyroxine; it corrects with refeeding, and thyroxine would only accelerate weight loss and cardiac risk. Second, the low oestrogen plus high cortisol plus malnutrition drives the osteoporosis, which unlike the other endocrine changes may not fully reverse, and oral oestrogen or calcium alone does not restore bone density while the patient stays underweight.

COMMON TRAP

Do not read the low thyroid hormones as hypothyroidism and start thyroxine, and do not be reassured by "normal" bloods. Laboratory results are frequently normal even in a seriously ill, low-weight patient, so a normal panel never excludes danger. The sick-euthyroid pattern reverses with feeding; giving thyroxine only worsens weight loss and the cardiac risk.

1.9 The refeeding flag and the hypophosphataemia hallmark

The paradox of getting better. The most dangerous moment can be the start of re-nourishment. Refeeding syndrome is the shift of fluid, electrolytes and minerals that occurs when a severely malnourished patient is fed too quickly: insulin surges as carbohydrate returns, pushing phosphate, potassium and magnesium into cells. Its hallmark is hypophosphataemia, and it can precipitate cardiac failure, arrhythmia and death. The preventive discipline is a single phrase: correct the electrolytes, give thiamine, and start slow, monitoring closely through the opening days.

Why it is flagged here. The exact starting-calorie ranges, the phosphate, potassium and magnesium thresholds and the monitoring schedule are worked out in the refeeding-syndrome topic in these notes; the point for the anorexia diagnosis is simply to name refeeding syndrome as the risk that a low-BMI patient carries into treatment, with hypophosphataemia as the signature.

TRAP **Refeeding too fast, and missing the phosphate.** The classic lethal error is to correct starvation rapidly; the falling phosphate of refeeding syndrome is the thing to pre-empt, so electrolytes are corrected and thiamine given *before* calories are pushed, and phosphate is watched daily through the first several days of feeding.

1.10 Screening: the SCOFF and the EAT-26

The five-question bedside screen. The SCOFF is a five-item verbal screen for anorexia and bulimia that takes about two minutes: *S*ick (making yourself vomit when uncomfortably full), *C*ontrol (lost control over eating), *O*ne stone (lost more than one stone, about 6.35 kg, in three months), *F*at (believe yourself fat when others say too thin), and *F*ood (food dominates life). Each "yes" scores one, and a total of **two or more** is a positive screen warranting fuller assessment, with a reported sensitivity around 84.6% and specificity around 89.6% in general-practice women (Luck et al. 2002); the original specialist-clinic study (Morgan, Reid and Lacey 1999)

reported a 100% sensitivity for anorexia and bulimia. The instrument itself is reproduced on the accompanying scale plate.

The self-report questionnaire. The EAT-26 (Eating Attitudes Test) is a 26-item self-report of eating attitudes and behaviours; a total score of **20 or more** is the conventional threshold prompting referral for clinical evaluation (Garner 1982). The EDE and its questionnaire form (EDE-Q) are the fuller research-standard interview and questionnaire but give dimensional scores rather than a single screening cut-off. All are aids to case-finding, not diagnoses in themselves.

INSTRUMENT	FORM	POSITIVE THRESHOLD
SCOFF	5-item verbal screen (Sick, Control, One stone, Fat, Food)	**≥ 2 "yes" answers**
EAT-26 (Eating Attitudes Test)	26-item self-report questionnaire	**Total ≥ 20 warrants assessment**
EDE-Q / EDE	Questionnaire / semi-structured interview	Dimensional; no single cut-off (reference standard)

The eating-disorder screens and their verified thresholds; SCOFF two-or-more is the number to hold, and the actual forms sit on the accompanying scale plate.

GOOD TO REMEMBER

- **SCOFF:** five verbal questions, one point each, a score of two or more is a positive screen for a probable eating disorder (sensitivity around 84.6%, specificity around 89.6%); it screens, it does not diagnose.
- **EAT-26:** a 26-item self-report; a total of 20 or more warrants clinical evaluation; a screening/severity aid, not a diagnostic instrument.

2 SCOFF POSITIVE CUT-OFF (YES ANSWERS)	**15** SEVERE ANOREXIA THRESHOLD (ADULT BMI, KG PER M SQUARED)	**1.4%** LIFETIME PREVALENCE IN WOMEN (0.2% IN MEN)	**6×** EXCESS MORTALITY VS GENERAL POPULATION

1.11 The India lens: non-fat-phobic anorexia and under-recognition

The fat phobia may be absent. A genuinely Indian and pan-Asian point: the explicitly stated fear of becoming fat is *relatively more often absent* in Asian populations, where the person rationalises the restriction as gastrointestinal discomfort, loss of appetite, or a culturally sanctioned religious fast rather than a wish to be thin, the "non-fat-phobic" presentation (DSM-5-TR 2022; ICD-11 CDDR). Both modern systems accommodate this precisely because Criterion B accepts persistent weight-defeating *behaviour* in place of a voiced fear. The transcultural framing is developed in the Consultation-liaison, geriatric and transcultural psychiatry notes; the applied lesson is to not withhold the diagnosis just because the patient never says "I want to be thin".

Under-recognition is the other reality. Eating disorders are under-detected in India, dismissed as ordinary dieting or as a physical complaint, and are still misread as a disease only of affluent urban young women; they occur across socioeconomic strata and in men. The clinical antidote is a low threshold to screen (the SCOFF at the bedside) and to weigh, take orthostatic vitals, and check potassium and the ECG in any young person with unexplained weight loss.

INDIA

Two things travel differently here. First, **non-fat-phobic anorexia** is relatively more common in Indian and other Asian patients, who attribute the restriction to abdominal discomfort, poor appetite or a religious fast; the diagnosis still stands on behaviour and a significantly low weight, so do not dismiss it for want of a stated fear of fatness. Second, eating disorders are widely under-recognised and stereotyped as an affluent-urban-female problem, missing men and lower-income patients; screen early with the SCOFF and always attach a weight, orthostatic vitals, a potassium and an ECG QTc.

WORKED EXAMPLE

A 17-year-old girl is brought by her mother for amenorrhoea and fainting. She is emaciated with fine downy **lanugo** on the back and forearms, cold peripheries, a pulse of 44 and lying-to-standing blood-pressure drop; BMI is 15.4. She denies wanting to be thin but eats tiny measured portions and exercises for hours. Bloods show potassium 3.0 and the ECG QTc is prolonged. This is anorexia nervosa, restricting subtype (no binge-purge), DSM-5-TR severe by BMI, ICD-11 with significantly low body weight; the **bradycardia**, **hypokalaemia** and QTc make her a medical-admission and refeeding-risk patient, and the absent stated fear does not exclude the diagnosis.

HOLD THIS

Anorexia nervosa is restriction-driven, significantly low body weight plus a fear of fatness (or behaviour that blocks weight gain) plus disturbed body-image or non-recognition of the danger; DSM-5-TR grades severity by BMI (severe 15 to 15.99, extreme under 15) and dropped the amenorrhoea criterion, ICD-11 uses BMI under 18.5 with significantly-low versus dangerously-low (under 14) grades; it kills more than any other psychiatric illness (six-fold, one in five by suicide), the SCOFF is positive at two, and the urgent complications are the prolonged QTc, hypokalaemia and refeeding hypophosphataemia.

2 · Refeeding syndrome

Refeeding syndrome is the group of potentially fatal fluid and electrolyte shifts that follow the reintroduction of nutrition, especially carbohydrate, into a severely malnourished body. It is the sharpest paradox in eating-disorder medicine: the patient who is sickest from starvation is the one most endangered by the treatment for it, so the danger arrives not from the illness but from feeding it back too fast. Because the psychiatrist is often the physician who admits and refeeds the profoundly underweight patient with anorexia nervosa, this is examinable as a hands-on emergency, not a footnote.

Why it matters, and how this note is framed. Two facts carry the topic. First, the biochemical hallmark is **hypophosphataemia**, a falling serum **phosphate** in the opening days of feeding, accompanied by falls in potassium and magnesium and by fluid and sodium retention. Second, the whole of prevention reduces to three moves: correct the electrolytes first, give **thiamine** before or with the first feed, and start the calories low and climb slowly. This is a management topic, so it is built from the verified guideline rows for cautious refeeding and the medical

stabilisation of anorexia; every rate and schedule below is drawn from that verified base, and any exact numeric threshold the parsed library could not confirm is flagged rather than invented.

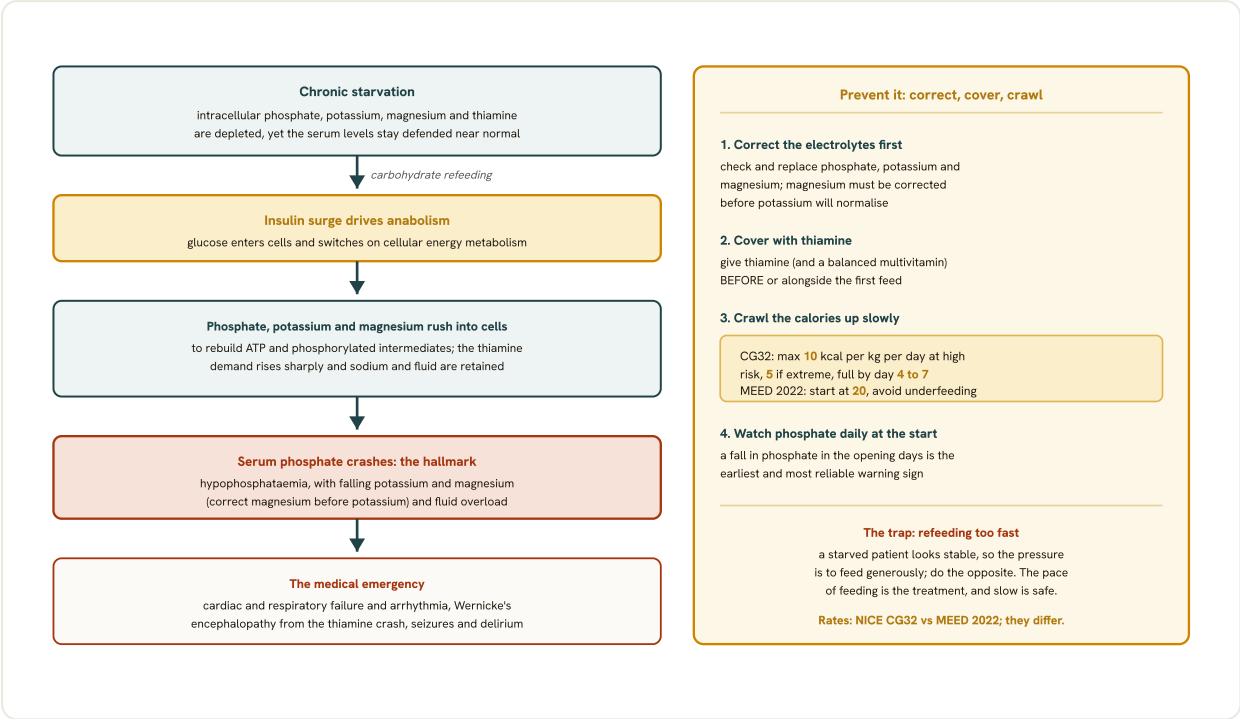


Fig 17.3 Refeeding syndrome. Starvation depletes the intracellular stores of phosphate, potassium, magnesium and thiamine while the serum levels stay defended near normal, so a routine blood test before feeding can look reassuring. When carbohydrate is reintroduced, the insulin surge switches anabolism back on and drives phosphate, potassium and magnesium into the cells to rebuild ATP, while the thiamine demand rises and sodium and fluid are retained. The serum pools then crash: the fall in phosphate is the hallmark and is what makes the syndrome lethal, and it is accompanied by hypokalaemia, hypomagnesaemia and fluid overload, producing cardiac and respiratory failure, arrhythmia, Wernicke's encephalopathy and seizures. Prevention is three moves: correct the electrolytes first (magnesium before potassium), cover with thiamine before the first feed, and crawl the calories up. The two numeric sources disagree and NICE NG69 sets no rate: NICE CG32 recommendation 1.4.8 caps the high-risk start at a maximum of 10 kcal per kg per day, uses only 5 at extreme risk with a body mass index under 14, and reaches full needs within 4 to 7 days, whereas RCPsych MEED CR233 (2022) starts at 20 kcal per kg per day, never below the immediate pre-admission intake, and warns against underfeeding. Quote whichever source the question names, and watch the phosphate daily. The pace of feeding is the treatment.

2.1 What refeeding syndrome is, and the deceptive normal serum level

The definition. Refeeding syndrome refers to the dangerous electrolyte and fluid shifts that occur when severely malnourished patients are refed too quickly; the clinical signature is fluid retention together with falling levels of phosphorus, magnesium and, less specifically, calcium (First Aid for Psychiatry). It is precipitated by the reintroduction of feeding, whether oral, enteral or parenteral, and the carbohydrate component is the main trigger.

The trap of the near-normal baseline. The catch that examiners love is that in the starved state the serum levels of phosphate, potassium and magnesium can sit near normal even though the intracellular and total-body stores are severely depleted, so a reassuring admission panel does not exclude risk. The fall only unmasks itself once feeding begins and the ions are driven out of the serum into the cells. The lesson is that risk is assessed from the degree of starvation and the feeding plan, not from a single normal set of electrolytes at presentation.

2.2 Pathophysiology: starvation depletion, then the insulin surge on carbohydrate

The starved state. Prolonged undernutrition switches the body to fat and protein catabolism, insulin secretion falls, and intracellular **phosphate**, potassium, magnesium and thiamine are steadily depleted while, as above, serum concentrations are defended and stay near-normal. The cell is running on empty even though the blood test looks acceptable.

The refeeding switch. When carbohydrate is reintroduced, blood glucose rises and insulin surges. Insulin drives glucose, and with it phosphate, potassium and magnesium, rapidly into the cells to rebuild ATP, phosphorylated intermediates and 2,3-diphosphoglycerate, so the already-depleted serum pools collapse. The same carbohydrate load sharply raises the demand for **thiamine**, an essential cofactor for glucose metabolism whose requirement rises with carbohydrate intake (KDT), and can outstrip depleted stores. Insulin also promotes renal sodium and water retention, expanding the extracellular volume. The mechanism is drawn together in the accompanying figure. This starvation-to-refeeding neuroendocrine backdrop, the wider hypothalamic-pituitary-gonadal, thyroid and adrenal changes of anorexia, is developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

MECHANISM IN ONE LINE

Starvation empties the intracellular stores while serum stays near-normal; carbohydrate refeeding triggers an insulin surge that pulls phosphate, potassium and magnesium into the cells and raises thiamine demand, so the serum pools crash and fluid is retained.

2.3 The hallmark: hypophosphataemia

Why phosphate is the marker. The defining biochemical abnormality of **refeeding syndrome** is hypophosphataemia. Phosphate is consumed on a large scale the moment anabolism restarts, because it is needed for ATP, for the phosphorylation of glucose entering the cell, and for 2,3-diphosphoglycerate in red cells; the newly insulin-stimulated cells strip it out of the serum faster than a depleted body can replace it. A falling serum phosphate in the first days of feeding is therefore the earliest and most reliable warning that refeeding syndrome is developing.

What low phosphate does. Because phosphate underpins cellular energy, severe hypophosphataemia is what makes the syndrome lethal: it impairs cardiac and respiratory muscle, red and white cell function and neuronal membranes, and is the proximate driver of the cardiac failure, arrhythmia and respiratory failure below. Serum phosphate is the single number watched most closely once feeding starts.

GOOD TO REMEMBER

- **Refeeding syndrome (defining criterion):** a fatal cluster of fluid and electrolyte shifts triggered by reintroducing nutrition (chiefly carbohydrate) into a severely malnourished patient; the defining biochemical criterion is *hypophosphataemia*, a falling serum phosphate in the opening days of feeding, alongside hypokalaemia, hypomagnesaemia and fluid/sodium retention; the discriminator from the starved baseline is that serum ions are near-normal until feeding drives them intracellularly.

2.4 The other shifts: hypokalaemia, hypomagnesaemia, and fluid and sodium retention

The two accompanying electrolyte falls. Insulin drives potassium into cells through the sodium-potassium pump, producing hypokalaemia, and shifts magnesium intracellularly, producing hypomagnesaemia. Both develop transiently during the early phases of refeeding even when the presenting electrolytes were normal (Tasman Psychiatry). Hypomagnesaemia matters doubly, because a low magnesium blocks the correction of potassium and prolongs the hypokalaemia, so the magnesium must be replaced for the potassium to normalise.

Fluid and sodium retention. The carbohydrate-driven insulin surge causes the kidney to retain sodium and water, expanding extracellular volume. In a heart already weakened by starvation, with reduced cardiac mass, this fluid load can precipitate peripheral oedema and, when refeeding is too rapid, congestive cardiac failure (Tasman Psychiatry). The salt-and-water retention is therefore not a benign cosmetic swelling but part of the cardiac danger.

ION OR COMPARTMENT	DIRECTION IN REFEEDING	MECHANISM AND CONSEQUENCE
Phosphate	**Falls, hypophosphataemia (the hallmark)**	Insulin drives it into cells for ATP, glucose phosphorylation, 2,3-DPG; drives cardiac, respiratory and neuronal failure
Potassium	Falls, hypokalaemia	Insulin-driven intracellular shift via the sodium-potassium pump; arrhythmia risk
Magnesium	Falls, hypomagnesaemia	**Intracellular shift; a low magnesium blocks correction of potassium**
Sodium and water	Retained	Carbohydrate/insulin-driven renal retention; oedema and volume overload, cardiac failure
Thiamine	Demand rises, stores deplete	**Cofactor for carbohydrate metabolism; deficiency risks Wernicke's encephalopathy**

The refeeding electrolyte and fluid shifts; the load-bearing points are hypophosphataemia as the hallmark and the rule that magnesium must be corrected before potassium will normalise.

2.5 The clinical consequences: cardiac, neurological, respiratory, muscular

The organ failures. The consequences follow directly from an energy-starved, electrolyte-depleted body being loaded too fast. The cardiac complications are the ones that kill: arrhythmia, sinus bradycardia, nonspecific electrocardiographic changes, QT prolongation and, with overly rapid refeeding, congestive cardiac failure and sudden death (Tasman Psychiatry). Neurologically, the surge in thiamine demand can precipitate Wernicke's encephalopathy (confusion, ophthalmoplegia, ataxia), and the electrolyte shifts can cause seizures and delirium.

Respiratory and muscular. Hypophosphataemia weakens the diaphragm and respiratory muscles and can cause respiratory failure, and the same energy failure of muscle produces rhabdomyolysis and profound weakness. The picture is thus a multi-organ collapse driven by

phosphate and thiamine depletion, which is why it is treated as a medical emergency and why the pace of feeding is the thing under a clinician's control.

SYSTEM	CONSEQUENCE OF REFEEDING SYNDROME
Cardiac	**Arrhythmia, bradycardia, QT prolongation, congestive cardiac failure, sudden death**
Neurological	Wernicke's encephalopathy (thiamine), seizures, delirium
Respiratory	Respiratory muscle weakness and failure (hypophosphataemia)
Musculoskeletal	Rhabdomyolysis, weakness
Haematological/immune	Haemolysis, leucocyte dysfunction, impaired immunity

Clinical consequences; the cardiac complications carry the mortality, and Wernicke's encephalopathy is the neurological reason thiamine is given before feeding.

GOOD TO REMEMBER

- **Wernicke's encephalopathy (in refeeding, criterion):** the triad of confusion, ophthalmoplegia and ataxia from thiamine deficiency, precipitated when carbohydrate refeeding raises thiamine demand beyond depleted stores; the defining prevention step is to give thiamine *before or with* the first carbohydrate, never after.

2.6 Identifying the high-risk patient

Who is at risk. Risk tracks the depth and duration of undernutrition, not the presenting electrolytes. The recognised high-risk features, drawn from the nutrition-support criteria that MARSIPAN and NICE adopt, are a very low body mass index, large recent unintentional weight loss, a period of little or no nutritional intake before feeding, and low pre-feeding levels of potassium, phosphate or magnesium; extreme risk is flagged by a very low BMI (in the verified eating-disorder guidance, a BMI under 14) or negligible intake over a prolonged period. The exact numeric cut-offs for each of these criteria are guideline-specific and are flagged below rather than stated from memory.

Beyond anorexia. The psychiatrist meets refeeding risk outside the eating-disorder clinic too. In severe alcohol dependence with little food intake before withdrawal, refeeding risk must be actively considered (Saunders, Addiction medicine), and it arises in chronic neglect, prolonged fasting and the post-critical-illness patient. The common thread is a sustained period of near-starvation followed by a feed, whatever the psychiatric context.

GOOD TO REMEMBER

- **High-risk identification (first step):** stratify by *depth and duration of starvation*, very low BMI, large recent weight loss, prolonged negligible intake, and low pre-feeding phosphate/potassium/magnesium, with a BMI under 14 marking extreme risk (verified NICE NG69 eating-disorder guidance); a near-normal admission electrolyte panel does *not* exclude risk, and the same risk applies in severe alcohol dependence and chronic neglect, not only anorexia.

2.7 Prevention: correct the electrolytes, cover with thiamine, crawl the calories up

The three moves. **Prevention** is the whole game, and it is built into every guideline: identify the at-risk patient, correct pre-existing electrolyte abnormalities, supplement phosphate, magnesium, potassium and thiamine from the outset, and begin feeding at a deliberately low energy level with a slow climb. The numeric supplementation schedule belongs to NICE CG32 (recommendation 1.4.8), not to NG69: oral thiamine 200 to 300 mg daily, vitamin B co strong and a balanced multivitamin immediately before and during the first 10 days of feeding, with *daily* potassium, phosphate and magnesium supplements unless pre-feeding plasma levels are high. Thiamine is given before or alongside the first carbohydrate, because loading glucose into a thiamine-deplete brain is what precipitates Wernicke's encephalopathy.

Correct first, do not chase. Electrolytes are replaced proactively rather than only when they fall, because waiting for hypophosphataemia to appear means waiting for the syndrome to start. Feeding is not withheld for a low phosphate; instead the phosphate is replaced while feeding continues cautiously. Thiamine and a balanced multivitamin and multimineral supplement are standard from the beginning.

MNEMONIC

CORRECT, COVER, CRAWL

Correct the electrolytes (replace phosphate, potassium, magnesium proactively); **Cover** with thiamine before or with the first feed; **Crawl** the calories up from a low starting rate. The three prevention moves for refeeding syndrome, in order.

RULE **Correct the electrolytes, give thiamine, start slow.** Refeeding syndrome is prevented, not treated: replace phosphate, potassium and magnesium proactively, give thiamine before or with the first carbohydrate, and begin feeding at a low energy level with a gradual climb.

GOOD TO REMEMBER

- **Prevention (the principle):** correct electrolytes first, cover with thiamine before or with feeding, and crawl the calories up from a low start, with daily phosphate, magnesium, potassium and thiamine supplementation (NICE CG32 recommendation 1.4.8; NICE NG69 2017 carries no numbers of its own and refers to MEED); a low phosphate is replaced *while* feeding continues cautiously, not a reason to starve the patient further.

2.8 The refeeding rate: start low, climb slow

The starting energy. The controllable variable is the **refeeding rate**, and this is the one place in the topic where the guidelines openly disagree. NICE NG69 (2017) carries *no* kcal figure at all: recommendation 1.11.10 asks only for a standard operating procedure that avoids both under-nutrition and refeeding syndrome, and refers the clinician to the Royal College of Psychiatrists' Medical Emergencies in Eating Disorders guidance. The numbers therefore come from two other places, and they do not agree. The general nutrition-support guidance, NICE CG32 (recommendation 1.4.8), starts the patient at high risk of refeeding problems at a *maximum* of **10 kcal per kg per day**, increasing slowly to meet or exceed full needs within **4 to 7 days**, and uses

only **5 kcal per kg per day** in extreme cases (for example a BMI under 14, or negligible intake for more than 15 days) with continuous cardiac-rhythm monitoring. The eating-disorder guidance, RCPsych MEED CR233 (2022), starts higher, at **20 kcal per kg per day** and never below the immediate pre-admission intake, builds the calories up swiftly, and warns explicitly against underfeeding. Quote whichever source the question names.

Slow enough to be safe. The rate is set low precisely because the insulin response scales with the carbohydrate delivered: feed cautiously and the intracellular shift is gentle enough for replacement to keep pace; feed fast and the serum phosphate, potassium and magnesium crash faster than they can be corrected. Historically some clinicians started even lower than these figures; the exact lowest-risk starting rate and the tightest escalation schedule differ between guidelines and are flagged below.

SOURCE	STARTING RATE (KCAL PER KG PER DAY)	NOTE
NICE NG69 2017 (eating disorders)	no kcal figure given	Recommendation 1.11.10: use a standard operating procedure that avoids under-nutrition *and* refeeding syndrome; refers to MEED
NICE CG32 1.4.8, high risk of refeeding problems	**maximum 10**	Increase slowly to meet or exceed full needs within 4 to 7 days
NICE CG32 1.4.8, extreme cases (BMI under 14, or negligible intake over 15 days)	**only 5**	Slowest start; continuous cardiac-rhythm monitoring
RCPsych MEED CR233 2022 (eating disorders)	**start at 20**	**Never below the immediate pre-admission intake; build up swiftly; avoid underfeeding**

The two numeric refeeding positions, and they disagree: NICE CG32 caps the high-risk start at 10 kcal per kg per day, RCPsych MEED CR233 2022 opens at 20 and warns against underfeeding. NICE NG69 itself sets no rate. Quote whichever source the question names.

10	5	20	4 to 7
NICE CG32 MAXIMUM START AT HIGH RISK (KCAL PER KG PER DAY)	CG32 EXTREME CASES, BMI UNDER 14 (KCAL PER KG PER DAY)	RCPSYCH MEED CR233 2022 START (KCAL PER KG PER DAY)	CG32 DAYS TO MEET OR EXCEED FULL NEEDS

GOOD TO REMEMBER

- **Refeeding rate (the value):** NICE NG69 gives no kcal figure at all, and the two sources that do disagree, so quote the one the question names. NICE CG32 1.4.8: a *maximum* of 10 kcal per kg per day at high risk, only 5 in extreme cases (BMI under 14), increasing slowly to meet or exceed full needs within 4 to 7 days. RCPsych MEED CR233 2022: start at 20 kcal per kg per day, no lower than the immediate pre-admission intake, build up swiftly and avoid underfeeding. Either way the rate is the one variable fully under the clinician's control and the single strongest lever against the syndrome.

2.9 Monitoring: what to watch, and when

What is monitored. **Monitoring** centres on the electrolytes that move: serum phosphate above all, plus potassium and magnesium, together with glucose, sodium and fluid balance, and clinical signs of cardiac overload. Physical monitoring in the underweight patient also covers weight, orthostatic blood pressure, pulse, temperature and the electrocardiogram (QTc), with the eating-disorder guidance emphasising potassium, magnesium and phosphate specifically (NICE NG69 2017).

The schedule. Electrolytes are checked frequently once feeding starts, monitored daily for the first week in the verified guidance, with the tightest surveillance over the opening days when the intracellular shift is steepest; the extreme-risk patient warrants continuous cardiac monitoring from the outset. As feeding stabilises and the electrolytes hold, the frequency is relaxed. The phosphate trend across the first three days is the earliest signal that the syndrome is developing.

TRAP **Refeeding too fast and trusting a normal admission panel.** The classic errors are pushing calories up quickly to correct weight and being reassured by near-normal presenting electrolytes; both miss the falling phosphate of the opening days. Feed slowly and re-check the electrolytes, do not chase the weight.

GOOD TO REMEMBER

- **Monitoring (the value):** watch phosphate, potassium and magnesium (plus glucose, sodium, fluid balance and the electrocardiogram), checked daily for the first week and most intensively over the opening days (NICE NG69 2017); a falling serum phosphate in the first three days is the earliest warning, and the extreme-risk patient needs continuous cardiac monitoring from the outset.

2.10 The guideline positions, and the Indian frame

MARSIPAN leads. For the medical stabilisation of the severely ill patient with anorexia, the lead guidance is MARSIPAN (Management of Really Sick Patients with Anorexia Nervosa; RCPsych, MARSIPAN 2014, updated as the Medical Emergencies in Eating Disorders guidance 2022). Its position is a coordinated medical-and-psychiatric approach: assess refeeding risk early, refeed cautiously, replace electrolytes and give thiamine, and monitor cardiac status closely, with escalation of care for the highest-risk patient. Alongside it, NICE NG69 (2017) sets the eating-disorder care pathway but carries no kcal figure of its own, asking at recommendation 1.11.10 only for a standard operating procedure that avoids both under-nutrition and refeeding syndrome and referring to MEED; the general nutrition-support guidance NICE CG32 (recommendation 1.4.8) supplies the numeric refeeding-risk criteria, the cautious maximum rate and the replacement doses; MEED CR233 (2022) supplies the higher eating-disorder-specific starting rate that CG32 disagrees with; and the Indian Psychiatric Society CPG (IPS 2017) frames eating-disorder care for local practice. Where an exact MARSIPAN threshold, dose or criterion could not be confirmed against the parsed library, it is flagged below rather than stated.

The Indian reality. Refeeding is a recognition problem before it is a resource problem, and phosphate, potassium, magnesium and thiamine replacement are all inexpensive and widely stocked in India.

INDIA

Eating disorders are under-recognised in India, and the atypical, non-fat-phobic presentation, weight loss framed as appetite loss or a somatic complaint rather than a fear of fatness, means the severely underweight patient can reach care late and profoundly starved, exactly the patient most at risk of refeeding syndrome. The psychiatrist also meets the risk in severe alcohol dependence with poor intake and in chronic self-neglect. The corrective is cheap and available: thiamine, phosphate, potassium and magnesium replacement cost little, so the failure that kills is not funding but not thinking of the syndrome and refeeding too fast. Correct the electrolytes, give thiamine first, and start the calories low.

HOLD THIS

Refeeding syndrome is carbohydrate-triggered, insulin-driven, and defined by *hypophosphataemia* with falling potassium and magnesium and fluid retention in a severely starved patient whose admission electrolytes looked normal; you prevent it, not treat it, by correcting electrolytes, giving thiamine before or with the first feed, and starting low, on whichever source the question names (NICE CG32 1.4.8: a maximum of 10 kcal per kg per day, only 5 if BMI is under 14, full needs within 4 to 7 days; RCPsych MEED CR233 2022: start at 20 and avoid underfeeding), with daily electrolyte monitoring for the first week.

3 · The management of anorexia nervosa

The **management of anorexia** nervosa is the topic where examiners test whether you can hold a hierarchy in your head: this is a disorder with the highest mortality in psychiatry, yet the treatment that saves lives is not a drug at all. The answer is a ladder. You decide *where* to treat (least restrictive, but escalate for medical danger), you stabilise the failing body (the medical-risk assessment and, if needed, admission), you restore weight through **nutritional rehabilitation** done slowly enough to avoid killing the patient by feeding them, and you deliver a manualised psychological therapy as the primary treatment. Medication sits off to one side, treating comorbidity, never inducing the weight gain. The single fact that anchors every answer is that recovery is driven by weight restoration plus a specialist talking therapy, and that **no drug is first-line.**

Why it matters clinically. This is a management topic, so the marks sit in the guideline-level plan, the setting, the medical stabilisation, the refeeding rate, the named therapies and the medication caveat, more than in the phenomenology, which belongs to the anorexia diagnosis topic and the eating-disorder differentiation grid. The lead position is NICE NG69 (2017), with the MARSIPAN framework for the medically compromised patient, then RANZCP and WFSBP where they add or qualify. The neuroendocrine axes wrecked by starvation (the hypothalamic-pituitary-gonadal, thyroid and adrenal changes) are developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes; the general cognitive-behavioural technique that CBT-ED specialises belongs to the Psychotherapies, clinical assessment, MSE and nosology notes; the fine detail of the refeeding electrolyte thresholds and the monitoring schedule is owned by the refeeding-syndrome topic and its diagram. This topic

leans on the differentiation grid and the accompanying refeeding figure rather than adding a new figure of its own.

3.1 The setting: least-restrictive care, an outpatient or a day-patient by default

Treat in the least restrictive place that is safe. Most patients with anorexia nervosa are managed as outpatients or on a day-patient basis; hospital admission is reserved for those at risk of medical or psychological compromise (RANZCP 2014). The principle is explicit: use the least restrictive environment, escalating only when the body or the risk demands it. NICE frames specialist eating-disorder services, whether the patient is having a specific intervention or not, as the setting where psychoeducation and coordinated multidisciplinary monitoring of weight, mental and physical health, and risk are provided (NICE NG69 2017).

What tips the decision to admit. Emergency admission is indicated for the patient with severe electrolyte imbalance, severe malnutrition, severe dehydration, or signs of incipient organ failure (NICE NG69 2017). The choice of setting is therefore a medical-risk decision as much as a psychiatric one, which is why the medical-risk assessment comes next.

GOOD TO REMEMBER

- **Setting (the where-to-treat step):** the governing value is *least restrictive that is safe*; anorexia nervosa is treated as an outpatient or a day patient in most instances, with admission reserved for medical or psychological compromise (severe electrolyte imbalance, severe malnutrition or dehydration, incipient organ failure).

3.2 Medical stabilisation: the medical-risk assessment and when to admit

Assess the risk before you feed. **Medical stabilisation** begins with a structured medical-risk assessment. Monitor weight, orthostatic (lying and standing) blood pressure, pulse, temperature and peripheral circulation, and check full blood count, urea and electrolytes with particular attention to potassium, magnesium and phosphate, liver function, glucose, an ECG for the QTc interval, and bone density by DEXA (consider a scan after one year of underweight in children and young people, after two years of underweight in adults, or earlier if there is bone pain or recurrent fractures; NG69 explicitly says not to use single measures such as BMI or duration of illness to drive decisions) (NICE NG69 2017). Frequency rises for the severely underweight or the rapidly losing patient.

MARSIPAN, the framework for the really sick patient. The MARSIPAN guidance (Management of Really Sick Patients with Anorexia Nervosa) stratifies medical risk from parameters such as BMI and rate of weight loss, bradycardia and postural blood-pressure drop, hypothermia, the core biochemistry (potassium, phosphate, magnesium, glucose), ECG changes, and muscle power gauged clinically by the sit-up-squat-stand manoeuvre, sorting patients into risk zones that dictate the urgency and the site of care. It is the medically-led companion to NICE NG69 and the reference point when a patient is too unwell for routine outpatient refeeding. Its exact red-zone numeric cut-offs are not reproduced here (see gaps) and are cross-referenced to the refeeding-syndrome topic.

GOOD TO REMEMBER

- **Medical stabilisation (the safety step):** the principle is *assess medical risk first, correct it before you push calories*; monitor weight, orthostatic BP, pulse, temperature, U&E (potassium, magnesium, phosphate), LFT, glucose, ECG (QTc) and DEXA, and use the MARSIPAN risk stratification to decide who is too unwell for outpatient care.

3.3 Refeeding safely: the low-and-slow principle and the daily electrolyte watch

Feeding can kill; feed slowly. **Nutritional rehabilitation** must be started cautiously to avoid refeeding syndrome, the fluid, electrolyte and mineral catastrophe that follows when a starved body meets a carbohydrate load: insulin surges, intracellular uptake of phosphate, potassium and magnesium empties the serum, and the hallmark is hypophosphataemia (NICE NG69 2017; Kaplan and Sadock CTP 2024). The instruction is therefore to start low and go slow, and the two sources that carry numbers disagree about how low. NICE NG69 gives no kcal figure: recommendation 1.11.10 asks only for a standard operating procedure that avoids both under-nutrition and refeeding syndrome, and refers to the RCPsych Medical Emergencies in Eating Disorders guidance. The general nutrition-support guidance NICE CG32 (recommendation 1.4.8) starts the high-risk patient at a maximum of 10 kcal per kg per day, and only 5 kcal per kg per day in extreme cases such as a BMI under 14, with oral thiamine and a balanced multivitamin before and during the first 10 days of feeding plus potassium, phosphate and magnesium supplements, increasing slowly to meet or exceed full needs within 4 to 7 days. RCPsych MEED CR233 (2022) starts higher, at 20 kcal per kg per day and no lower than the immediate pre-admission intake, builds up swiftly and warns against underfeeding. Quote whichever source the question names.

Watch the electrolytes early and often. Monitor electrolytes daily through the first week, when the risk of the intracellular shift is highest, checking phosphate over the first three days especially, and give thiamine from the outset to pre-empt Wernicke encephalopathy. The precise phosphate, potassium and magnesium thresholds and the full monitoring schedule are owned by the refeeding-syndrome topic and its diagram; the message to carry into a management answer is the sequence *correct the electrolytes, give thiamine, start slow*.

SOURCE AND CLINICAL STATE	STARTING RATE (KCAL PER KG PER DAY)	SUPPLEMENT DAILY	ESCALATION
NICE CG32 1.4.8, high risk of refeeding problems	**maximum 10**	Phosphate, magnesium, potassium, thiamine	Increase slowly to meet or exceed full needs within 4 to 7 days
NICE CG32 1.4.8, extreme (e.g. BMI under 14)	**only 5**	Phosphate, magnesium, potassium, thiamine	Continuous cardiac-rhythm monitoring, electrolytes daily
RCPsych MEED CR233 2022, eating disorders	**start at 20**	Phosphate, magnesium, potassium, thiamine	Build up swiftly, never below the pre-admission intake
NICE NG69 2017, eating disorders	no kcal figure given	Recheck electrolytes daily	**Standard operating procedure only; refers to MEED**

The two numeric refeeding positions in anorexia nervosa, and they disagree: NICE CG32 caps the high-risk start at 10 kcal per kg per day, RCPsych MEED CR233 2022 opens at 20 and warns against underfeeding, and NG69 sets no rate at all. Quote whichever source the question names; exact electrolyte thresholds are held in the refeeding-syndrome topic and the accompanying refeeding figure.

TRAP **Refeeding too fast.** Piling on calories to correct a dangerously low weight is the classic lethal error: the carbohydrate load drives phosphate, potassium and magnesium into cells, hypophosphataemia precipitates cardiac failure, arrhythmia and death. Start low (NICE CG32: a maximum of 10 kcal per kg per day, only 5 if extreme; RCPsych MEED CR233 2022 opens at 20 and warns against underfeeding, so quote the source the question names), supplement phosphate and thiamine, and check electrolytes daily through the first week.

GOOD TO REMEMBER

- **Refeeding (the nutritional-rehabilitation safety step):** the hallmark of refeeding syndrome is *hypophosphataemia* and the prevention is *correct the electrolytes, give thiamine, start slow*; open low on NICE CG32 (a maximum of 10 kcal per kg per day, only 5 if extreme with a BMI under 14, full needs within 4 to 7 days) or at 20 kcal per kg per day on RCPsych MEED CR233 2022, which warns against underfeeding, quoting whichever the question names; supplement phosphate, magnesium, potassium and thiamine, and monitor electrolytes daily through the first week.

3.4 Nutritional rehabilitation: weight restoration is the treatment goal

Healthy weight is the target, not an afterthought. NICE is explicit that helping the person reach a healthy body weight or BMI for their age is a key treatment goal, because weight gain is what unlocks the psychological, physical and quality-of-life recovery (NICE NG69 2017). Once refeeding is safely under way, the calorie prescription is escalated toward weight restoration within a multidisciplinary plan; dietary counselling is offered only as part of that multidisciplinary approach, alongside an age-appropriate oral multivitamin and multimineral supplement until the diet meets reference values (NICE NG69 2017). WFSBP adds that zinc supplementation may be considered as an adjunct (WFSBP grade B evidence, 2011).

Bone and endocrine sequelae. Consider a bone-mineral-density scan after one year of underweight in the young and after two years in adults (not repeated more than once a year), and for young women aged 13 to 17 with long-standing low weight, low bone density and a bone age

over 15, transdermal 17-beta-estradiol with cyclic progesterone may be considered (NICE NG69 2017). The starvation endocrinopathy that drives the bone loss (the suppressed hypothalamic-pituitary-gonadal axis, the low-T3 state) is developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

PEARL

In anorexia nervosa, food is the medicine and weight is the vital sign. Almost every physical and cognitive abnormality, the bradycardia, the amenorrhoea, the concrete rigid thinking, the low bone density, is downstream of the starved state and reverses, at least partly, with weight restoration. This is why the plan refuses to treat the low weight as a side issue: restore the weight and most of the pathology follows it back toward normal.

GOOD TO REMEMBER

- **Nutritional rehabilitation (the weight-restoration step):** the governing value is that *reaching a healthy weight/BMI is the key treatment goal* because weight gain unlocks recovery; deliver it in a multidisciplinary plan with an oral multivitamin-multimineral supplement (zinc as a possible adjunct), and screen bone density by DEXA after one year (young) or two years (adults) of underweight.

3.5 Psychological therapy is the primary treatment in adults: CBT-ED, MANTRA, SSCM

The first-line psychological choice. For adults with anorexia nervosa, NICE offers a choice of three manualised psychological therapies as first-line: individual eating-disorder-focused cognitive behavioural therapy (CBT-ED), the Maudsley Anorexia Nervosa Treatment for Adults (MANTRA), or Specialist Supportive Clinical Management (SSCM) (NICE NG69 2017). CBT-ED runs typically to 40 sessions over about 40 weeks. If all three are unacceptable, contraindicated or ineffective, eating-disorder-focused focal psychodynamic therapy (FPT) is the next option (NICE NG69 2017). RANZCP concurs at the guideline level: use specialist, therapist-led, manualised psychological therapies across all age groups, within a multi-axial approach that addresses nutritional, medical and psychological aspects together (RANZCP 2014).

Therapy is primary, not adjunctive. The talking therapy is not an add-on to feeding; it is the treatment that changes the disorder, delivered in parallel with weight restoration. The general CBT technique on which CBT-ED is built belongs to the Psychotherapies, clinical assessment, MSE and nosology notes; this topic owns the disorder-specific therapies.

RULE **Weight plus a specialist therapy, and no drug first-line.** The primary treatment of anorexia nervosa is nutritional rehabilitation to a healthy weight *plus* a manualised psychological therapy (in adults CBT-ED, MANTRA or SSCM; in the young, family-based treatment). Medication has no established role in inducing weight gain: *no drug first-line*.

WORKED EXAMPLE

A 24-year-old woman with a BMI of 15.5, amenorrhoeic, restricting and over-exercising but medically stable, is seen in a specialist eating-disorder clinic. The correct plan is outpatient care (least restrictive, she is not medically compromised), a multidisciplinary weight-restoration programme with dietetic input and a multivitamin-multimineral supplement, and a choice of first-line psychological therapy, CBT-ED, MANTRA or SSCM, agreed with her. She does not need, and should not be started on, an antidepressant or an antipsychotic to make her gain weight; if she had comorbid depression that persisted after some weight gain, that would be treated on its own merits, with ECG monitoring given the cardiac risk at low weight.

3.6 The three adult therapies up close: CBT-ED, MANTRA and SSCM

What each therapy is. **CBT-ED** is the eating-disorder-specific adaptation of CBT: it targets the over-evaluation of shape, weight and control, the dietary rules and the safety behaviours, and it builds regular eating and behavioural experiments that disconfirm the feared consequences of weight gain, all while working toward weight restoration. **MANTRA**, the Maudsley model, is a manualised individual therapy built around the maintaining factors of the illness (a rigid, detail-focused, harm-avoidant cognitive style, unhelpful beliefs about the value of anorexia to the self, and interpersonal and emotional-avoidance patterns), working collaboratively to shift them. **SSCM** combines supportive psychotherapy with clinical management: education, careful physical and weight monitoring, and a focus on the core anorexic symptoms that keep the patient underweight, without a specific psychological technique. All three are first-line and chosen by patient preference and availability.

THERAPY	WHAT IT IS	POPULATION AND COURSE
CBT-ED	Eating-disorder-focused CBT: over-evaluation of shape/weight/control, dietary rules, regular eating, behavioural experiments	Adults, first-line; typically 40 sessions over about 40 weeks
MANTRA	Maudsley individual model targeting the cognitive style and beliefs that maintain the illness	Adults, first-line
SSCM	Supportive psychotherapy plus clinical management; education, monitoring, focus on core anorexic symptoms	Adults, first-line
FPT	Eating-disorder-focused focal psychodynamic therapy	Adults, second-line if the three above fail or are unacceptable

The adult first-line psychological therapies for anorexia nervosa and the second-line psychodynamic option (NICE NG69 2017); chosen by patient preference and local availability.

GOOD TO REMEMBER

- **CBT-ED, MANTRA and SSCM (the adult primary therapies):** the one value is that *all three are first-line and equivalent*, chosen by patient preference; CBT-ED (typically 40 sessions over about 40 weeks) targets the over-evaluation of shape and weight, MANTRA targets the maintaining cognitive style, SSCM pairs supportive therapy with clinical monitoring, and FPT is the second-line fallback.

3.7 Children and young people: family-based treatment first

Treat the family, not just the child. For children and young people with anorexia nervosa, the first-line treatment is anorexia-nervosa-focused family therapy (FT-AN), the manualised **family-based treatment** in which parents are coached to take charge of refeeding and weight restoration before control is gradually handed back to the young person as they recover (NICE NG69 2017; RANZCP 2014). It is delivered as single-family therapy or as combined single- and multi-family work, typically over 18 to 20 sessions across about one year. If FT-AN is unacceptable, contraindicated or ineffective, the alternatives are individual CBT-ED or adolescent-focused psychotherapy for anorexia nervosa (AFP-AN) (NICE NG69 2017).

Why the family is the lever. In the young, still-dependent patient the parents are the practical agents of weight restoration, which is why the evidence base (originally the Maudsley model) puts family work, not individual therapy, at the front of the line for this age group.

GOOD TO REMEMBER

- **Family-based treatment (the first-line therapy in the young):** the anchor is that *FT-AN is first-line for children and young people*, parents lead refeeding then hand control back; typically 18 to 20 sessions over about one year, single- or multi-family, with individual CBT-ED or AFP-AN as the fallback.

3.8 No drug is first-line: medication, comorbidity and the cardiac caveat

The rule stated plainly. Do not offer medication as the sole treatment for anorexia nervosa (NICE NG69 2017). There is **no drug first-line**: no agent has an established role in inducing weight gain, and the pharmacology that works is aimed at comorbidity, treated on its own merits and preferably once some weight has been regained. If an SSRI is considered (for comorbid depression or OCD), remember that the evidence for efficacy in the low-weight patient is poor and the cardiac risk (QTc prolongation) is increased at low body weight, so an ECG and electrolyte check accompany any such prescription (NICE NG69 2017). The deep SSRI pharmacology, including fluoxetine (Indian brands Prodep, Fludac, Flunil), which is the licensed drug for *bulimia* and not for anorexia, is developed in the Mood disorders: pharmacotherapy notes.

Olanzapine, the only agent with a signal. Low-dose olanzapine (of the order of 2.5 to 5 mg per day) may have a small weight-gain effect and can help the severe, unremitting, ruminative patient, but it is explicitly not first-line and not for routine use (NICE NG69 2017); WFSBP grades the olanzapine weight-gain signal as grade B and other atypicals as weaker (WFSBP 2011). The

through-line for an answer: medication is adjunctive and comorbidity-directed, never the treatment that restores weight.

TRAP **Prescribing a drug to make the patient gain weight.** Reaching for an antidepressant, or an antipsychotic, as the way to treat anorexic low weight is the classic management error: no drug is first-line and none reliably induces weight gain. Weight is restored by nutrition and a specialist therapy; medication only treats comorbidity, with an ECG because the QTc is vulnerable at low weight.

GOOD TO REMEMBER

- **Medication in anorexia (no drug first-line):** the one value is that *no drug is first-line and none induces weight gain reliably*; do not offer medication as the sole treatment, treat comorbidity on its merits (SSRI cautiously, poor low-weight efficacy and QTc risk, ECG advised), and reserve low-dose olanzapine (2.5 to 5 mg per day) as a non-routine adjunct, not a first-line agent.

3.9 Guideline convergence, compulsory treatment and the enduring illness

Where the guidelines land. Read together, the guidelines converge: least-restrictive setting, medical stabilisation with safe refeeding, weight restoration as the goal, a manualised psychological therapy as the primary treatment, and medication kept for comorbidity (NICE NG69 2017; RANZCP 2014; WFSBP 2011). For the small group who lack capacity because of the eating disorder, refuse treatment and face a significant risk to life or long-term health, compulsory treatment under mental-health legislation may be considered, coordinated with a hospital ethics committee; in India the Mental Healthcare Act 2017 supported-admission provision (Section 89) may apply, and the co-occurring physical illness is treated under the ordinary treatment and consent provisions of that admission, not under Section 105, which deals with the question of mental illness in a judicial process (MHCA 2017). In chronic, severe and enduring anorexia nervosa, a harm-minimisation approach is adopted rather than repeated coercive weight restoration (RANZCP 2014).

GUIDELINE	SETTING	PRIMARY TREATMENT	MEDICATION STANCE
NICE NG69 2017	Least restrictive; admit for medical/psychological compromise	Adults: CBT-ED, MANTRA or SSCM. Young: FT-AN first-line	**Not the sole treatment; no drug first-line; olanzapine non-routine**
MARSIPAN 2014	Medical risk stratification decides site and urgency for the sick patient	Safe, low-and-slow refeeding under medical oversight	Medical management, not drug-led weight gain
RANZCP 2014	Outpatient or a day patient in most instances; least restrictive	Specialist therapist-led manualised therapy; family-based in the young	Harm minimisation in chronic (SEED) illness

GUIDELINE	SETTING	PRIMARY TREATMENT	MEDICATION STANCE
WFSBP 2011	Multidisciplinary	Nutritional and psychological rehabilitation	Olanzapine grade B (weight gain), zinc adjunct grade B; not first-line

Guideline-level management of anorexia nervosa, NICE NG69-led with MARSIPAN for the medically compromised, converging on least-restrictive care, safe refeeding, psychological therapy as primary and no drug first-line (verified from the drug-guideline supplement).

INDIA

Two India-specific points earn marks. First, the atypical, non-fat-phobic presentation: the absence of an expressed intense fear of weight gain ("fat phobia") is relatively more common in Asian populations, where dietary restriction is attributed to a culturally sanctioned complaint such as gastrointestinal discomfort, or to cultural or religious motives such as fasting, so an Indian patient can meet criteria for anorexia nervosa with prominent low weight but little overt shape-and-weight talk (DSM-5-TR 2022; ICD-11 CDDR). Missing this, and calling a non-fat-phobic starving patient "not anorexia", is the classic error. Second, eating disorders remain under-recognised and under-served in India, which delays the medical-risk assessment and safe refeeding that this ladder depends on. Where capacity is lost and life is at risk, compulsory care runs through the Mental Healthcare Act 2017 (supported admission under Section 89; Section 105 is *not* the physical-illness provision, it covers the question of mental illness in a judicial process), coordinated with the hospital ethics committee.

10 or 20
REFEEDING START (KCAL PER KG PER DAY): CG32 CAPS AT 10 (5 IF EXTREME), MEED 2022 OPENS AT 20

40
CBT-ED SESSIONS OVER ABOUT 40 WEEKS IN ADULTS (NICE NG69)

18 to 20
FT-AN FAMILY-THERAPY SESSIONS OVER ABOUT ONE YEAR IN THE YOUNG

None
DRUG IS FIRST-LINE FOR ANOREXIA (MEDICATION HAS NO WEIGHT-GAIN ROLE)

HOLD THIS

The management of anorexia nervosa is a ladder: treat in the least restrictive safe setting, stabilise the body (medical-risk assessment, MARSIPAN, safe low-and-slow refeeding to pre-empt hypophosphataemia), restore weight as the treatment goal, and deliver the primary treatment, a manualised psychological therapy (adults: CBT-ED, MANTRA or SSCM; young: family-based treatment), while no drug is first-line and medication only treats comorbidity.

4 · Bulimia nervosa

The normal-weight eating disorder. **Bulimia nervosa** is the disorder of the **binge-purge cycle**: recurrent episodes of binge eating with a sense of loss of control, followed by recurrent inappropriate compensatory behaviour to undo the calories, in a person whose self-worth is hostage to weight and shape and whose body weight is typically normal or above normal. That last fact is why it hides: unlike anorexia nervosa, there is no emaciation to give it away, so the examiner tests whether you can recognise it from the behaviour and read the physical footprint of purging on the body. This note owns both halves of the exam question: it *teaches* the features, the ICD-11 and DSM-5-TR criteria with their frequency and duration, and the **medical**

complications of purging (the electrolyte derangement and **hypokalaemia**, the metabolic alkalosis, **Russell's sign**, dental erosion, parotid swelling, and the oesophageal and cardiac risks), and it delivers the guideline-anchored *management*.



Fig 17.4 The bulimia nervosa cycle links rigid dietary restraint with hunger or negative affect, binge eating, compensatory behaviour, brief relief and shame that renews further restraint.

Why the management matters. This is a management topic, so the marks sit in the stepped-care plan and the one licensed drug. The lead position is NICE NG69 (2017): a psychological therapy first (guided self-help, then eating-disorder-focused CBT), with medication never the sole treatment. There is one drug to know cold, fluoxetine at a dose *higher* than its antidepressant dose, and one drug that is dangerous here. The deep SSRI pharmacology (fluoxetine's kinetics, adverse effects and interactions) is developed in the Mood disorders: pharmacotherapy notes; the general cognitive-behavioural technique that CBT-ED specialises belongs to the Psychotherapies, clinical assessment, MSE and nosology notes. The accompanying figure maps the binge-purge cycle and the purging complications onto the body; the SCOFF form sits on the accompanying scale plate.

4.1 The clinical picture: the binge-purge cycle

One cycle, four moving parts. Bulimia nervosa is built from a self-perpetuating loop. First, a *binge*: eating, in a discrete period usually under two hours, an amount of food definitely larger than most people would eat in similar circumstances, accompanied by a *sense of loss of control*, the inability to stop or limit what is eaten (DSM-5-TR 2022). The binge is usually secret, driven most often by negative affect, and continues until the person is uncomfortably or painfully full. Second, the guilt and fear of weight gain that follow. Third, a *compensatory behaviour* to undo it: most commonly self-induced vomiting, or misuse of laxatives, diuretics or other medications, fasting, or excessive exercise. Fourth, transient relief, then renewed dietary restraint that primes the next binge. The over-evaluation of shape and weight sits at the centre, keeping the whole cycle turning.

The weight is the giveaway that there is no giveaway. Because the binges and the purging roughly cancel, the person with bulimia nervosa is characteristically of *normal or above-normal weight* (Kaplan and Sadock CTP 2024). This is the single most useful discriminator from the binge-purge subtype of anorexia nervosa, where the weight is significantly low, and it is why bulimia nervosa is so often missed on inspection alone.

GOOD TO REMEMBER

- **Bulimia nervosa (the syndrome):** the defining criterion is the recurrent *binge-purge cycle*, binge eating with a sense of loss of control plus recurrent inappropriate compensatory behaviour (most often self-induced vomiting), with self-evaluation unduly influenced by weight and shape; the discriminating clinical fact is that the weight is *typically normal or above normal*, not low.

4.2 DSM-5-TR criteria and the severity bands

The five criteria to state. DSM-5-TR sets five criteria (DSM-5-TR 2022). *A*, recurrent episodes of binge eating (both the large amount, A1, and the sense of lack of control, A2). *B*, recurrent inappropriate compensatory behaviours to prevent weight gain (self-induced vomiting; misuse of laxatives, diuretics or other medications; fasting; or excessive exercise). *C*, the binge eating *and* the compensatory behaviours both occur, on average, **at least once a week for 3 months**. *D*, self-evaluation is unduly influenced by body shape and weight. *E*, the disturbance does not occur exclusively during episodes of anorexia nervosa (so a low-weight binge-purge patient is coded as anorexia nervosa, binge-purge type, not as bulimia nervosa).

Severity is scored on the compensatory behaviour. DSM-5-TR grades current severity by the average number of episodes of inappropriate compensatory behaviour per week, and this is the band examiners like to test.

DSM-5-TR SEVERITY	COMPENSATORY BEHAVIOUR (EPISODES PER WEEK)
Mild	1 to 3
Moderate	4 to 7
Severe	**8 to 13**
Extreme	**14 or more**

DSM-5-TR severity grading for bulimia nervosa by the average weekly frequency of inappropriate compensatory behaviour (DSM-5-TR 2022); severity may be raised for other symptoms or functional disability.

GOOD TO REMEMBER

- **DSM-5-TR criteria (the diagnostic anchor):** binge eating with loss of control *plus* recurrent compensatory behaviour, both on average *at least once a week for 3 months*, with self-evaluation unduly influenced by weight/shape, and *not* exclusively during anorexia nervosa; severity is banded by compensatory episodes per week (mild 1 to 3, moderate 4 to 7, severe 8 to 13, extreme 14 or more).

4.3 ICD-11 criteria and the frequency-duration discriminator

Where the two systems diverge. ICD-11 (6B81) requires frequent, recurrent binge eating (loss of control, eating notably more or differently than usual) *and* repeated inappropriate compensatory behaviour to prevent weight gain, each occurring **once a week or more over a period of at least 1 month**, with an excessive preoccupation with body weight or shape and marked distress or functional impairment (ICD-11 CDDR). The high-yield discriminator is the timeframe: *ICD-11 asks for at least one month, DSM-5-TR asks for three months*. ICD-11 also notes that self-induced vomiting, the commonest compensatory behaviour, typically occurs within an hour of the binge.

The historical anchor. Bulimia nervosa was first delineated by Gerald Russell in 1979 as an "ominous variant" of anorexia nervosa, and his name is attached to the hand sign of chronic self-induced vomiting (below). Where the person meets full criteria but at lower frequency or shorter duration, the residual category is *bulimia nervosa of low frequency and/or limited duration*, coded under OSFED (DSM-5-TR) or "other specified" in ICD-11.

FRAMEWORK	BINGE + COMPENSATORY FREQUENCY AND DURATION	WEIGHT AND BOUNDARY
DSM-5-TR	**On average at least once a week for 3 months**	Normal or above; excluded if only during anorexia nervosa
ICD-11 (6B81)	**Once a week or more over at least 1 month**	Not significantly low weight (else anorexia nervosa, binge-purge pattern)
ICD-10 (historical)	Recurrent overeating with pre-occupation and craving	Morbid dread of fatness; often past anorexic episode

The frequency-and-duration thresholds compared; the number to hold is the split, DSM-5-TR three months against ICD-11 one month, both at once weekly (DSM-5-TR 2022; ICD-11 CDDR).

RULE **Once weekly, but three months versus one month.** Both systems require binge eating and compensatory behaviour at least once a week; the duration is the discriminator, *three months in DSM-5-TR, one month in ICD-11*, and the patient is not significantly underweight (or the diagnosis becomes anorexia nervosa, binge-purge type).

4.4 Distinguishing bulimia from its neighbours

Three look-alikes. The differential turns on weight and on whether purging is present. *Anorexia nervosa, binge-purge subtype* shares the binge-purge behaviour but the weight is *significantly low*,

and by the exclusion rule that low-weight patient is diagnosed as anorexia nervosa, not bulimia nervosa. *Binge-eating disorder* shares the binges and the loss of control but has *no* regular compensatory behaviour, so the person is commonly overweight or obese and does not purge. *Purging disorder* (an OSFED presentation) is recurrent purging to control weight *without* objective binges. The presence of purging plus objective binges plus a non-low weight is what pins the label to bulimia nervosa.

DISORDER	OBJECTIVE BINGES	COMPENSATORY PURGING	TYPICAL WEIGHT
Bulimia nervosa	Yes	**Yes, recurrent**	Normal or above
Anorexia nervosa, binge-purge type	Yes	Yes	**Significantly low**
Binge-eating disorder	Yes	No	Overweight or obese
Purging disorder (OSFED)	No	Yes	Normal

Bulimia nervosa against its differentials; the two questions are "are there objective binges?" and "is there recurrent purging at a non-low weight?" (DSM-5-TR 2022).

GOOD TO REMEMBER

- **Boundary rule (the discriminator):** objective binges plus recurrent purging at a *normal or above-normal* weight is bulimia nervosa; the same behaviour at a significantly *low* weight is anorexia nervosa binge-purge type; binges *without* compensation is binge-eating disorder; purging *without* binges is purging disorder.

4.5 Medical complications: the footprint of purging

The body records the vomiting. The **medical complications** of bulimia nervosa come almost entirely from the compensatory behaviours, above all self-induced vomiting (Kaplan and Sadock CTP 2024). Repeated acid vomit dissolves the lingual dental enamel (erosion and multiple caries), swells the parotid and salivary glands (sialadenosis, with a raised serum amylase), and, over time, lays down Russell's sign, the callus or abrasion over the knuckles of the dominant hand where the teeth scrape the skin during gag-induced vomiting. The dangerous consequences are biochemical and cardiac. The two findings that demand urgent evaluation are a prolonged QTc on the ECG and marked hypokalaemia.

The electrolyte and acid-base signature. Recurrent vomiting loses hydrogen and chloride and drives a hypochloraemic, hypokalaemic metabolic alkalosis; laxative misuse instead loses bicarbonate in the stool and tends toward a metabolic acidosis. *Hypokalaemia* is the killer: a low serum potassium is a particularly dangerous imbalance that precipitates cardiac arrhythmia, so potassium is monitored in anyone who purges (Kaplan and Sadock CTP 2024). Forceful vomiting also risks the oesophagus, oesophagitis, Mallory-Weiss mucosal tears with haematemesis, and, rarely, catastrophic oesophageal or gastric rupture, while ipecac (emetine) abuse can cause a skeletal and cardiac myopathy.

SYSTEM	SIGN OR ABNORMALITY	MECHANISM / NOTE
Oral / dental	**Erosion of dental enamel (perimylolysis), multiple caries**	Acid gastric contents dissolve the lingual enamel with chronic vomiting
Salivary	Swollen parotid and salivary glands (sialadenosis), raised serum amylase	Recurrent self-induced vomiting; the "chipmunk" facies
Hands	**Russell's sign: knuckle calluses / abrasions**	Teeth scraping the dorsum of the hand during gag-induced vomiting
Electrolyte	**Hypokalaemia, hypochloraemia, hyponatraemia**	Loss through vomiting and purging; hypokalaemia is the dangerous one
Acid-base	Metabolic alkalosis (vomiting); metabolic acidosis (laxatives)	Vomiting loses hydrogen and chloride; laxatives lose bicarbonate
Cardiac	**Prolonged QTc, arrhythmia; ipecac cardiomyopathy**	Driven by hypokalaemia and QTc; urgent findings on the ECG
Oesophageal / gastric	Oesophagitis, Mallory-Weiss tears, rare oesophageal or gastric rupture	Forceful vomiting; gastric distension from bingeing
Gastrointestinal (lower)	Constipation, cathartic (atonic) colon, rectal prolapse	Chronic laxative misuse and dependence

Medical complications of bulimia nervosa by system; the eye-catchers are Russell's sign, parotid swelling and dental erosion, and the two that kill are hypokalaemia and a prolonged QTc (Kaplan and Sadock CTP 2024).

TRAP **A normal weight is falsely reassuring.** The classic error is to discount an eating disorder because the patient looks well and weighs normally, and to miss the silent *hypokalaemia* and prolonged QTc of covert purging. Weigh, ask directly about bingeing and vomiting, look for Russell's sign, parotid swelling and dental erosion, and always check potassium and an ECG.

GOOD TO REMEMBER

- **Complications of purging (the criterion sign to seek):** the physical footprint is dental erosion, parotid swelling and Russell's sign; the biochemistry is a *hypochloraemic, hypokalaemic metabolic alkalosis* from vomiting; and the two urgent findings that must be actively sought are marked *hypokalaemia* and a *prolonged QTc*, because hypokalaemia drives fatal arrhythmia.

4.6 Management, the NICE NG69 stepped plan: guided self-help first

Psychological therapy leads, in a defined order. The lead guideline is NICE NG69 (2017), and its first step for adults with bulimia nervosa is bulimia-nervosa-focused guided self-help: structured self-help materials supported by four to nine brief supportive sessions over about 16 weeks (NICE NG69 2017). If guided self-help is unacceptable, contraindicated or ineffective after four weeks, the next step is individual eating-disorder-focused cognitive behavioural therapy (CBT-ED), typically 20 sessions over about 20 weeks. For children and young people the first-line psychological treatment is *bulimia-nervosa-focused family therapy* (FT-BN) (NICE NG69 2017).

NICE is explicit that medication is *not* offered as the sole treatment for bulimia nervosa, and that ineffective physical therapies (transcranial magnetic stimulation, acupuncture, weight training, yoga, warming therapy) should not be used.

Where the other guidelines land. RANZCP (2014) puts therapist-led CBT as the first-line psychological treatment and allows an antidepressant, topiramate or orlistat (the last in comorbid obesity) as adjunctive or alternative medication. This is the point where NICE (self-help first, then CBT-ED) and RANZCP (CBT first) differ in emphasis while agreeing that a talking therapy, not a drug, is primary.

GOOD TO REMEMBER

- **NICE NG69 stepped care (the management order):** the value is *a psychological therapy first, medication never alone*; adults start with bulimia-nervosa-focused *guided self-help* (4 to 9 sessions over about 16 weeks), stepping up to individual *CBT-ED* (about 20 sessions over 20 weeks) if that fails after four weeks; young people get FT-BN; RANZCP places therapist-led CBT first-line.

4.7 CBT-ED, the definitive psychological treatment

The best-evidenced therapy. **CBT-ED** is the eating-disorder-specific form of cognitive behavioural therapy and has the strongest evidence base in bulimia nervosa, established across dozens of controlled trials as the most effective single treatment (Lewis Child and Adolescent Psychiatry; NICE NG69 2017). It targets the machinery of the binge-purge cycle directly: it establishes a pattern of regular eating to break the restrict-binge see-saw, dismantles dietary rules and the compensatory behaviours, and works on the over-evaluation of shape and weight that drives the whole loop. A typical course runs to about 20 sessions over 20 weeks. The general CBT technique on which it is built is developed in the Psychotherapies, clinical assessment, MSE and nosology notes; this topic owns the disorder-specific adaptation.

Therapy is primary, drug is adjunctive. The through-line for an answer is that CBT-ED (or, as a first step in NICE, guided self-help built on the same model) is the treatment that changes the disorder, and any medication rides alongside it rather than replacing it.

GOOD TO REMEMBER

- **CBT-ED (the primary therapy):** the anchor is that *eating-disorder-focused CBT is the best-evidenced treatment for bulimia nervosa*; it installs regular eating, targets dietary rules, purging and the over-evaluation of shape and weight, typically 20 sessions over about 20 weeks, and medication is adjunctive to it, never a substitute.

4.8 Fluoxetine, the one licensed drug, at 60 mg per day

The drug to know cold. If one pharmacological fact is tested on this topic, it is this: fluoxetine is the medication of choice and the licensed drug for bulimia nervosa, and it works at a dose *higher* than its antidepressant dose. Fluoxetine is traditionally prescribed at 20 to 40 mg per day for depressive disorders, but studies show that a higher dose, **60 mg per day**, is more effective at disrupting binge eating and purging, and even at that higher dose it is better tolerated than the older alternatives (Kaplan and Sadock CTP 2024). WFSBP (2023) names fluoxetine as the first-line pharmacological treatment for bulimia nervosa in adults (its strongest recommendation

grade). The effect is largely independent of whether the patient is depressed, so it is not merely treating a comorbid mood disorder. In India, fluoxetine is widely available and inexpensive, led by the brands Prodep, Fludac and Flunil; the deep pharmacology (kinetics, adverse effects, the long half-life, CYP interactions) is cross-referenced to the Mood disorders: pharmacotherapy notes.

RULE **Fluoxetine 60 mg per day is THE licensed drug for bulimia.** The one antibulimic dose to memorise is fluoxetine *60 mg per day*, the antibinge dose that sits above the 20 to 40 mg antidepressant range; it is the medication of choice and licensed for bulimia nervosa, given alongside, not instead of, a psychological therapy.

WORKED EXAMPLE

A 22-year-old woman of normal weight (BMI 22) discloses that she binges several evenings a week and then makes herself vomit; she has knuckle calluses, bilateral parotid fullness, and a serum potassium of 3.1 with a borderline-prolonged QTc. This is bulimia nervosa. The correct plan is to correct and monitor the potassium, arrange an ECG, and start a psychological therapy, bulimia-nervosa-focused guided self-help stepping up to CBT-ED per NICE NG69. If a drug is added for the bingeing and purging, the answer is **fluoxetine** titrated to 60 mg per day, alongside the therapy. She should not be started on bupropion (see below), and normal weight does not make the hypokalaemia any less dangerous.

GOOD TO REMEMBER

- **Fluoxetine (the licensed drug):** the one value is *60 mg per day*, above the 20 to 40 mg antidepressant dose, as the antibinge dose; fluoxetine is the medication of choice and the licensed agent for bulimia nervosa (WFSBP 2023 first-line), works whether or not the patient is depressed, and is given *with* a psychological therapy, not alone.

4.9 The rest of the drug shelf, and the one to avoid

Adjuncts and alternatives. Beyond fluoxetine, topiramate reduces binge eating and purging and is recommended by WFSBP (2023) and offered by RANZCP (2014) as an adjunct or alternative, though its cognitive and paraesthetic side effects limit tolerability. Older tricyclic antidepressants can reduce bulimic symptoms but carry a moderate risk-benefit ratio and are dangerous in overdose (WFSBP 2011). Because eating-disorder patients on medication may develop electrolyte disturbance, bradycardia, hypokalaemia or QT prolongation, NICE NG69 (2017) advises ECG monitoring for anyone whose drug could compromise cardiac function.

The contraindication that is a favourite question. Bupropion is *contraindicated* in bulimia nervosa: it lowers the seizure threshold, and actively purging patients had an unacceptably high rate of seizures, so it is not used in current or past bulimia or anorexia nervosa (Kaplan and Sadock CTP 2024). Naming bupropion as an antidepressant for a bulimic patient is a classic exam trap.

TRAP **Reaching for bupropion.** Bupropion is contraindicated in bulimia nervosa because it lowers the seizure threshold and precipitated seizures in actively purging patients; the antidepressant that is *indicated and licensed* here is fluoxetine at 60 mg per day, not bupropion.

GOOD TO REMEMBER

- **Other drugs and the caution (the value):** topiramate is the evidenced adjunct or alternative (WFSBP 2023; RANZCP 2014) and tricyclics are second-line with a poor overdose margin; monitor the ECG on any cardiac-risk drug (NICE NG69 2017); and *bupropion is contraindicated* because it lowers the seizure threshold in purging patients.

4.10 Screening, guideline convergence and the India lens

Case-finding and where the guidelines meet. The bedside screen is the SCOFF, the same five-item verbal tool used for anorexia nervosa (Sick, Control, One stone, Fat, Food), positive at **two or more** "yes" answers and reproduced on the accompanying scale plate. Read together, the guidelines converge: a psychological therapy is primary (NICE NG69 guided self-help then CBT-ED; RANZCP therapist-led CBT), medication is never the sole treatment, and where a drug is used the licensed choice is fluoxetine at 60 mg per day.

GUIDELINE	FIRST-LINE PSYCHOLOGICAL	MEDICATION STANCE
NICE NG69 2017	**Guided self-help, then CBT-ED; FT-BN in the young**	Not the sole treatment; ECG-monitor cardiac-risk drugs
RANZCP 2014	Therapist-led CBT first-line	Antidepressant, topiramate or orlistat as adjunct/alternative
WFSBP 2023	Psychotherapy embedded	**Fluoxetine first-line; topiramate to reduce binge/purge**
WFSBP 2011	Psychotherapy embedded	Tricyclics usable, moderate risk-benefit

Guideline-level management of bulimia nervosa, NICE NG69-led, converging on a psychological therapy first and fluoxetine as the licensed drug (verified from the drug-guideline supplement; WFSBP fluoxetine and dose from Kaplan and Sadock CTP 2024).

INDIA

Bulimia nervosa is under-recognised in India, and doubly hidden: unlike anorexia nervosa it leaves no visible emaciation, the binges and vomiting are intensely secret and shaming, and the presentation is often to a physician or dentist with dental erosion, parotid swelling or unexplained **hypokalaemia** rather than to a psychiatrist. The stereotype of the affluent urban young woman misses men and lower-income patients. The clinical antidotes are a low threshold to screen (the SCOFF), a direct question about bingeing and self-induced vomiting in any young person with normal weight and a low potassium or eroded teeth, and reassurance that the licensed, cheap and available drug, **fluoxetine** (Prodep, Fludac, Flunil), sits behind an accessible first-line therapy.

PEARL

Bulimia nervosa is the eating disorder you diagnose by *asking*, not by looking. The weight is normal, so the tells are behavioural and physical residue: the secret binge-purge cycle on history, and Russell's sign, parotid fullness, eroded teeth and a quietly low potassium on examination. Treat the cycle with CBT-ED and, if a drug is needed, fluoxetine at 60 mg per day.

60	2	3	8 to 13
FLUOXETINE DOSE FOR BULIMIA (MG PER DAY); THE LICENSED DRUG	SCOFF POSITIVE SCREEN (YES ANSWERS)	DSM-5-TR MINIMUM DURATION (MONTHS AT ONCE WEEKLY)	SEVERE BULIMIA (COMPENSATORY EPISODES PER WEEK)

HOLD THIS

Bulimia nervosa is the recurrent binge-purge cycle, binge eating with loss of control plus recurrent compensatory behaviour (most often self-induced vomiting), at least once weekly for three months in DSM-5-TR (one month in ICD-11), in a person of normal or above-normal weight; the footprint of purging is Russell's sign, parotid swelling, dental erosion and a hypokalaemic metabolic alkalosis with the deadly duo of hypokalaemia and a prolonged QTc; management is a psychological therapy first (NICE NG69 guided self-help then CBT-ED), medication never alone, and the one licensed drug is fluoxetine at 60 mg per day, with bupropion contraindicated.

5 · Binge eating disorder

Binge eating disorder (BED) is the eating disorder examiners use to test one clean discrimination: it is **recurrent binge eating with loss of control, but without the regular compensatory behaviour that defines bulimia.** Take away the self-induced vomiting, the laxatives, the fasting and the driven exercise, and a bulimia-shaped binge picture becomes binge eating disorder. It is the most common eating disorder, it sits alongside overweight and obesity rather than emaciation, and its management is a guideline-led ladder in which a psychological therapy, not a drug, is the primary treatment.

Why it matters clinically. This is a hybrid topic. The diagnosis half turns on three things you must be able to state cold: the binge (a discrete period of overeating with loss of control eating), the associated features and marked distress, and the absence of regular compensation. The management half is a guideline plan led by NICE NG69 (2017): binge-eating-disorder-focused guided self-help first, then group CBT-ED, with medication kept adjunctive and weight loss explicitly not a therapy target. The general cognitive-behavioural technique that CBT-ED specialises belongs to the Psychotherapies, clinical assessment, MSE and nosology notes, and the high-dose bulimia pharmacology of fluoxetine belongs to the Mood disorders: pharmacotherapy notes. This topic leans on the differentiation grid and the accompanying scale plate rather than adding a figure of its own.

5.1 What binge eating disorder is: the recurrent binge with loss of control

The binge, defined. A binge is eating, in a discrete period of time (usually under two hours), an amount of food that is definitely larger than most people would eat in a similar period under similar circumstances, accompanied by a **sense of lack of control** (DSM-5-TR 2022, Criterion A). The loss of control is the core: the inability to stop once started, or, in longer-standing illness, a generalised feeling of uncontrolled eating even where the acute out-of-control quality has faded. ICD-11 broadens this usefully, allowing the binge to be "objective" (a genuinely large amount) or "subjective" (an amount that is normal in quantity but experienced as a binge), because the defining experience is the loss of control, not the calorie count (ICD-11 CDDR).

Recurrent, and distressing. The pattern must be a **recurrent binge**, not an isolated lapse: on average at least once per week for three months (DSM-5-TR 2022, Criterion D; ICD-11 uses "once a week or more over three months"). The binge eating is marked by significant distress (DSM-5-TR 2022, Criterion C), the shame and secrecy that make patients conceal it, so most binge eating happens alone and hidden.

MNEMONIC

RAG (Rapid, Alone, Guilt) around a Loss-of-control binge

The core of a binge eating disorder episode is a *Loss-of-control* binge; the three most memorable of the five associated features are eating *Rapidly*, eating *Alone* from embarrassment, and *Guilt* afterwards. Loss of control is required; three or more of the five features are required.

5.2 The five associated features and the "three of five" rule

Marked distress plus three of five. Beyond the binge itself, the diagnosis requires marked distress and at least three of five associated behavioural features (DSM-5-TR 2022, Criterion B): eating much more rapidly than normal; eating until feeling uncomfortably full; eating large amounts of food when not feeling physically hungry; eating alone because of feeling embarrassed by how much one is eating; and feeling disgusted with oneself, depressed, or very guilty afterward. These are the phenomenology of a compulsive, secretive, affect-driven episode; negative affect is the most common trigger.

CRITERION	REQUIREMENT
A. The binge	**Discrete period (usually under two hours), amount definitely larger than most would eat, with a sense of lack of control**
B. Associated features (three or more)	Eating much more rapidly than normal
B (feature)	Eating until uncomfortably full
B (feature)	Eating large amounts when not physically hungry
B (feature)	Eating alone from embarrassment at the amount
B (feature)	Feeling disgusted, depressed or very guilty afterward
C. Distress	**Marked distress about the binge eating**
D. Frequency	**On average at least once per week for three months**
E. No compensation	**Not regularly accompanied by inappropriate compensatory behaviour; not occurring exclusively during anorexia nervosa or bulimia nervosa**

The binge eating disorder criteria (DSM-5-TR 2022; ICD-11 6B82 aligns, adding the objective/subjective binge distinction). The instrument forms are held on the accompanying scale plate.

GOOD TO REMEMBER

- **Binge eating disorder (the defining criteria):** the anchor is a *recurrent binge with loss of control, marked distress, three or more of five associated features, at least once per week for three months, and no regular compensation*; loss of control is required, the "three of five" is the behavioural gate, and the absence of compensation is what separates it from bulimia.

5.3 The discriminator: binge without compensation

Take away the compensation and it is BED. The single fact that fixes the diagnosis is **binge without compensation**: binge eating disorder shares recurrent binge eating with bulimia nervosa but lacks the regular inappropriate compensatory behaviour (vomiting, laxatives, fasting, driven exercise) that bulimia requires (DSM-5-TR 2022). A second, softer discriminator: unlike bulimia, patients with binge eating disorder do not show marked sustained dietary restriction between binges, and the sequence is reversed, dieting typically *follows* the binge eating in BED, whereas dysfunctional dieting usually *precedes* binge eating in bulimia (DSM-5-TR 2022). The three eating-disorder diagnoses are mutually exclusive for a single episode, so a patient who binges and purges is bulimia, not BED.

FEATURE	BINGE EATING DISORDER	BULIMIA NERVOSA
Recurrent binge with loss of control	**Yes**	Yes
Regular inappropriate compensation	**Absent (the discriminator)**	Present (defining)
Dietary restriction between binges	Not marked; dieting follows binges	Marked; dieting precedes binges
Typical body weight	Overweight or obese (but distinct from obesity)	Often normal weight
Treatment response	**Higher remission rates**	Lower remission rates

Binge eating disorder versus bulimia nervosa; the presence or absence of regular compensatory behaviour is the pivotal discriminator (DSM-5-TR 2022).

RULE **Recurrent binge, loss of control, no regular compensation.** If the binges are recurrent and out of control but there is no regular purging, fasting or driven exercise, the diagnosis is binge eating disorder, not bulimia nervosa. The compensation is the fork in the road.

5.4 Frequency, severity bands and the ICD-11 framing

Severity is graded by binge frequency. Once the diagnosis is made, DSM-5-TR grades severity purely by the average number of binge-eating episodes per week: mild is 1 to 3, moderate 4 to 7, severe 8 to 13, and extreme 14 or more (DSM-5-TR 2022). ICD-11 does not use the same numeric grid but allows the diagnosis to be assigned after a shorter period (for example one month) when multiple binges per week cause significant distress (ICD-11 CDDR). Remission is more common than in bulimia or anorexia, sometimes spontaneously, and crossover to another eating disorder is uncommon.

DSM-5-TR SEVERITY	FREQUENCY (BINGE EPISODES PER WEEK)
Mild	**1 to 3**
Moderate	**4 to 7**
Severe	8 to 13
Extreme	14 or more

DSM-5-TR severity bands for binge eating disorder, graded by weekly binge frequency (severity may be raised for greater distress or disability).

GOOD TO REMEMBER

- **Severity grading (the frequency step):** the anchor value is that *DSM-5-TR grades binge eating disorder by binge episodes per week*, mild 1 to 3, moderate 4 to 7, severe 8 to 13, extreme 14 or more; ICD-11 keeps the "once a week over three months" threshold and may diagnose after one month if binges are frequent and distressing.

5.5 Association with obesity and the metabolic risk

Sits with obesity, but is not obesity. Binge eating disorder occurs in normal-weight, overweight and obese individuals and is reliably associated with overweight and obesity in treatment-seeking samples, carrying the attendant metabolic and cardiovascular morbidity, the weight-related quality-of-life loss, and increased health-care use (DSM-5-TR 2022). But it is distinct from simple obesity: most obese people do not binge; compared with weight-matched obese controls without the disorder, those with BED eat more in laboratory studies, place higher overvaluation on shape and weight, and carry far more psychiatric comorbidity, most commonly major depressive disorder and alcohol use disorder. Crucially, that comorbidity tracks the *severity of the binge eating*, not the degree of obesity (DSM-5-TR 2022).

The clinical implication. This is why weight loss is the wrong therapeutic target (see the management half): the disorder is a psychiatric one that happens to co-travel with obesity, and treating the obesity does not treat the binge eating. Screen the overweight or obese patient who describes secret, out-of-control eating with the eating-disorder screen on the accompanying scale plate rather than reaching only for a weight-loss plan.

PEARL

Binge eating disorder is the eating disorder of the medical and bariatric clinic, not the emaciation ward. It is over-represented among people seeking weight-loss treatment, and the binge eating almost always predates the weight-loss attempt rather than being caused by it. Ask any patient presenting for obesity management about secret, rapid, out-of-control eating; you will find binge eating disorder hiding behind a body mass index far more often than behind a low weight.

5.6 Management, the NICE NG69 lead: guided self-help then CBT-ED

Psychological therapy is the primary treatment. Leading with NICE NG69 (2017): for adults with binge eating disorder, offer a binge-eating-disorder-focused guided self-help programme as the first step. If guided self-help is unacceptable, contraindicated, or ineffective after four weeks, offer group eating-disorder-focused cognitive behavioural therapy (CBT-ED); if group CBT-ED is

unavailable or declined, offer individual CBT-ED (NICE NG69 2017). Children and young people are offered the same treatments as adults (NICE NG69 2017). RANZCP concurs at guideline level that individual therapist-led CBT is the best-evidenced psychological treatment for the disorder (RANZCP 2014).

Weight loss is not the target. NICE is explicit: explain to patients that psychological treatment has a limited effect on body weight, and weight loss is not itself a therapy target (NICE NG69 2017). The goal is to stop the binge eating and the distress it causes; any weight change is a separate, secondary matter managed on its own merits.

TRAP **Chasing weight loss as the treatment.** Treating binge eating disorder as if it were obesity, prescribing a diet and a weight-loss target, is the classic error: NICE says weight loss is not a therapy target and psychological treatment has limited effect on weight. Treat the binge eating with guided self-help and CBT-ED; manage weight, if at all, separately.

GOOD TO REMEMBER

- **Psychological therapy (the first-line step):** the one value is that *binge-eating-disorder-focused guided self-help is first-line, then group CBT-ED, then individual CBT-ED* (NICE NG69 2017), and that *weight loss is not a therapy target*; the goal is to stop the binge eating and its distress, not to slim the patient.

5.7 Pharmacotherapy: adjunctive, never the sole treatment

Medication is an add-on, not a substitute. Do not offer medication as the sole treatment for binge eating disorder (NICE NG69 2017, strong); NICE keeps the psychological therapies primary and does not license a specific drug for the disorder in the UK. Where a drug is used, it sits within a plan that includes psychotherapy and, where relevant, nutritional counselling and treatment of medical complications (WFSBP 2011). The named agents, drawn from the guidelines and the licensing position:

- **Lisdexamfetamine** is the one drug with a specific regulatory licence for binge eating disorder (US FDA), a prodrug stimulant given at 50 to 70 mg per day (initial 30 mg per day, titrated), and is the first medication ever approved for the disorder (Stahl, Prescriber's Guide). It reduces binge frequency; it is a Schedule-controlled stimulant and is not a NICE-recommended UK option.
- An **SSRI, sertraline**, is supported for binge eating disorder (WFSBP 2011, grade A), and RANZCP lists an antidepressant as an adjunctive or alternative option (RANZCP 2014).
- **Topiramate**, the antiepileptic, reduces binge eating (WFSBP 2011, grade A; RANZCP 2014), useful where weight is a concern given its anorectic effect.
- **Orlistat**, the pancreatic lipase inhibitor, is considered for the patient with comorbid obesity, aiding weight but with little direct effect on the binge eating itself (RANZCP 2014; New Oxford Textbook).

GOOD TO REMEMBER

- **Lisdexamfetamine and the adjuncts (the medication step):** the anchor value is that *medication is adjunctive, never the sole treatment* (NICE NG69 2017); lisdexamfetamine (50 to 70 mg per day) is the only agent specifically licensed for binge eating disorder (US FDA, Stahl), with the SSRI sertraline and topiramate (both WFSBP grade A) and orlistat (for comorbid obesity) as the other named options.

5.8 Guideline convergence and the Indian picture

Where the guidelines land. Read together they converge: a psychological therapy is primary (guided self-help then CBT-ED per NICE NG69; individual CBT per RANZCP), weight loss is not the treatment goal, and medication is adjunctive within a psychotherapy-anchored plan (NICE NG69 2017; RANZCP 2014; WFSBP 2011). The one point of divergence is regulatory rather than clinical: only lisdexamfetamine holds a specific licence, and only in the US.

GUIDELINE / SOURCE	PRIMARY TREATMENT	MEDICATION STANCE
NICE NG69 2017	Guided self-help first, then group CBT-ED, then individual CBT-ED; weight loss not a target	**Not the sole treatment; no UK-licensed drug**
RANZCP 2014	Individual therapist-led CBT (best-evidenced)	Antidepressant or topiramate as adjunct; orlistat if comorbid obesity
WFSBP 2011	Psychotherapy plus nutritional counselling	Sertraline (grade A), topiramate (grade A)
US FDA (Stahl)	Adjunct to psychological therapy	**Lisdexamfetamine 50 to 70 mg per day, the only licensed agent**

Guideline-level management of binge eating disorder, NICE NG69-led, converging on a psychological therapy as primary and medication as adjunctive (verified from the drug-guideline supplement; the FDA licence and dose from Stahl).

INDIA

Two India-specific points earn marks. First, under-recognition: eating disorders, and binge eating disorder in particular, are substantially under-recognised in Indian practice, and because binge eating disorder hides behind overweight rather than emaciation it is especially easy to miss in the diabetes, cardiac and bariatric clinics where these patients actually present. Ask the overweight patient with secret, out-of-control eating the eating-disorder screen rather than assuming simple obesity. Second, drug availability: lisdexamfetamine, the only agent with a specific licence for binge eating disorder, is a US FDA licence and the drug is not marketed in India, so Indian practice necessarily leans on the psychological therapies with off-label SSRI (sertraline) or topiramate as the adjunct where one is used. (This availability point is a clinical-practice observation and is flagged for local verification.)

1	3 of 5	50 to 70	4 to 7
BINGE EPISODES FOR DIAGNOSIS, MINIMUM (PER WEEK, OVER THREE MONTHS)	ASSOCIATED FEATURES REQUIRED (WITH MARKED DISTRESS AND LOSS OF CONTROL)	LISDEXAMFETAMINE, THE ONLY LICENSED AGENT (MG PER DAY)	DSM-5-TR MODERATE SEVERITY (BINGE EPISODES PER WEEK)

WORKED EXAMPLE

A 38-year-old man attending a diabetes clinic, BMI 34, discloses that two or three evenings a week he eats a very large amount of food rapidly, alone, after the household is asleep, cannot stop once he starts, and feels disgusted and guilty afterward. He never vomits, fasts or over-exercises to compensate, and does not diet restrictively between episodes. This is binge eating disorder (recurrent binge, loss of control, three or more associated features, marked distress, no compensation), moderate severity by DSM-5-TR frequency. The correct plan is binge-eating-disorder-focused guided self-help first, escalating to group then individual CBT-ED if it fails, with the explicit message that weight loss is not the treatment target; if a drug is added it is adjunctive (an SSRI such as sertraline, or topiramate), not a substitute for the therapy, and lisdexamfetamine is unavailable to him in India.

HOLD THIS

Binge eating disorder is recurrent binge eating with loss of control and marked distress but no regular compensatory behaviour (the discriminator from bulimia); it co-travels with obesity yet is distinct from it; and management is led by NICE NG69, binge-eating-disorder-focused guided self-help then CBT-ED, with weight loss explicitly not a target and medication only ever adjunctive (lisdexamfetamine 50 to 70 mg per day the sole licensed agent, US FDA; sertraline or topiramate the other named options).

6 · Avoidant/restrictive food intake disorder (ARFID)

The eating disorder without the body image. **Avoidant/restrictive food intake disorder** (ARFID) is the disorder of restricted eating that is *not* driven by any wish to be thin. The person avoids or restricts food because of the sensory qualities of food, an apparent lack of interest in eating, or a fear of an aversive consequence such as choking or vomiting, and this **food avoidance** produces weight loss, nutritional deficiency, dependence on supplements or feeds, or psychosocial impairment. What it lacks is the whole engine of anorexia: there is **no body-image disturbance**, no overvaluation of weight and shape, and no fear of gaining weight. That single absence is the examiner's discriminator and the reason the topic exists.

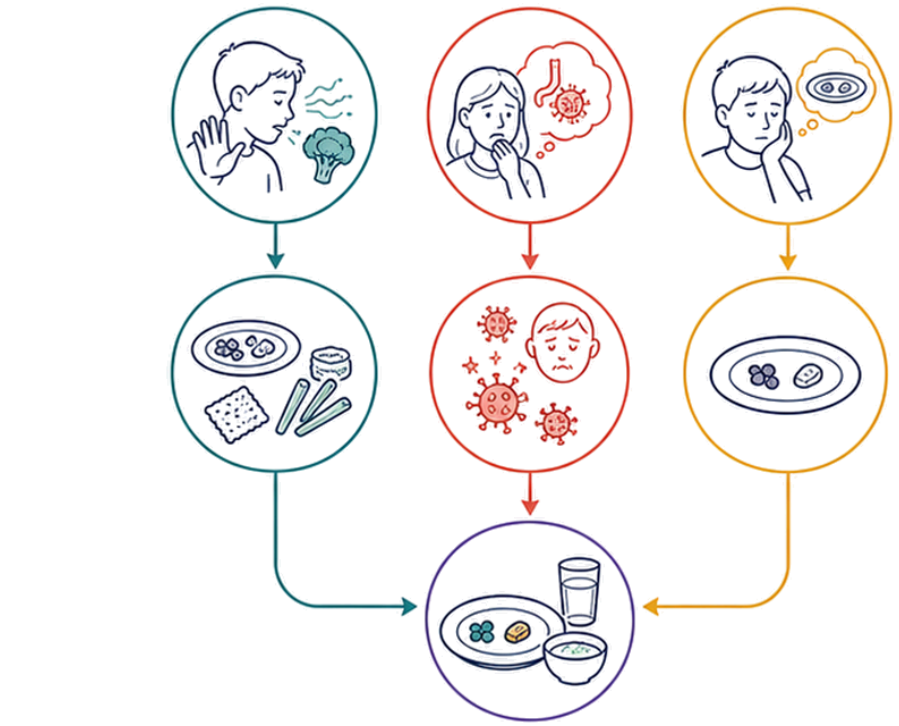


Fig 17.5 Avoidant/restrictive food intake disorder may arise from sensory sensitivity, fear of aversive consequences or low interest in food, leading to inadequate intake without weight-shape overvaluation.

A DSM-5 creation. ARFID was introduced in DSM-5 (carried into DSM-5-TR) to replace and widen the old DSM-IV "feeding disorder of infancy or early childhood", extending it to older children, adolescents and adults; ICD-11 then adopted the same category (6B83). The full name, *avoidant restrictive food intake disorder*, is worth stating in the viva because the components name the syndrome: avoidance or restriction of intake, with functional and nutritional consequences, and without the weight-and-shape psychopathology of anorexia. This note owns the diagnosis and the discrimination from anorexia; the SSRIs sometimes used for comorbid anxiety are detailed in the Mood disorders: pharmacotherapy notes, and the family and cognitive-behavioural techniques in the Psychotherapies, clinical assessment, MSE and nosology notes.

6.1 The DSM-5-TR criteria: an eating disturbance plus one consequence

Criterion A is a disturbance with a consequence. DSM-5-TR criterion A is an eating or feeding disturbance (for example, an apparent lack of interest in eating or food, avoidance based on the sensory characteristics of food, or concern about the aversive consequences of eating) that is associated with *one or more* of four consequences: significant weight loss (or, in a growing child, a

failure to make expected weight gain or faltering growth); significant nutritional deficiency; dependence on **enteral feeding or oral nutritional supplements**; or marked interference with psychosocial functioning (DSM-5-TR 2022).

The exclusions do the diagnostic work. Criterion B excludes restriction better explained by unavailability of food or by a culturally sanctioned practice (a religious fast is not ARFID). Criterion C is the pivotal one: the disturbance does not occur only during anorexia or bulimia, *and there is no disturbance in the way body weight or shape is experienced*. Criterion D excludes restriction fully attributable to a concurrent medical condition or better explained by another mental disorder, unless it exceeds what that condition usually causes.

GOOD TO REMEMBER

- **ARFID (the syndrome):** an eating/feeding disturbance from sensory-based avoidance, low interest in food, or fear of aversive consequences, plus at least one of four consequences (weight loss or faltering growth, nutritional deficiency, dependence on enteral feeding or oral nutritional supplements, or marked psychosocial impairment); the defining exclusion is Criterion C, no body-image disturbance and no overvaluation of weight or shape, which is what separates it from anorexia.

6.2 The three drivers of restriction

Same restriction, three routes in. DSM-5-TR frames the food avoidance through three prototypical, non-exclusive drivers, and naming them is the fastest way to show you understand the disorder.

Sensory-based avoidance

Restriction driven by the appearance, colour, smell, texture, temperature or taste of food; the "selective", "choosy" or "picky" eater and food neophobia, often refusing whole food groups or particular brands, and overlapping with autism-spectrum sensory sensitivity.

Apparent lack of interest in eating or food

A longstanding low appetite, poor recognition of hunger, or simple lack of drive to eat, so intake falls without any conscious avoidance of a feared outcome.

Fear of aversive consequences

A conditioned avoidance following, or in anticipation of, a frightening experience such as choking, vomiting or a traumatic gastrointestinal procedure; the person restricts to prevent the feared event, not to lose weight.

6.3 The line from anorexia nervosa

One question settles it. Is the restriction motivated by weight or shape concern? If the person restricts to be thin, fears fatness, or overvalues weight and shape, it is anorexia nervosa; if the restriction is sensory, appetite-driven or fear-of-consequence driven and body image is intact, it is ARFID. Both can present with a significantly low weight and the same starvation physiology (bradycardia, hypothermia, anaemia), so the differentiation is psychological, not physical. The figure alongside lays the two side by side.

FEATURE	ARFID	ANOREXIA NERVOSA
Body-image / weight-shape overvaluation	**Absent (no body-image disturbance)**	Present and central
Fear of weight gain / drive for thinness	Absent	Present, or weight-defeating behaviour
Reason for restriction	**Sensory aversion, low interest/appetite, or fear of choking or vomiting**	To lose weight or avoid becoming fat
Typical age at onset	Infancy or early childhood	Adolescence or early adulthood
Sex distribution	More often male than in anorexia	Strongly female
Weight	Low or faltering growth (may be normal)	Significantly low (required)

ARFID versus anorexia nervosa; the discriminator is the presence or absence of body-image disturbance and weight/shape overvaluation, not the weight itself (DSM-5-TR 2022; New Oxford Textbook of Psychiatry).

RULE **No body-image disturbance is the line.** Restricted eating with weight loss but no overvaluation of weight or shape and no fear of fatness is ARFID, not anorexia; the absence of the body-image psychopathology is the diagnosis, even when the weight is dangerously low.

GOOD TO REMEMBER

- **ARFID versus anorexia (the discriminator):** both can reach a significantly low weight, but ARFID has intact body image and no drive for thinness, restricting for sensory, appetite or aversive-consequence reasons; anorexia is defined by weight/shape overvaluation and fear of weight gain. Ask why the person restricts.

6.4 The typical presentation, comorbidity and epidemiology

A disorder of childhood, more often male. ARFID most commonly begins in infancy or early childhood and can persist into adulthood. Compared with anorexia, patients are younger, more likely to be male, more likely to carry a comorbid medical condition or an anxiety disorder, and less likely to have a mood disorder (New Oxford Textbook of Psychiatry). The strongest associations are with autism spectrum disorder and neurodevelopmental conditions (the sensory subtype), with anxiety disorders, and with low bone mineral density from chronic undernutrition. Very young infants may present with food refusal, gagging or vomiting and failure to engage with the caregiver at feeds.

Prevalence is uncertain but not trivial. The community prevalence is not established, but among paediatric eating-disorder inpatients ARFID accounts for roughly **5% to 14%** of admissions, so it is a real and separable slice of eating-disorder practice rather than a rarity (New Oxford Textbook of Psychiatry).

3	4	14%
RECOGNISED DRIVERS OF RESTRICTION	CRITERION A CONSEQUENCES (AT LEAST ONE REQUIRED)	UPPER ARFID SHARE OF PAEDIATRIC ED INPATIENTS (FROM 5%)

TRAP **Dismissing it as ordinary fussy eating.** The classic error is to write off ARFID as a phase of picky eating and miss the weight loss, nutritional deficiency or supplement dependence that defines it; conversely, do not label a restrictor as ARFID if body-image concern is actually present, because that is anorexia.

6.5 Management in brief, and the Indian frame

Multidisciplinary, and no first-line drug. There are no randomised trials and no established medication for ARFID; management rests on a multidisciplinary team providing medical stabilisation, nutritional rehabilitation and psychological treatment, with family therapy central for a child so that parents can manage intake. Feared-consequence presentations respond to graded exposure and cognitive-behavioural work; sensory presentations to structured food-chaining and desensitisation. Where drugs are used they are adjuncts of unproven efficacy: SSRIs (for example fluoxetine or sertraline) for a comorbid anxiety disorder, mirtazapine or olanzapine to promote weight gain, and the antihistaminic appetite stimulant cyproheptadine, all off-label and evidence-thin (Maudsley Guidelines). The dosing of the antidepressants sits in the Mood disorders: pharmacotherapy notes, and the exposure and family techniques in the Psychotherapies, clinical assessment, MSE and nosology notes.

GOOD TO REMEMBER

- **ARFID management (the value):** no drug is first-line and none is licensed; the treatment is multidisciplinary nutritional rehabilitation plus psychological therapy (family-based for children, graded exposure for the choking/vomiting-fear type, sensory desensitisation for the selective type), with SSRIs, mirtazapine, olanzapine or cyproheptadine used only as unproven off-label adjuncts (New Oxford Textbook of Psychiatry; Maudsley Guidelines).

INDIA

Two Indian realities meet in this diagnosis. First, eating disorders are widely under-recognised here, and a child's restrictive or "choosy" eating with faltering growth is easily normalised as fussiness rather than assessed, so ARFID reaches care late and undernourished. Second, ARFID is easy to confuse with the **non-fat-phobic** anorexia presentation that is relatively common in Indian and other Asian patients, where a person rationalises restriction as poor appetite or abdominal discomfort. The discriminator is the same one question: is there any overvaluation of weight or shape? If yes, it is anorexia despite the somatic framing; if the body image is genuinely intact, it is ARFID. Weigh the child, plot growth, and screen for the anxiety and neurodevelopmental comorbidity that so often sits underneath.

HOLD THIS

ARFID is restricted eating from sensory-based avoidance, an apparent lack of interest in food, or fear of an aversive consequence (choking, vomiting), causing weight loss or faltering growth, nutritional deficiency, dependence on supplements or feeds, or psychosocial impairment, with no fear of fatness and no body-image disturbance; it is a DSM-5 creation (also ICD-11 6B83), usually starts in early childhood and more often in boys, and is managed by a multidisciplinary team with no first-line drug.

7 · The aetiology and neurobiology of eating disorders

Why one disorder becomes an eating disorder. No single gene, family or magazine causes an eating disorder; each arises where a heritable temperament meets a developmental window and a culture that rewards thinness. The examiner tests this as a **biopsychosocial** synthesis, so the safe answer names risk from three tiers at once and refuses a single cause. This note owns the causal model: the **aetiology of eating disorders** (the genetic and heritability data, the temperament and personality risk, the sociocultural and family factors, the life-event triggers) and the **neurobiology of eating disorders** (the appetite-regulation circuitry, the hypothalamic homeostatic control, leptin and ghrelin, the serotonin and dopamine systems, the reward and cognitive-control circuits, and the interoception literature).

The diagnoses themselves are set out in the anorexia-nervosa, bulimia-nervosa and binge-eating-disorder topics in these notes; the neuroendocrine axes that fail in the starved state (the hypothalamic-pituitary-gonadal, thyroid and adrenal changes) are derived in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and used here only in causal form. What follows is the machinery: which risks load the dice before the illness, and which brain systems keep it running once weight is lost. The single most useful teaching point sits underneath the whole account, that many of the "biological findings" in a low-weight patient are *consequences* of starvation rather than its cause, which is why the state-versus-trait distinction runs through every subtopic.

7.1 The biopsychosocial model as the organising frame

Three tiers, one threshold. The **biopsychosocial** model holds that eating disorders emerge from an interaction of predisposing, precipitating and perpetuating factors across biological, psychological and social tiers, none sufficient alone. A heritable vulnerability (a particular temperament, a susceptibility to anxiety or affective instability, or a neurocircuitry difference) is expressed only under adverse conditions such as ill-judged dieting or emotional stress, and is then locked in by the effects of starvation itself. This gene-environment framing is why the aetiology of eating disorders is written as a convergence, not a chain.

Predispose, precipitate, perpetuate. A clean way to hold it is by timing: *predisposing* factors (genes, temperament, family and cultural context) set the vulnerability; a *precipitant* (a diet that "works", a life event, puberty) tips a susceptible person over; and *perpetuating* factors (the neuroendocrine and cognitive effects of the starved or binge-purge state) hold the disorder in place and make it self-reinforcing.

RULE **No single cause; name three tiers.** Eating disorders are multifactorial and biopsychosocial. A heritable temperament, a precipitating stressor or diet, and a perpetuating starved or binge-purge state converge, so the correct answer refuses a monocausal ("it is just the media") account.

7.2 Genetics and heritability

The disorders run in families and twins. Family studies show an increased risk of anorexia nervosa and bulimia nervosa in the relatives of affected probands, and more binge-eating disorder among the first-degree relatives of people with binge-eating disorder. Twin studies

comparing identical with fraternal pairs give heritability estimates of roughly **33% to 84%** for anorexia nervosa, **28% to 83%** for bulimia nervosa, and **41% to 57%** for binge-eating disorder, with the remaining variance attributed largely to unique (non-shared) environment; adoption data for disordered-eating symptoms fall in the same high range (Kaplan and Sadock 2024). The wide bands reflect small early samples, but the message is consistent, that these are substantially heritable conditions.

Candidate genes and the modern reframe. Linkage work put signals on chromosome 1 near the serotonin 1D receptor gene (HTR1D) and the delta-opioid receptor gene (OPRD1), and the BDNF Met66 variant has been associated with the *restricting* type of anorexia nervosa, consistent with the disorder's serotonergic, reward and neurotrophic biology. Early candidate-gene and small genome-wide studies were largely non-replicating; the field has since moved to large collaborative genome-wide association studies, which point to overlap of anorexia nervosa with *metabolic and anthropometric* traits as well as psychiatric ones, an emerging reframe of anorexia as partly a "metabo-psychiatric" condition rather than a purely psychological one.

GOOD TO REMEMBER

- **Heritability of the eating disorders:** twin-study estimates are roughly 33% to 84% for anorexia nervosa, 28% to 83% for bulimia nervosa and 41% to 57% for binge-eating disorder; substantial genetic loading with the rest largely non-shared environment, and the candidate signals cluster on serotonergic (HTR1D), opioid (OPRD1) and neurotrophic (BDNF) genes.

7.3 Temperament and personality risk

The anorexic and bulimic temperaments differ. A meta-analysis of the Temperament and Character Inventory found significantly higher *harm avoidance* and *persistence* in anorexia nervosa than in bulimia nervosa, binge-eating disorder or controls, whereas *novelty seeking* was elevated specifically in bulimia nervosa, which also shows greater impulsivity and low self-directedness (Kaplan and Sadock 2024). The restricting anorexic tends toward an anxious, rigid, over-controlled style; the bulimic toward an impulsive, dysregulated one, mirroring the behaviours of restriction versus binge-purge.

Perfectionism is the signature trait. Perfectionism was the psychological feature first tied to anorexia nervosa; higher scores track lower body weight, more eating rituals and less motivation to change, and are most severe where obsessive-compulsive personality disorder or obsessive-compulsive disorder co-occur. Trait anxiety, a common accompaniment, predicts a lower likelihood of recovery. Crucially, harm avoidance falls and reward dependence rises after weight restoration, a reminder that some "traits" are partly state effects of starvation.

PEARL

Read the temperament off the behaviour: **harm avoidance, persistence and perfectionism** load the over-controlled, anxious restricting anorexic; **novelty seeking, impulsivity and low self-directedness** load the dysregulated bulimic. This is why obsessive-compulsive traits cluster with anorexia and impulse-control and affective-dysregulation problems cluster with bulimia.

7.4 Sociocultural and family factors

The thin ideal, internalised. The social tier is the internalisation of a culturally transmitted *thin ideal*: exposure to media and peer messages that equate slimness with worth, body dissatisfaction, and dieting as the normative response, amplified in weight-sensitive settings (ballet, modelling, gymnastics, wrestling). Sociocultural pressure is neither necessary nor sufficient, but it shapes which vulnerable individuals cross into disordered eating and gives the illness its content (the fear of fatness, the over-valuation of shape).

Family influence, without blame. Family factors include parental psychiatric illness (eating disorders, anxiety, affective disorders and substance use aggregate in families), parental attitudes to weight and eating, and interaction patterns. The modern reading is that the family is a legitimate arena for *treatment* (family-based therapy is first-line for young people, set out in the anorexia-management topic in these notes) rather than a place to assign cause; the old "psychosomatic family" typology is not an evidence-based aetiology.

7.5 Life-event triggers and the developmental window

Adolescence is the vulnerable window. Onset clusters in adolescence and early adulthood because puberty, identity formation and the surge in body concern coincide with rising autonomy over eating; puberty and age themselves moderate the genetic influence on eating-disorder traits. The commonest precipitant is a diet that "works", producing early praise or a sense of control that becomes self-reinforcing as weight falls.

Stressors and adversity as precipitants. Life events (loss, transition, bullying about weight, interpersonal or family stress) and, in a subset, childhood adversity or trauma act as non-specific precipitants that tip a predisposed person over the threshold. They are risk-raising rather than disorder-specific, which is why the same adversity elsewhere produces mood or anxiety pathology instead.

7.6 The homeostatic appetite-regulation circuit

Where appetite is computed. Normal **appetite regulation** is a distributed network, but its homeostatic core is the hypothalamic arcuate nucleus, which holds two opposing neuron populations. One expresses pro-opiomelanocortin and releases alpha-melanocyte-stimulating hormone (an *anorexigenic*, satiety signal); the other co-expresses neuropeptide Y, agouti-related peptide and GABA (an *orexigenic*, hunger signal). The two are mutually inhibitory and project to the paraventricular nucleus (satiety) and the lateral hypothalamic area (feeding, via orexin and melanin-concentrating hormone) (Kaplan and Sadock 2024).

The melanocortin switch. The opposing arcuate signals converge on a single receptor, the melanocortin-4 receptor: alpha-MSH is its agonist (dampening intake) and agouti-related peptide its inverse agonist (driving intake). Loss-of-function mutations in the melanocortin-4 receptor or in pro-opiomelanocortin are the commonest monogenic human obesity, seen in about **1% to 2%** of people with obesity, which shows how much of intake this one node sets. Downstream, the mesolimbic dopamine projection from the ventral tegmental area to the nucleus accumbens adds the *hedonic* layer that homeostasis alone does not.

GOOD TO REMEMBER

- **Arcuate two-population model:** pro-opiomelanocortin/alpha-MSH neurons are anorexigenic (satiety) and the neuropeptide Y/agouti-related peptide/GABA neurons are orexigenic (hunger); they act oppositely on the melanocortin-4 receptor, with alpha-MSH the agonist and agouti-related peptide the inverse agonist. Leptin excites the anorexigenic set and inhibits the orexigenic set; ghrelin does the reverse.

7.7 Leptin and ghrelin: the two hormones to know

Leptin, the adiposity signal. Leptin is a hormone secreted by adipocytes in proportion to fat mass; its physiological job is to *defend against underweight* (a fall in leptin powerfully increases eating and lowers energy expenditure, while a rise above the usual level does little). In anorexia nervosa serum leptin is markedly low and tracks the loss of adipose tissue, rising as weight is regained, and the same low leptin drives the suppression of the reproductive axis and the amenorrhoea. It is almost certainly a *consequence* of the low weight, not a cause. The leptin (ob) gene was cloned in 1994, and the name comes from the Greek *leptos*, "thin".

Ghrelin, the hunger signal. Ghrelin is a peptide released mainly by enteroendocrine cells of the stomach; plasma levels rise before meals and during fasting and fall after eating, making it the principal circulating *orexigenic* signal (it acts on the arcuate nucleus and on reward nodes such as the ventral tegmental area and nucleus accumbens). In anorexia nervosa ghrelin is *elevated* and falls toward normal with weight gain, read as an unheeded hunger drive; in bulimia nervosa the post-meal suppression of ghrelin is blunted, consistent with impaired post-ingestive satiety that may permit binges.

HORMONE	SOURCE AND DIRECTION	ANOREXIA NERVOSA	BULIMIA NERVOSA
Leptin	Adipocytes; anorexigenic (satiety), defends against underweight, rises with fat mass	**Markedly low; rises as weight is regained (drives amenorrhoea)**	Variable / near-normal
Ghrelin	Stomach; orexigenic (hunger), rises before meals, falls after eating	**Elevated; falls toward normal with weight gain**	Blunted post-meal suppression (impaired satiety)

The two examinable appetite hormones and their direction of change; leptin falls and ghrelin rises in the starved anorexic state, both largely as consequences of low weight (Kaplan and Sadock 2024).

MNEMONIC

LEPTIN LEAN, GHRELIN GROWLS

Leptin from fat says "we are fat enough" (Greek *leptos*, thin), an anorexigenic satiety signal that is *low* when the anorexic is lean; **Ghrelin** is the growling-stomach hunger hormone that rises before meals and is *high* in anorexia nervosa, an ignored drive to eat.

TRAP **Calling starvation biology the cause.** The low leptin, high ghrelin, sick-euthyroid pattern and high cortisol of a low-weight patient are largely *state* effects of starvation that reverse with refeeding, not proof of a primary hormonal cause; reading them as causal (or as a hormone disorder to correct) is the classic reverse-causation error.

7.8 The serotonin and dopamine systems

Serotonin, anxiety and restraint. Of all the transmitter systems the serotonin eating disorder link is the most studied, because serotonin is both anxiogenic and inhibitory to feeding, exploration and sexual behaviour, all of which are suppressed in anorexia nervosa. PET studies of *recovered* patients (studied off the confounding starved state) show reduced 5-HT2A receptor binding in the insula, cingulate and temporal cortex, and the degree of binding change correlates positively with harm avoidance, tying the serotonin abnormality to the anxious temperament; in bulimia nervosa altered orbitofrontal serotonin binding maps instead onto impulsivity. This is the neurochemical rationale behind fluoxetine's role in bulimia nervosa (developed in the bulimia-nervosa and Mood disorders: pharmacotherapy notes).

Dopamine and altered reward. The dopamine reward system is also disturbed: recovered anorexia-nervosa women show increased dopamine D2/3 receptor availability in the ventral striatum and an altered striatal response to food and monetary reward, so the normal link between a rewarding stimulus and the striatal "wanting" signal is uncoupled. One reading is that in anorexia nervosa restraint is experienced as rewarding and eating as anxiety-provoking, an inversion of the usual valence of food.

GOOD TO REMEMBER

- **Serotonin and dopamine in the eating disorders:** recovered anorexia nervosa shows reduced 5-HT2A binding (insula and cingulate) that correlates with harm avoidance, and increased striatal dopamine D2/3 availability with altered reward processing; bulimia nervosa maps onto orbitofrontal serotonin changes and impulsivity. Studying recovered patients separates trait from the state effects of starvation.

RULE **Study the recovered brain to find the trait.** Because starvation itself distorts every measure, the reliable neurobiological signatures (reduced 5-HT2A binding tied to harm avoidance, altered striatal reward) come from *recovered* patients; a finding present only in the ill state is a state marker, not a cause.

7.9 Reward, cognitive control and interoception

Three circuits carry the pathology. The neurobiology of eating disorders converges on three overlapping systems: *taste and reward* processing (ventral striatum, orbitofrontal cortex and the mesolimbic dopamine projection), *cognitive and inhibitory control* (dorsolateral prefrontal and frontostriatal circuits, over-active in the rigid restraint of anorexia, under-active in the disinhibited binge of bulimia and binge-eating disorder), and *interoception*. The balance between an over-controlling executive system and a dysregulated reward system helps explain why the same broad biology yields restriction in one patient and bingeing in another.

The interoceptive insula. Interoception, the sensing of internal bodily states such as hunger, fullness and affect, is served by the anterior insula, and it is disturbed across the eating disorders: anorexic patients show altered insular responses to taste and an impaired reading of hunger and satiety, so the normal interoceptive signals that should start and stop a meal are mis-weighted. This interoceptive account links the appetite abnormality to the body-image disturbance and is one of the more active research frontiers.

33–84%	28–83%	57%	1994
AN TWIN-STUDY HERITABILITY RANGE	BN TWIN-STUDY HERITABILITY RANGE	BED HERITABILITY (UPPER TWIN ESTIMATE)	YEAR THE LEPTIN (OB) GENE WAS CLONED

7.10 The India lens: culture, the thin ideal and under-recognition

The sociocultural story is not only Western. The thin-ideal account was built on affluent Western samples, yet the classic Indian and pan-Asian presentation is the *non-fat-phobic* anorexia, in which the person attributes restriction to abdominal discomfort, poor appetite or a religious fast rather than a stated wish to be thin. This both complicates a purely sociocultural aetiology (the fear of fatness is not universal) and matters practically, because the diagnosis still stands on behaviour and a significantly low weight. As the globalised thin ideal reaches urban India, presentations are rising and shifting toward the Western fat-phobic pattern, so the cultural tier is a moving target here.

Under-recognition is the clinical reality. Eating disorders are under-detected in India, dismissed as ordinary dieting or a physical complaint and stereotyped as an affluent-urban-female problem, so men and lower-income patients are missed; the genetic, temperamental and interoceptive vulnerabilities described above are not culture-bound even where the presentation is atypical. The applied lesson from the aetiology is a low threshold to screen (the SCOFF, in the anorexia-nervosa topic in these notes) rather than to wait for a textbook fear of fatness.

INDIA

Two aetiological points travel differently here. First, the **non-fat-phobic** presentation is relatively common in Indian and Asian patients, undercutting a purely thin-ideal causal story and reminding you the biology (heritable temperament, altered serotonin, dopamine and interoception) is not culture-bound. Second, as the globalised thin ideal spreads to urban India, incidence is rising even as eating disorders stay widely under-recognised, so weigh, screen and take the risk seriously in men and lower-income patients too, not only affluent young women.

WORKED EXAMPLE

A 16-year-old girl develops anorexia nervosa after a "successful" diet before an exam. The biopsychosocial formulation writes the causes in tiers: *predisposing*, a family history of anxiety and her own perfectionism and high harm avoidance (heritable temperament, with candidate serotonergic and neurotrophic loading); *precipitating*, the pubertal window, exam stress and the diet that drew praise; *perpetuating*, the starved state itself, low leptin and high ghrelin, a 5-HT2A and striatal-reward picture that makes restraint feel rewarding and eating anxiety-provoking, and mis-read interoceptive hunger and satiety signals. No tier alone explains her; together they do.

HOLD THIS

Eating disorders are biopsychosocial and substantially heritable (twin estimates roughly 33% to 84% for anorexia nervosa); a perfectionistic, harm-avoidant temperament plus a precipitant (dieting, puberty, stress) meets an appetite-regulation circuit (the arcuate pro-opiomelanocortin/alpha-MSH satiety versus neuropeptide Y/agouti-related peptide hunger neurons acting on the melanocortin-4 receptor) tuned by leptin (low in anorexia, defends against underweight) and ghrelin (high in anorexia, the hunger signal), with reduced 5-HT2A binding tied to harm avoidance, altered striatal dopamine reward, and disturbed insular interoception; most hormonal findings in a low-weight patient are consequences of starvation, not its cause.

8 · Pica, rumination and other feeding disorders

The feeding disorders below the famous eating disorders. Beneath anorexia, bulimia and binge-eating sit three quieter diagnoses the syllabus still expects you to define crisply: **pica**, **rumination disorder**, and the residual "**other feeding disorders**" that capture presentations falling short of a full syndrome. They are grouped with the eating disorders because each is a persistent disturbance of eating or eating-related behaviour that harms physical health or functioning, but they carry no drive for thinness and no body-image psychopathology. The reward in a viva is precise criterion recall, the developmental and comorbidity context (they cluster with intellectual disability and autism), and two or three sharp discriminators.

Small topic, clean marks. DSM-5-TR and ICD-11 both give each entity its own code (ICD-11: **6B84 Pica**, **6B85 Rumination-regurgitation disorder**, **6B8Y** other specified and **6B8Z** unspecified). This note owns the definitions, the developmental frame and the brief management; the full anorexia and bulimia syndromes have their own notes, the SSRI dosing used for comorbidity sits in the Mood disorders: pharmacotherapy notes, and the behavioural and family techniques in the Psychotherapies, clinical assessment, MSE and nosology notes.

8.1 Pica: the persistent eating of non-nutritive substances

Four criteria, and a suggested floor age. Pica is the persistent eating of **non-nutritive substances** (paper, soap, cloth, hair, soil, chalk, paint, metal, pebbles, charcoal, clay, starch or ice) over a period of at least one month (Criterion A), that is inappropriate to the person's developmental level (Criterion B) and is not part of a culturally supported or socially normative practice (Criterion C); if it occurs within another disorder or in pregnancy, it counts only when severe enough to warrant independent attention (Criterion D). A minimum age of **2 years** is suggested, to exclude the ordinary mouthing and swallowing of objects by infants (DSM-5-TR 2022).

Two exclusions carry the diagnosis. Criterion B and Criterion C are what the examiner is testing. The substance must be developmentally out of place (a toddler mouthing a toy is not pica; a school-age child eating chalk daily may be), and it must not be a sanctioned cultural practice, because in several communities the eating of earth or clay is a valued or normative behaviour rather than a disorder.

RULE **Non-nutritive, non-food, out of place, not cultural.** Pica is diagnosed only when the eaten substance is nutritionally empty, developmentally inappropriate (suggested floor of two years) and outside any culturally sanctioned practice; take away any one of those and it is not pica.

8.2 Pica: the classic subtypes and the real danger

Name the substance, name the risk. Pica is traditionally sub-labelled by what is eaten, and the medical danger tracks the specific substance rather than the behaviour itself.

Geophagia

Eating of earth, soil, mud or clay; the commonest form worldwide, frequent in pregnancy and where soil is culturally used, and a route to parasitic infection and lead exposure.

Pagophagia

Compulsive eating of ice; the form most tightly linked to iron-deficiency anaemia and often the first clue to it.

Amylophagia

Eating of raw starch (uncooked rice, flour, laundry starch), again associated with pregnancy and iron deficiency.

Trichophagia and coprophagia

Eating of hair (risking a trichobezoar and bowel obstruction) and of faeces; the hair form overlaps with trichotillomania.

The complications are what kill. Pica reaches medical attention through its consequences: broken teeth, choking, intestinal obstruction or perforation, a **bezoar**, infection (toxoplasmosis, toxocariasis from soil or faeces) and **lead or other poisoning**. It is significantly associated with anaemia, low haemoglobin and low plasma zinc, though the direction of causation is uncertain (New Oxford Textbook of Psychiatry). Prevalence is roughly **5%** among school-age children, and a worldwide meta-analysis put it near **28%** in pregnancy or the postpartum period.

GOOD TO REMEMBER

- **Pica (the syndrome):** persistent eating of non-nutritive, non-food substances for at least one month, developmentally inappropriate (suggested minimum age two years) and not culturally sanctioned; the defining discriminator from anorexia is that the substance is nutritionally empty and not eaten to control weight, and the danger (obstruction, bezoar, lead poisoning, infection) tracks the specific item ingested (DSM-5-TR 2022; New Oxford Textbook of Psychiatry).

WORKED EXAMPLE

A pregnant woman is brought with weeks of compulsively crunching ice and, on questioning, eating small amounts of raw rice. Her haemoglobin is low. This is pagophagia with amylophagia, developmentally inappropriate and not a sanctioned practice, so it meets pica; the pica is best read as a flag for iron-deficiency anaemia, which is corrected while the eating is monitored. Contrast this with a woman from a community where a little clean earth is eaten in pregnancy as an accepted custom: Criterion C removes that from the diagnosis.

8.3 Rumination disorder: repeated, effortless regurgitation

Bring it up, re-chew, re-swallow or spit. Rumination disorder is the repeated regurgitation of food over at least one month, where the regurgitated food may be re-chewed, re-swallowed or spat out (Criterion A); the behaviour is *not* attributable to a gastrointestinal or other medical condition such as gastro-oesophageal reflux or pyloric stenosis (Criterion B), does not occur exclusively during anorexia, bulimia, binge-eating disorder or ARFID (Criterion C), and when it sits inside another disorder must be severe enough to warrant separate attention (Criterion D). The regurgitation is frequent, at least several times a week and typically each day (DSM-5-TR 2022).

The signature is that it is effortless and calm. Previously swallowed food is brought up without apparent nausea, retching or disgust, often preceded only by an urge or a belching sensation, and the regurgitant is recognisable and may taste pleasant, tending to stop once it turns acidic. In infants and in people with intellectual disability the act appears to serve a self-soothing or self-stimulating function, akin to other repetitive behaviours; infants show a characteristic straining, back-arching posture with tongue-sucking movements.

TRAP **Reading rumination as vomiting or reflux.** The classic error is to chase regurgitation as gastro-oesophageal reflux or vomiting and miss the psychiatric diagnosis; rumination is effortless, painless, without nausea or retching, brings up recognisable pleasant-tasting food, and is a diagnosis made only once genuine gastrointestinal disease is excluded.

PEARL

A quiet nosological difference is worth a mark: DSM-5-TR allows rumination disorder to be diagnosed across the lifespan, *including in infancy*, whereas ICD-11 states it should *not* be diagnosed in infants and frames the regurgitation as intentional and relatively easy to induce. Same phenomenon, two thresholds.

GOOD TO REMEMBER

- **Rumination disorder (the syndrome):** repeated, effortless regurgitation of food for at least one month, re-chewed, re-swallowed or spat out, with no nausea or retching, once a gastrointestinal cause (reflux, pyloric stenosis, achalasia, Sandifer syndrome) is excluded and it is not confined to another eating disorder; the discriminator from vomiting is the calm, painless, non-nauseated bringing-up of pleasant recognisable food (DSM-5-TR 2022).

8.4 The other feeding disorders: the residual categories

Clinically real, but sub-threshold or unnamed. The "**other feeding disorders**" are the two residual boxes: other specified feeding or eating disorder (OSFED; ICD-11 6B8Y), where the clinician states why the full criteria are not met, and unspecified feeding or eating disorder (UFED; ICD-11 6B8Z), used when the reason is not specified or information is incomplete, as in an emergency setting. OSFED is not a soft or trivial category, it is often the commonest eating-disorder diagnosis in the community.

Five OSFED presentations are worth naming. DSM-5-TR lists them explicitly.

Atypical anorexia nervosa

All anorexia criteria are met except that, despite significant weight loss, weight is within or above the normal range; the physiological complications can still be severe.

Bulimia / binge-eating disorder of low frequency or limited duration

The full behavioural pattern, but below the frequency or duration threshold of the parent diagnosis.

Purging disorder

Recurrent purging (self-induced vomiting, laxative or diuretic misuse) to influence weight or shape, in the absence of binge eating.

Night eating syndrome

Recurrent eating after waking from sleep, or excessive intake after the evening meal, with awareness and recall, causing distress and not better explained by binge-eating disorder or a circadian shift.

GOOD TO REMEMBER

- **Other feeding disorders (the residual categories):** OSFED (6B8Y) names the reason full criteria are unmet, UFED (6B8Z) does not; the five OSFED exemplars are atypical anorexia nervosa (weight normal or above despite the illness), low-frequency or limited-duration bulimia and binge-eating disorder, purging disorder (purging without binges) and night eating syndrome; the defining move is that a clinically significant eating disturbance is present but sits below a named threshold (DSM-5-TR 2022).

8.5 The shared developmental and comorbidity thread

One question opens all three. Pica and rumination in particular cluster with intellectual developmental disorder and autism spectrum disorder, begin most often in childhood, and can serve a self-soothing or self-stimulating function; both can also arise in otherwise typically developing children and persist or first appear in adults. Screening for neurodevelopmental disorder, neglect and understimulation, and for the medical consequences, belongs in every assessment. The figure alongside sets the three residual feeding disorders next to their discriminators.

ENTITY	DEFINING FEATURE	KEY DISCRIMINATOR
Pica	Eating of non-nutritive, non-food substances for at least one month	**Developmentally inappropriate and not culturally sanctioned; substance not eaten to control weight**
Rumination disorder	Effortless repeated regurgitation, re-chewed or spat out, for at least one month	**No nausea or retching; not due to a gastrointestinal condition; not confined to another eating disorder**
Atypical anorexia (OSFED)	Full anorexia picture despite weight in or above the normal range	Weight is not significantly low, so it falls outside anorexia proper
Shared context	Onset usually in childhood; self-soothing function common	Strong link to intellectual disability and autism; screen for both

The three residual feeding disorders and the single discriminating question that separates each from its neighbours (DSM-5-TR 2022; ICD-11).

2	5%	28%	1 to 2%
MINIMUM SUGGESTED AGE FOR PICA (YEARS)	PICA PREVALENCE, SCHOOL-AGE CHILDREN	PICA IN PREGNANCY OR POSTPARTUM (META-ANALYSIS)	RUMINATION DISORDER, GRADE-SCHOOL CHILDREN

8.6 Management in brief: assess, correct, behavioural first

No first-line drug; behaviour and the underlying deficit lead. There are no adequately powered randomised trials for either pica or rumination, so treatment is pragmatic. For pica, begin with a thorough medical and psychological assessment, treat any complication (obstruction, poisoning, infection) and correct an identified deficiency such as iron-deficiency anaemia, which may reduce the behaviour, although supplementation trials have been negative and resolution is not guaranteed; the best-evidenced psychological approach is behavioural, with applied behaviour analysis and reinforcement-plus-response-reduction procedures, delivered by a multidisciplinary team. Medication is reserved for comorbidity: an SSRI such as fluoxetine (Indian brands Prodep, Fludac, Flunil) where depression or obsessive-compulsive features co-occur, and methylphenidate where ADHD co-occurs, both on case-report evidence only.

Rumination is treated behaviourally across all ages. After excluding gastrointestinal disease (reflux, achalasia, gastroparesis, Sandifer syndrome; manometry with impedance can help), the mainstay is behavioural. Diaphragmatic breathing, which competes with the urge to regurgitate, is the first-line technique for children, adolescents and adults; in young children, changing feeding posture, distraction at onset and parent-directed work are added. Antidepressant dosing is detailed in the Mood disorders: pharmacotherapy notes and the wider behavioural frame in the Psychotherapies, clinical assessment, MSE and nosology notes.

GOOD TO REMEMBER

- **Pica and rumination management (the value):** no drug is first-line and none is licensed for either; treat the medical complications, correct any deficiency (iron), and lead with behavioural therapy (applied behaviour analysis for pica, diaphragmatic breathing for rumination across all ages), reserving an SSRI or methylphenidate only for comorbid depression, OCD or ADHD on weak evidence (New Oxford Textbook of Psychiatry).

INDIA

Three Indian realities meet here. First, *geophagia* and the eating of raw starch are genuinely common in pregnancy and in some communities, so Criterion C does heavy lifting: earth-eating that is a sanctioned local custom is not pica, whereas the same behaviour causing anaemia, obstruction or lead exposure is. Second, the high background rate of iron-deficiency anaemia in Indian women and children makes pagophagia and amylophagia frequent and clinically useful red flags for anaemia that are easily dismissed as habit. Third, feeding and eating disorders are broadly under-recognised in India, and the **non-fat-phobic** presentations that dominate here mean a clinician must actively ask why a person is eating, or not eating, rather than assume the classic picture. Weigh, check haemoglobin, and consider lead where pica is chronic.

HOLD THIS

Pica is the persistent eating of non-nutritive, non-food substances for at least one month, developmentally inappropriate and not culturally sanctioned (suggested floor of two years); rumination disorder is repeated, effortless, non-nauseated regurgitation for at least one month once gastrointestinal disease is excluded; the "other feeding disorders" (OSFED and UFED) catch sub-threshold or unspecified presentations such as atypical anorexia; all three cluster with intellectual disability and autism, carry no drive for thinness, and are led by behavioural treatment with no first-line drug.

9 · Atypical eating disorders, orthorexia and OSFED

The residual bin that is not a dustbin. Not every disordered eater fits the tidy boxes of anorexia, bulimia, binge-eating disorder, ARFID, pica or rumination. A large share of real, impairing eating pathology sits just outside those thresholds, and the classifications capture it in a residual category: **other specified feeding or eating disorder** (OSFED) in DSM-5-TR, the successor to the old DSM-IV EDNOS. This note owns that residual space, plus two entities the exam loves to test at its edges: orthorexia nervosa, a pathological preoccupation with "healthy" or "pure" eating that is not a formal diagnosis, and the **non-fat-phobic** anorexia presentation that is comparatively common in Indian and other Asian patients.

Why it earns exam time. The whole point of these categories is to stop the clinician dismissing a genuine, dangerous disorder because it misses a threshold by a hair. An **atypical anorexia** patient can be normal-weight and still be in starvation physiology; a non-fat-phobic patient can deny any fear of fatness and still be dying of anorexia. The examiner's trap, and the clinical error, is the same sentence: "that is not a real eating disorder." The diagnosis lives in this note; the nutritional rehabilitation and psychological therapies that follow are detailed in the anorexia-management material, and the general cognitive-behavioural and family techniques in the Psychotherapies, clinical assessment, MSE and nosology notes.

9.1 OSFED and USFED: the two residual categories

OSFED names the reason; USFED does not. DSM-5-TR provides two residual codes for presentations that cause clinically significant distress or impairment but do not meet the full criteria for any specific feeding or eating disorder. **Other specified feeding or eating disorder** (OSFED, F50.89) is used when the clinician wants to state the specific reason the presentation falls short, recorded as "other specified feeding or eating disorder" followed by the reason, for example "bulimia nervosa of low frequency". Unspecified feeding or eating disorder (USFED, F50.9) is used when the clinician chooses not to specify a reason, or when information is insufficient to be more precise, as in an emergency setting (DSM-5-TR 2022).

A residual code is not a mild code. OSFED is emphatically not a diagnosis of triviality. Many OSFED presentations, atypical anorexia in particular, carry the same medical danger as their full-threshold counterparts; the label describes which criterion is not met, not how sick the patient is. ICD-11 mirrors the structure with its own residual categories.

GOOD TO REMEMBER

- **OSFED versus USFED (the discriminator):** both are residual codes for a clinically significant feeding or eating disturbance that misses full criteria; OSFED (F50.89) is chosen when the clinician *states* the specific reason it falls short (e.g. "bulimia nervosa of low frequency"), USFED (F50.9) when the reason is not specified or information is insufficient (DSM-5-TR 2022).

9.2 The five named OSFED presentations

Learn the list; the reason for each is the answer. DSM-5-TR names five prototypical OSFED presentations. For every one, the whole disorder is present except a single missing element, and that missing element is exactly what the examiner wants you to name.

OSFED PRESENTATION	WHAT IS MET	THE SINGLE MISSING ELEMENT
Atypical anorexia nervosa	All anorexia criteria, with significant weight loss	**Weight is within or above the normal range**
Bulimia nervosa (low frequency and/or limited duration)	All bulimia criteria	**Binge-purge cycles on average less than once a week and/or for less than three months**
Binge-eating disorder (low frequency and/or limited duration)	All binge-eating-disorder criteria	Binges on average less than once a week and/or for less than three months
Purging disorder	Recurrent purging to influence weight or shape	**No binge eating (purging occurs without binges)**
Night eating syndrome	Recurrent night eating with awareness and recall, causing distress or impairment	Not better explained by binge-eating disorder, sleep-wake change or local norms

The five DSM-5-TR OSFED exemplars; in each, name the one criterion that is not met, because that is the diagnosis (DSM-5-TR 2022).

5	<3	2
NAMED OSFED PRESENTATIONS IN DSM-5-TR	LIMITED-DURATION THRESHOLD (MONTHS)	SCOFF SCREEN POSITIVE CUT-OFF (OF FIVE)

TRAP **Reading "subthreshold" as "safe".** Do not treat an OSFED label as a reassurance; atypical anorexia and purging disorder carry the same electrolyte and cardiac risk as the full syndromes, so the medical work-up is unchanged by the qualifier.

9.3 Atypical anorexia nervosa: the weight is not the diagnosis

All the anorexia, minus the low weight. **Atypical anorexia nervosa** is the OSFED presentation in which every criterion for anorexia is met, including significant weight loss and the whole cognitive engine of weight and shape overvaluation, except that despite that weight loss the person's weight remains within or above the normal range. DSM-5-TR is explicit that adults who are not underweight by population standards, for example a body mass index of 19.0 kg/m^2 or above, should not be diagnosed with anorexia nervosa but may warrant atypical anorexia nervosa instead. Crucially, these patients "may experience many of the physiological complications associated with anorexia nervosa": bradycardia, hypotension, electrolyte disturbance and

amenorrhoea can all appear at a normal weight if the *rate* and *magnitude* of loss are large (DSM-5-TR 2022).

RULE **Rate of loss, not the number on the scale.** A normal or high absolute weight does not exclude anorexic physiology; a large, rapid loss with intact weight-shape overvaluation is atypical anorexia and is medically managed as anorexia.

GOOD TO REMEMBER

- **Atypical anorexia nervosa (the criterion):** all anorexia criteria are met, including the weight-and-shape overvaluation and significant weight loss, but the weight is within or above the normal range (DSM-5-TR anchors this at an adult body mass index of about 19.0 kg/m^2 or above); the physiological complications of starvation can still be present, so it is coded and treated as a serious eating disorder, not a mild one.

9.4 Non-fat-phobic anorexia: food refusal without the stated fear of fatness

The engine can be silent. A recognised variant, comparatively common in Asian and Indian populations, is **non-fat-phobic** anorexia, in which the patient shows the weight loss and the food refusal of anorexia but does *not* voice the classic intense fear of gaining weight or of becoming fat. Instead the dietary restriction is rationalised through a more culturally sanctioned complaint, most often gastrointestinal discomfort ("bloating", "no appetite", "food does not suit me"), or through cultural and religious motives such as fasting. Both DSM-5-TR and ICD-11 note this presentation and instruct that the absence of an *expressed* fat phobia does not exclude anorexia: if collateral history, observation or longitudinal course supports an underlying preoccupation with, or behaviour aimed at, weight and shape, the diagnosis stands (DSM-5-TR 2022; ICD-11 CDDR).

Screen actively, because it hides. Under-recognition is the rule when the presenting language is somatic, so a low-friction case-finding tool earns its place. The five-item SCOFF questionnaire is the standard screen; a score of two or more affirmative answers (out of five) is a positive screen that warrants full eating-disorder assessment. The instrument itself is reproduced in the accompanying scale plate. The somatic framing and its overlap with medical presentations connect to the Somatic-symptom, sexual, impulse-control disorders and suicide notes and the transcultural material in the Consultation-liaison, geriatric and transcultural psychiatry notes.

MNEMONIC

S·C·O·F·F

Sick (do you make yourself sick when uncomfortably full), **C**ontrol (have you lost control over eating), **O**ne stone (lost more than about 6.35 kg in a three-month span), **F**at (do you believe yourself fat when others say thin), **F**ood (does food dominate your life). Two or more "yes" answers is a positive screen.

RULE **Absence of stated fat-phobia does not exclude anorexia.** If the restriction is driven by inferable weight-shape concern behind a somatic or cultural rationale, it is anorexia; treat the food refusal, not the offered excuse.

TRAP **"She never said she wanted to be thin, so it is not anorexia."** The classic error is to reject a non-fat-phobic or atypical presentation as "not a real eating disorder"; the fear of fatness may be unexpressed, denied, or culturally recoded as GI complaint, while the starvation is entirely real.

GOOD TO REMEMBER

- **Non-fat-phobic anorexia (the criterion):** weight loss and food refusal with the underlying anorexic drive present but the fear of weight gain not verbally expressed, the restriction attributed instead to gastrointestinal discomfort or cultural or religious reasons; both DSM-5-TR and ICD-11 retain the anorexia diagnosis when collateral or longitudinal evidence supports weight-shape motivation, so screen (SCOFF two or more of five) rather than take the somatic story at face value.

INDIA

This is the most India-relevant slice of eating-disorder practice. The **non-fat-phobic** pattern is comparatively common here, so an adolescent who has lost dangerous weight but frames it as "gas", "acidity" or "no hunger" is easily routed through gastroenterology rather than psychiatry, and eating disorders are under-recognised across Indian settings for exactly this reason. The remedy is a low threshold to weigh, plot the trajectory, take collateral from family, and screen actively; do not require the textbook sentence about fearing fatness before you take the illness seriously. The same somatising instinct that hides anorexia here also drives the over-medicalisation of distress, so the transcultural lens in the Consultation-liaison, geriatric and transcultural psychiatry notes applies directly.

9.5 Purging disorder and night eating syndrome

Two well-characterised residual entities. Beyond the subthreshold variants, two OSFED presentations are distinct enough to have their own literature, though neither is a standalone formal category in DSM-5 or ICD-11.

Purging disorder

Recurrent purging behaviour to influence weight or shape (self-induced vomiting; misuse of laxatives, diuretics or other medications) in the *absence* of objective binge eating; the missing bulimic binge is the whole distinction, and body weight is typically normal.

Night eating syndrome

Recurrent episodes of night eating, evening hyperphagia after the evening meal and/or nocturnal awakenings with food ingestion, with full awareness and recall of the eating, causing distress or impairment, and not better explained by an altered sleep-wake cycle, local norms, binge-eating disorder or another disorder. The awareness and recall separate it from the parasomnia of sleep-related eating.

GOOD TO REMEMBER

- **Purging disorder (the criterion):** recurrent purging to control weight or shape *without* binge eating; the absent binge is what separates it from bulimia nervosa.
- **Night eating syndrome (the criterion):** recurrent evening or nocturnal eating with *awareness and recall*; the retained awareness distinguishes it from the sleep-related eating parasomnia, which is amnesic.

9.6 Orthorexia nervosa: a preoccupation, not a diagnosis

An obsession with purity, not thinness. Orthorexia nervosa, a term coined by the physician Steven Bratman in 1997, describes a pathological preoccupation with eating food perceived as "healthy", "clean" or "pure". The drive is not toward a thin body but toward dietary righteousness: escalating self-imposed rules about food quality and preparation, mounting time and anxiety spent policing the diet, guilt or distress when rules are broken, and social withdrawal to protect the regimen. In the extreme it produces genuine malnutrition and impairment. Critically, orthorexia is **not** a formal diagnosis in DSM-5-TR or ICD-11; proposed criteria exist but are not validated, and in exam terms it is best framed as a described phenomenon on the boundary of an eating disorder and obsessive-compulsive spectrum pathology, captured, where impairing, under OSFED rather than as a category of its own.

GOOD TO REMEMBER

- **Orthorexia nervosa (the defining feature):** a pathological preoccupation with the perceived healthiness or purity of food, with rigid escalating rules, distress when they are broken, and functional or nutritional harm; the fixation is on food *quality*, not on weight or shape, and it is *not* a formal DSM-5-TR or ICD-11 diagnosis (Bratman, 1997).

HOLD THIS

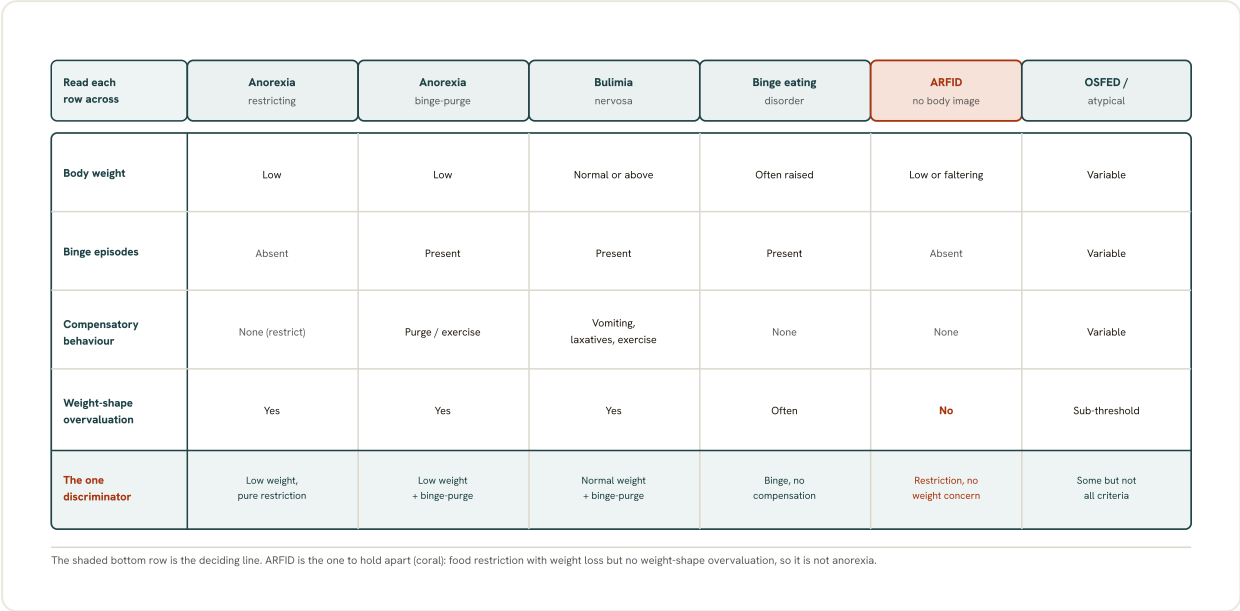
OSFED (other specified feeding or eating disorder) is the DSM-5-TR residual category, successor to EDNOS, for clinically significant eating pathology that misses full criteria by one element; its five exemplars are atypical anorexia (all anorexia features but weight within or above the normal range), low-frequency/limited-duration bulimia and binge-eating disorder (less than once a week and/or under three months), purging disorder (purging without binges) and night eating syndrome; the non-fat-phobic anorexia common in India is still anorexia when weight-shape drive is inferable behind a somatic rationale; and orthorexia, a preoccupation with "pure" eating, is a described phenomenon, not a formal diagnosis. The one trap is calling any of these "not a real eating disorder".

10 · Discriminating the eating disorders

The step that turns six syndromes into one decision. Every eating-disorder topic in these notes teaches a single entity in full; this note is the **differentiation** step that lays them side by side and asks the one question that separates each from its neighbour. The examiner rarely gives you a textbook case; the marks are in telling anorexia nervosa restricting from anorexia nervosa binge-purge, telling anorexia from bulimia nervosa, telling bulimia from binge eating disorder, and telling all four from ARFID and from the residual OSFED presentations. The whole map collapses onto a small set of axes: the *weight* (significantly low versus normal-or-above), the presence of an objective *binge*, the presence of a **compensatory behaviour**, the presence or absence of **body image** and weight-shape overvaluation, and the *medical picture* that follows from each.

Why this note exists. The individual diagnoses are owned by their own topics in these notes; this one owns the *discrimination*, the decision tree and the master grid that the exam draws its viva questions from. Two of the axes do most of the work: *weight* forks anorexia (and its atypical

variant) from the rest, and *compensatory behaviour* forks bulimia from binge eating disorder, while *body image* is the axis that pulls ARFID out of the whole family. The accompanying figure typesets these axes as a decision grid, and the eating-disorder screens sit on the accompanying scale plate; the guideline-anchored treatment that each label buys is developed in the individual management topics in these notes.



Read each row across	Anorexia restricting	Anorexia binge-purge	Bulimia nervosa	Binge eating disorder	ARFID no body image	OSFED / atypical
Body weight	Low	Low	Normal or above	Often raised	Low or faltering	Variable
Binge episodes	Absent	Present	Present	Present	Absent	Variable
Compensatory behaviour	None (restrict)	Purge / exercise	Vomiting, laxatives, exercise	None	None	Variable
Weight-shape overvaluation	Yes	Yes	Yes	Often	No	Sub-threshold
The one discriminator	Low weight, pure restriction	Low weight + binge-purge	Normal weight + binge-purge	Binge, no compensation	Restriction, no weight concern	Some but not all criteria

The shaded bottom row is the deciding line. ARFID is the one to hold apart (coral): food restriction with weight loss but no weight-shape overvaluation, so it is not anorexia.

Fig 17.6 The eating disorders discriminated. Read each row across the six presentations. Body weight separates the low-weight anorexias from the normal-or-above bulimia and the often-raised binge eating disorder; the presence of a binge separates restricting anorexia from the rest; and the compensatory behaviour separates bulimia and binge-purge anorexia (which purge) from binge eating disorder (which does not). The deciding line is the bottom row: anorexia is low weight with restriction, bulimia is normal weight with binge-purge, binge eating disorder is bingeing without compensation, and ARFID, the one most often mislabelled, is food restriction with weight loss but no overvaluation of weight or shape, so the body-image disturbance that defines anorexia is simply absent. OSFED and atypical anorexia meet some but not all of the full criteria.

10.1 The five axes that do all the work

Learn the axes, not the cases. Every discrimination in the family is settled by asking, in order, about five variables. Naming them in this sequence is the fastest route through any differentiation question, because each answer prunes the tree.

Weight

Significantly low (from restriction) versus normal-or-above. The first fork: a significantly low, restriction-driven weight points to anorexia nervosa; a normal or raised weight points toward bulimia nervosa, binge eating disorder or a residual presentation.

The binge

Present or absent. An objective binge (a discrete overeating episode with loss of control) is required for bulimia and for binge eating disorder, and defines the binge-purge subtype of anorexia; it is absent in restricting anorexia, in ARFID and in purging disorder.

Compensatory behaviour

Present or absent. Recurrent inappropriate compensation (self-induced vomiting, laxatives, diuretics, fasting, driven exercise) defines bulimia and is what its absence removes to leave binge eating disorder.

Body image and weight-shape overvaluation

Present or absent. Overvaluation of weight and shape is central to anorexia and bulimia and partly present in binge eating disorder, but it is *absent* in ARFID, which is the disorder without a body image disturbance.

The medical picture

The physiological footprint each pattern leaves: starvation physiology and refeeding risk at low weight, a hypokalaemic alkalosis and Russell's sign with purging, and metabolic morbidity with binge-driven obesity.

MNEMONIC

Weight? · Binge? · Compensation? · Body-image?

Four questions in order settle almost every eating-disorder differentiation. **Weight** low or not (anorexia versus the rest); **Binge** present or not (bulimia and binge eating disorder versus restricting anorexia and ARFID); **Compensation** present or not (bulimia versus binge eating disorder); **Body-image** overvaluation present or not (the eating disorders proper versus ARFID). The fifth axis, the medical picture, then tells you how urgent the patient is.

10.2 The master differentiation grid

The whole family on one page. The grid below reads each entity against the five axes; the highlighted cell in each row is the discriminator that pins that label, the single answer that no neighbour shares. The figure alongside renders the same information as a branching decision tree. Read any real patient down the columns and the diagnosis falls out of the pattern rather than out of a remembered vignette.

DISORDER	TYPICAL WEIGHT	OBJECTIVE BINGE	COMPENSATORY BEHAVIOUR	BODY IMAGE / WEIGHT-SHAPE OVERVALUATION	MEDICAL SIGNATURE
Anorexia nervosa, restricting	Significantly low	**Absent (no binge or purge in the last three months)**	None (dieting, fasting, over-exercise)	Present and central	Starvation physiology; refeeding risk
Anorexia nervosa, binge-purge	**Significantly low (the fork from bulimia)**	Present	Present (vomiting, laxatives, diuretics)	Present and central	Hypokalaemia, alkalosis, prolonged QTc; refeeding risk
Bulimia nervosa	Normal or above	Present	**Present, recurrent (the defining feature)**	Present and central	Hypokalaemic hypochloraemic alkalosis, Russell's sign, dental erosion, prolonged QTc

DISORDER	TYPICAL WEIGHT	OBJECTIVE BINGE	COMPENSATORY BEHAVIOUR	BODY IMAGE / WEIGHT-SHAPE OVERVALUATION	MEDICAL SIGNATURE
Binge eating disorder	Overweight or obese	Present	**Absent (no regular compensation)**	Partly present (overvaluation common, not required)	Metabolic and cardiovascular morbidity of obesity
ARFID	Low or faltering growth (may be normal)	Absent	None	**Absent (no body image disturbance)**	Nutritional deficiency, faltering growth, supplement or feed dependence
Atypical anorexia (OSFED)	**Within or above the normal range despite marked loss**	Absent (restricting pattern)	None or purging	Present and central	Starvation physiology can occur at a normal weight
Purging disorder (OSFED)	Normal	**Absent (purging without a binge)**	Present (purging to control weight)	Present	Electrolyte disturbance from purging

The eating-disorder differentiation grid; in each row the highlighted cell is the one axis that fixes the label, and the two axes that decide most cases are weight (low versus normal-or-above) and compensatory behaviour (present versus absent) (DSM-5-TR 2022; ICD-11 CDDR; Kaplan and Sadock CTP 2024).

RULE **Three questions before you name it.** Ask "is the weight significantly low?", "is there an objective binge?" and "is there a compensatory behaviour?"; those three answers separate restricting anorexia, binge-purge anorexia, bulimia and binge eating disorder, and a fourth question, "is body image intact?", peels ARFID away from all of them.

10.3 Restricting versus binge-purge anorexia

Same low weight, split by the last three months. Within anorexia nervosa the subtype is decided by behaviour over the recent three-month window at a still significantly low weight. The *restricting* subtype loses weight through dieting, fasting or excessive exercise with *no* recurrent binge eating or purging in that window, the classic pure restrictor. The *binge-purge* subtype has engaged, over the same window, in recurrent binge eating or purging (self-induced vomiting, or misuse of laxatives, diuretics or enemas), while the weight remains significantly low. Crossover between the two over the illness course is common, so the label describes the current picture, not the lifetime one, and clinically the binge-purge subtype carries the higher electrolyte and cardiac risk.

GOOD TO REMEMBER

- **Anorexia subtypes (the discriminator):** both share a significantly low, restriction-driven weight and the same body-image psychopathology; the split is the presence of recurrent binge eating or purging in the last three months, absent in the restricting subtype and present in the binge-purge subtype, which carries the greater hypokalaemia and cardiac risk.

10.4 Binge-purge anorexia versus bulimia nervosa: the weight fork

Identical behaviour, decided by the scale. The binge-purge subtype of anorexia and bulimia nervosa can look behaviourally identical, the same objective binge followed by the same compensatory behaviour. The discriminator is weight, and it is enforced by an exclusion rule: if the patient is at a *significantly low* weight, the diagnosis is anorexia nervosa, binge-purge subtype; if the weight is *normal or above*, it is bulimia nervosa (DSM-5-TR Criterion E: bulimia is not diagnosed if the disturbance occurs exclusively during anorexia nervosa). Bulimia is therefore the normal-weight eating disorder, and because there is no emaciation to give it away it is diagnosed by asking, not by looking. Its timeframe threshold is once weekly for three months in DSM-5-TR and once weekly for one month in ICD-11.

FEATURE	ANOREXIA NERVOSA, BINGE-PURGE	BULIMIA NERVOSA
Objective binge	Yes	Yes
Compensatory behaviour	Yes	Yes, recurrent
Typical weight	**Significantly low**	**Normal or above**
Coding rule	Low weight wins: coded as anorexia	Only if not exclusively during anorexia

The weight fork between binge-purge anorexia and bulimia nervosa; when binge-purge behaviour occurs, the weight decides the label and the low-weight patient is always coded as anorexia (DSM-5-TR 2022).

TRAP **A normal weight is falsely reassuring.** The classic error is to discount an eating disorder because the patient looks well and weighs normally, missing the silent hypokalaemia and prolonged QTc of covert purging; a normal weight moves the label from anorexia to bulimia, it does not lower the medical danger.

GOOD TO REMEMBER

- **Bulimia nervosa (the criterion boundary):** objective binges plus recurrent compensatory behaviour at a *normal or above-normal* weight is bulimia nervosa; the identical behaviour at a significantly *low* weight is anorexia nervosa, binge-purge subtype, because the low-weight exclusion rule always codes to anorexia.

10.5 Bulimia versus binge eating disorder: the compensation fork

Take away the compensation and it is binge eating disorder. Binge eating disorder shares the recurrent binge and the loss of control with bulimia nervosa but lacks the regular inappropriate **compensatory behaviour** that bulimia requires. Remove the vomiting, the laxatives, the fasting and the driven exercise from a bulimia-shaped picture and what remains is binge eating disorder. A softer second discriminator: in bulimia dysfunctional dieting usually *precedes* the binge,

whereas in binge eating disorder dieting typically *follows* it, and the patient is commonly overweight or obese rather than of normal weight. The three eating-disorder diagnoses are mutually exclusive for a single episode, so a patient who both binges and purges is bulimia, not binge eating disorder.

RULE **The compensation is the fork in the road.** Recurrent binge with loss of control *plus* regular compensatory behaviour is bulimia nervosa; the same recurrent binge *without* regular compensation is binge eating disorder. Ask whether the binge is undone, not just whether it happens.

GOOD TO REMEMBER

- **Binge eating disorder (the discriminator):** recurrent binge eating with loss of control and marked distress but *no* regular compensatory behaviour; it co-travels with overweight and obesity, dieting follows the binge rather than preceding it, and it is the single most common eating disorder.

10.6 ARFID: the disorder without a body image

One axis pulls it out of the family. ARFID (avoidant/restrictive food intake disorder) is restricted eating that is *not* driven by any wish to be thin. The person avoids or restricts food because of its sensory qualities, an apparent lack of interest in eating, or a fear of an aversive consequence such as choking or vomiting, and this produces weight loss or faltering growth, nutritional deficiency, dependence on supplements or feeds, or psychosocial impairment. What it lacks is the whole engine of anorexia: no fear of weight gain and no disturbance of **body image** or overvaluation of weight and shape. Because both ARFID and anorexia can reach a dangerously low weight with the same starvation physiology, the differentiation is psychological, not physical, and it is settled by a single question, "why does the person restrict?". If the answer is to be thin or to avoid becoming fat, it is anorexia; if it is sensory aversion, low appetite or fear of a feared event, and the body image is intact, it is ARFID.

RULE **No body image disturbance is the line.** Restricted eating with weight loss but no overvaluation of weight or shape and no fear of fatness is ARFID, not anorexia; the absence of the body image psychopathology is the diagnosis, even when the weight is dangerously low.

GOOD TO REMEMBER

- **ARFID (the discriminator):** restriction from sensory aversion, apparent lack of interest in food, or fear of an aversive consequence, with the same possible low weight as anorexia but *no* body image disturbance and no drive for thinness; ask why the person restricts, because the motive, not the weight, separates it from anorexia.

10.7 OSFED, atypical and non-fat-phobic anorexia: subthreshold is not safe

The residual bin that is not a dustbin. A large share of real, impairing eating pathology misses full criteria by a single element and lands in OSFED (other specified feeding or eating disorder), the DSM-5-TR successor to the old EDNOS. Its named exemplars each keep the whole syndrome minus one item: atypical anorexia nervosa is every anorexia feature, including significant weight loss and the weight-shape overvaluation, except that the weight stays within or above the normal

range (DSM-5-TR anchors this at an adult BMI of about **19 kg per m squared** or above); purging disorder is recurrent purging without objective binges; and low-frequency or limited-duration bulimia and binge eating disorder fall below once weekly and/or under three months. A parallel high-yield variant is non-fat-phobic anorexia, in which the patient shows the weight loss and food refusal but does not voice the fear of fatness, rationalising the restriction as gastrointestinal discomfort, poor appetite or a religious fast. Both DSM-5-TR and ICD-11 keep the anorexia diagnosis when collateral or longitudinal evidence supports an underlying weight-shape drive. The single trap across all of these is the same sentence: "that is not a real eating disorder."

TRAP **Reading "subthreshold" or "non-fat-phobic" as "not anorexia".** Atypical anorexia and purging disorder carry the same electrolyte and cardiac risk as the full syndromes, and a large rapid loss can produce starvation physiology at a normal weight; the qualifier names the missing criterion, not a milder illness, so the medical work-up is unchanged.

GOOD TO REMEMBER

- **OSFED atypical anorexia (the criterion):** all anorexia criteria met, including significant weight loss and body-image overvaluation, but the weight is within or above the normal range (adult BMI about 19 kg per m squared or above); starvation physiology can still be present, so it is coded and treated as a serious eating disorder, and non-fat-phobic anorexia remains anorexia when weight-shape drive is inferable behind a somatic rationale.

INDIA

This is the most India-relevant slice of the differentiation. The **non-fat-phobic** presentation is comparatively common in Indian and other Asian patients, so an adolescent who has lost dangerous weight but frames it as "gas", "acidity" or "no appetite" is easily routed through gastroenterology rather than psychiatry, and eating disorders are widely under-recognised across Indian settings for exactly this reason, still stereotyped as a disease only of affluent urban young women when they occur across strata and in men. The remedy is the same low-friction discipline every time: weigh the patient, plot the trajectory, take collateral, and screen actively with the SCOFF rather than requiring the textbook sentence about fearing fatness before taking the illness seriously. The same instinct to somatise distress that hides anorexia here is developed in the Consultation-liaison, geriatric and transcultural psychiatry notes.

10.8 What the differentiation buys you: it changes the treatment

The label is not academic; it re-routes the management. Each fork above sends the patient down a different treatment path, and getting the discrimination right is what makes the plan right. *No drug is first-line for anorexia nervosa*: the primary treatment is nutritional rehabilitation plus a psychological therapy, and medication is at best adjunctive. Cross the weight fork into *bulimia nervosa* and the picture changes: a psychological therapy still leads (NICE NG69 guided self-help stepping up to CBT-ED), but here there is one licensed drug to know cold, fluoxetine at **60 mg per day**, above its 20 to 40 mg antidepressant dose and the medication of choice for bulimia (WFSBP 2023 first-line; brands in India include Prodep, Fludac and Flunil). Cross the compensation fork into *binge eating disorder* and the therapy is again psychological with weight loss explicitly *not* a target, and the only specifically licensed agent is lisdexamfetamine at 50 to 70

mg per day (US FDA, not marketed in India). *ARFID* has no first-line drug at all and is managed by a multidisciplinary team. The deep antidepressant pharmacology of fluoxetine at the high bulimia dose is developed in the Mood disorders: pharmacotherapy notes, and the general cognitive-behavioural technique in the Psychotherapies, clinical assessment, MSE and nosology notes.

RULE **The fork picks the drug.** No drug is first-line for anorexia; fluoxetine 60 mg per day is the one licensed drug for bulimia; lisdexamfetamine is the only agent specifically licensed for binge eating disorder; and ARFID has no first-line drug, so the differentiation directly selects the pharmacology.

GOOD TO REMEMBER

- **Treatment fork (the value anchor):** anorexia has *no* first-line drug (nutrition plus psychotherapy); bulimia's one licensed drug is *fluoxetine 60 mg per day* alongside CBT-ED; binge eating disorder's only specifically licensed agent is *lisdexamfetamine* (50 to 70 mg per day, US FDA) with weight loss not a therapy target; and ARFID has no first-line drug, managed by a multidisciplinary team.

2	60	18.5	19
SCOFF POSITIVE CUT-OFF (YES ANSWERS, OF FIVE)	FLUOXETINE DOSE FOR BULIMIA (MG PER DAY)	ICD-11 ANOREXIA WEIGHT THRESHOLD (ADULT BMI, KG PER M SQUARED)	ATYPICAL ANOREXIA WEIGHT FLOOR (ADULT BMI, KG PER M SQUARED)

WORKED EXAMPLE

Four young women present in one clinic. The first, BMI 15, eats tiny measured portions, exercises for hours, fears fatness, and has not binged or purged: anorexia nervosa, restricting subtype. The second, BMI 15, binges and vomits several times weekly: still anorexia nervosa, binge-purge subtype, because the low weight wins. The third, BMI 22, binges and vomits several times weekly with knuckle calluses and a potassium of 3.1: bulimia nervosa, the normal weight moving the label but not the danger. The fourth, BMI 34, binges alone at night, cannot stop, feels disgusted afterward, but never vomits, fasts or over-exercises: binge eating disorder. Same behaviours, four labels, decided by weight and by the presence of compensatory behaviour, and each label sends her down a different treatment path.

HOLD THIS

Differentiate the eating disorders on five axes, weight, binge, compensatory behaviour, body image and the medical picture: significantly low restriction-driven weight with intact body-image overvaluation is anorexia (restricting if no binge-purge, binge-purge if present), the same binge-purge behaviour at a normal-or-above weight is bulimia, recurrent binges without regular compensation is binge eating disorder, restricted eating with no body image disturbance is ARFID, and every-criterion-but-one presentations (atypical anorexia at a normal weight, non-fat-phobic anorexia, purging disorder) are OSFED and are never "not a real eating disorder"; the fork then picks the drug, no first-line agent for anorexia, fluoxetine 60 mg per day for bulimia, lisdexamfetamine for binge eating disorder, none for ARFID.

Sleep-wake disorders

11 · Normal sleep physiology, architecture and polysomnography

Every sleep-wake disorder in this band is read against a template, and that template is **normal sleep physiology**. Sleep is not the switching-off of the brain but an actively generated, tightly staged process that cycles through predictable states across the night; you cannot call insomnia, narcolepsy, obstructive sleep apnoea or a parasomnia abnormal until you know what the healthy **sleep architecture** looks like. This foundation topic is placed first for exactly that reason, and it earns its keep because the same handful of numbers, the stage percentages, the ninety-minute cycle, the normal REM latency and the polysomnographic indices, recur as the discriminators in every disorder that follows.

Why it matters, and how this note is framed. Two engines run underneath the whole topic. The first is the sleep switch and its drives: an **ascending arousal system** that holds the forebrain awake, a sleep-promoting nucleus that switches it off, and a two-drive timing model that decides when the flip happens. The second is the measurement layer: **polysomnography**, the EEG, EOG and EMG montage that lets you score the stages and read the apnoea-hypopnea and limb-movement indices. The sleep neurochemistry and the ascending-arousal anatomy are developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and the Functional Neuroanatomy and Neurophysiology notes; the sleep architecture, the hypnogram and polysomnography are owned here. Every percentage and index below is drawn from the parsed sources, and the one value the library confirmed only in part, the exact split between the light stages, is flagged rather than dressed up.

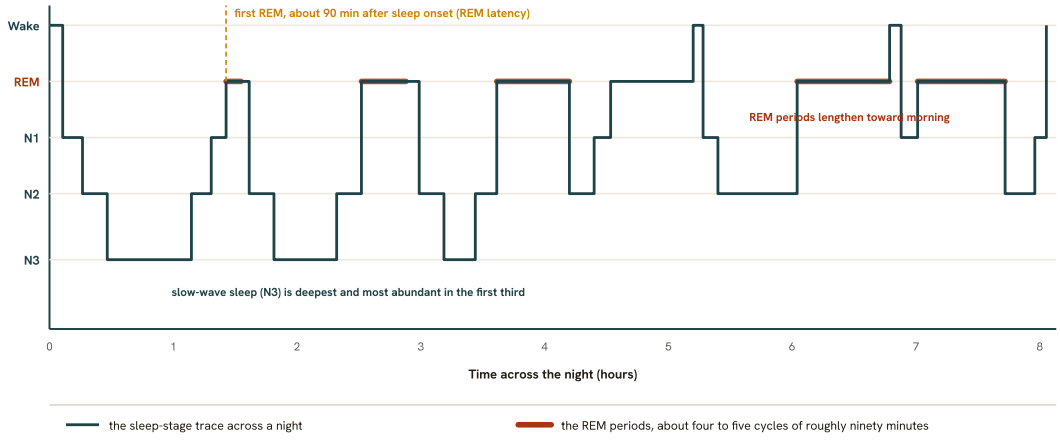


Fig 17.7 The sleep-architecture hypnogram. A normal night runs in four to five cycles of about ninety minutes, each descending from light N1 and N2 into deep slow-wave N3 sleep and then rising into a period of REM. The first REM period arrives about ninety minutes after sleep onset, the normal REM latency, and a shortened REM latency is a soft marker of depression and of narcolepsy. The architecture is not uniform across the night: slow-wave N3 sleep is deepest and most abundant in the first third and fades later, while the REM periods lengthen toward morning, so most deep sleep is early and most dreaming sleep is late. The stage percentages, the cycle length and the REM latency are the values to hold; the neurochemistry that generates these states is developed in the Neurochemistry, neuroendocrinology, neuroimaging and basic psychopharmacology notes and the Functional neuroanatomy and neurophysiology notes.

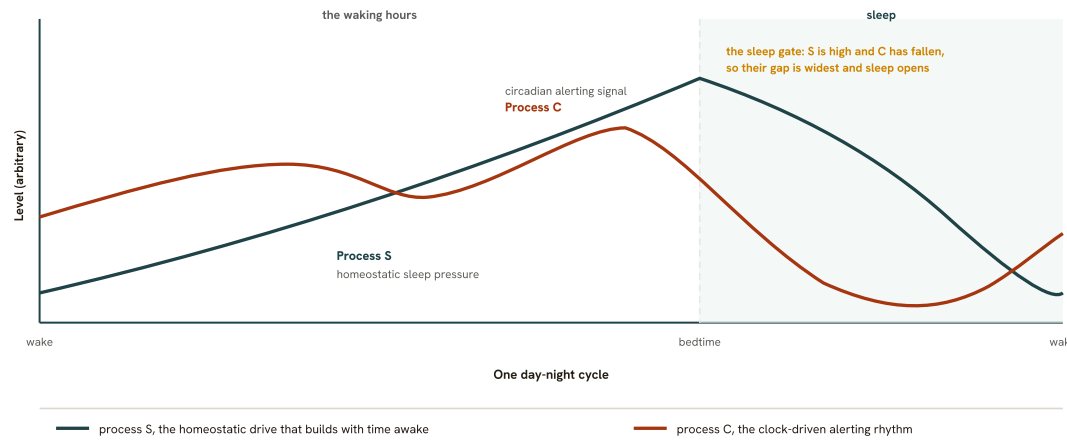


Fig 17.8 The two-process model of sleep regulation. Two independent processes set when we sleep. Process S is the homeostatic sleep pressure that builds steadily with every hour awake and discharges across sleep, so the longer the prior wakefulness the deeper the ensuing slow-wave sleep. Process C is the circadian alerting signal from the suprachiasmatic clock, which counter-intuitively rises through the evening (the wake-maintenance zone that makes it hard to fall asleep early) and then falls overnight to a trough in the early hours. Sleep opens when the gap between the two is widest, with S high and C fallen, and it consolidates through the night; the model explains why sleep deprivation deepens sleep, why the early-hours circadian trough is when lapses and errors peak, and why shifting the clock (the circadian disorders) or the drive (insomnia) disturbs sleep.

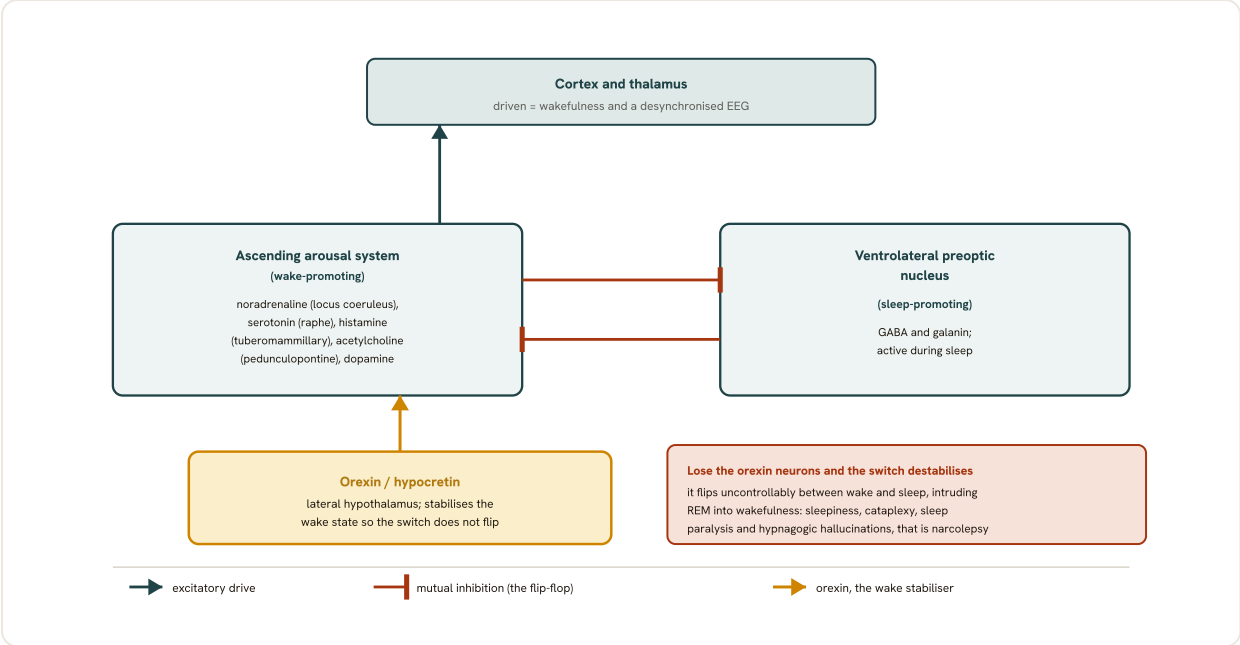


Fig 17.9 The ascending arousal system and the sleep-wake flip-flop switch. Wakefulness is driven by the ascending arousal system, a set of brainstem and hypothalamic monoaminergic and cholinergic nuclei that project up to the cortex; sleep is driven by the ventrolateral preoptic nucleus, which uses GABA and galanin. The two mutually inhibit each other, and mutual inhibition makes a flip-flop switch that snaps cleanly between wake and sleep and avoids dozing in between. The orexin (hypocretin) neurons of the lateral hypothalamus stabilise the wake side of the switch. When these neurons are lost, as in narcolepsy type 1, the switch becomes unstable and flips uncontrollably, so sleep and REM phenomena intrude into wakefulness as the tetrad of excessive sleepiness, cataplexy, sleep paralysis and hypnagogic hallucinations. The neurotransmitter systems themselves are developed in the Neurochemistry, neuroendocrinology, neuroimaging and basic psychopharmacology notes.

11.1 Two states of sleep: NREM and REM

The basic division. Human sleep alternates between two fundamentally different states: non-rapid eye movement (NREM) sleep, which has three stages of progressively deeper unconsciousness, and rapid eye movement (REM sleep), the dreaming, near-paralysed state whose brain activity resembles waking (New Oxford Textbook). Across a night the body passes in sequence through the NREM stages and then into REM, and repeats. Arousal threshold rises with each successive NREM stage while eye movement and muscle activity fall, so the depth of sleep is genuinely graded, not a single flat plateau.

Why the two states are taught apart. NREM and REM are opposites on almost every axis: NREM has high muscle tone, slow rolling or absent eye movements and slow high-voltage EEG, whereas REM has muscle atonia, bursts of rapid eye movement and a fast low-voltage EEG. Recalled, elaborate dreaming belongs to REM sleep; the fragmentary thought of NREM is rarely remembered. This split is the backbone of the parasomnia distinction later, where the NREM arousal disorders (sleepwalking, night terrors) arise out of slow-wave sleep and nightmare disorder and REM sleep behaviour disorder arise out of REM.

11.2 The NREM stages: N1, N2 and N3

The three stages and their EEG signatures. The **sleep stages** of NREM are defined electrographically. **N1** is the drowsy transition from wake, with attenuation and slowing of the waking alpha (8 to 12 Hz) rhythm and slow rolling eye movements. **N2** is the defining light-sleep stage, marked by two signature graphoelements, the sleep spindles (brief 11 to 16 Hz sigma

bursts) and the K-complexes, both appearing at the onset of stage 2 (New Oxford Textbook; Kaufman). **N3** is slow-wave sleep, dominated by high-amplitude slow delta (0.5 to 2 Hz) activity; it is the deepest, most restorative NREM stage and is the physical-recuperation portion of the night. The stage labels N1, N2 and N3 are the current names; older Rechtschaffen-and-Kales scoring split slow-wave sleep into stages 3 and 4.

NREM STAGE	EEG SIGNATURE	EOG / EMG AND ROLE
N1 (light transition)	Attenuation/slowing of alpha; low-voltage mixed frequency	Slow rolling eyes; muscle tone preserved; the doorway into sleep
N2 (light sleep)	**Sleep spindles (sigma bursts) and K-complexes**	Eyes slow or still; the single largest share of the night
N3 (slow-wave sleep)	**High-amplitude delta, 0.5 to 2 Hz**	Eyes still; deepest, most restorative; slow-wave parasomnias arise here

The three NREM stages by EEG signature; the load-bearing pairing is spindles and K-complexes marking N2 and delta activity marking N3.

GOOD TO REMEMBER

- **NREM stages (the identifiers):** N1 is alpha dropout with rolling eyes; *N2 is defined by sleep spindles and K-complexes*; N3 is slow-wave (delta) sleep, the deepest and most restorative stage. Spindles and K-complexes are the N2 signature and the commonest single graphoelements asked at the console.

11.3 REM sleep: the paradoxical state

Why it is called paradoxical. In REM sleep the EEG becomes low-voltage and fast, closely resembling the waking record, yet the sleeper is behaviourally asleep and the postural muscles are actively paralysed, hence paradoxical sleep. Bursts of rapid conjugate eye movement give the state its name, autonomic activity becomes irregular, and vivid narrative dreaming occurs. The muscle atonia is generated actively in the pons (the perilocus coeruleus region drives the eye movements, atonia and dreaming), and its failure is the substrate of REM sleep behaviour disorder, a synucleinopathy prodrome developed in the Dementias and neurocognitive disorders notes and the Neurology foundations for psychiatrists notes.

What REM does on the montage. On **polysomnography**, REM is scored from the triad of a wake-like low-voltage fast EEG, phasic rapid eye movements on the EOG, and a silent chin EMG reflecting atonia (Kaufman). That last channel matters clinically: loss of the normal REM atonia (REM sleep without atonia) is the polysomnographic marker of REM sleep behaviour disorder.

11.4 Sleep architecture: the stage percentages and the normal REM latency

How the night divides. In a healthy young adult the night distributes across the stages in a stable pattern. Light N2 sleep takes the largest single share, slow-wave N3 a smaller block loaded into the first third of the night, and REM sleep accounts for a verified **20 to 25%** of total sleep time, its proportion rising with each successive cycle (New Oxford Textbook). N1 is a thin transitional sliver. These proportions are the reference against which a disorder is called abnormal, for

example the reduced slow-wave sleep and increased N1 of ageing, or the elevated REM percentage of rebound after deprivation.

The normal REM latency. After sleep onset the sleeper descends through NREM and reaches the first REM period after roughly ninety minutes; this interval is the **REM latency**, and it starts at about **90 minutes** and lasts about ten minutes on that first pass (Kaufman). A shortened REM latency is a high-yield abnormality: a sleep-onset REM period, REM appearing within about fifteen minutes of falling asleep, points to narcolepsy, and a reduced REM latency is a classic (if non-specific) finding in major depression, cross-referenced to the mood chapters.

STAGE	SHARE OF TOTAL SLEEP (%)	NOTE
N1 (light transition)	about 5	Thin sliver; increases with age and with fragmentation
N2 (light sleep)	**about 45 to 55**	Largest single share of the night
N3 (slow-wave sleep)	about 15 to 20	Front-loaded into the first third; falls with age
REM sleep	**20 to 25**	Verified; proportion rises across successive cycles

Adult sleep architecture; the REM share (20 to 25%) is directly source-verified, and the N1/N2/N3 split is the standard sleep-medicine approximation (see gaps).

RULE **The first REM period comes at about ninety minutes.** Normal REM latency is roughly 90 minutes; a sleep-onset REM period (REM within about fifteen minutes) is pathological and points to narcolepsy, and a short REM latency is a recognised depression marker.

11.5 The NREM-REM cycle and the hypnogram

The ninety-minute cycle. The two states alternate in a regular cycle of roughly ninety minutes (the first cycle is a little shorter, 70 to 100 minutes; later cycles run 90 to 120 minutes), and four to five such cycles complete a night (New Oxford Textbook; Kaufman). The internal balance of the cycle shifts as the night goes on: slow-wave N3 dominates the early cycles and fades, while REM periods lengthen and cluster into the last third of the night. This is why the vivid dream a person recalls is usually the final one, and why early-morning waking exposes the REM-rich end of sleep.

Reading the hypnogram. Plotting the scored stage against clock time produces the hypnogram, the conventional single-page map of a night's **sleep architecture** (the accompanying figure). It shows the descent into slow-wave sleep early, the cyclic climbs into REM about every ninety minutes, the shrinking of N3 and the lengthening of REM towards morning. The hypnogram is the visual grammar of the whole band: insomnia flattens and fragments it, apnoea peppers it with arousals, and narcolepsy plants REM at the very start.

GOOD TO REMEMBER

- **The cycle and hypnogram (the values):** NREM and REM alternate about every *90 minutes*, with 4 to 5 cycles per night; slow-wave sleep front-loads the night and REM back-loads it. The hypnogram is the stage-versus-time map read in every sleep disorder.

11.6 The two-process model of sleep regulation

Two drives, one gate. The timing of sleep is explained by the two-process model, which sets a homeostatic drive against a circadian one (Borbely; New Oxford Textbook). **Process S**, the homeostatic sleep pressure, builds steadily the longer one is awake and dissipates during sleep; its likeliest chemical substrate is adenosine, which accumulates in the brain across waking and whose blockade by caffeine is why coffee fights sleepiness. **Process C**, the circadian drive for wakefulness, is generated by the suprachiasmatic nucleus and rises through the day to oppose the mounting sleep pressure, then falls in the evening. The figure alongside plots the two curves.

The sleep gate. We stay awake through the day because Process C climbs in step with Process S and cancels it; sleep is triggered in the evening when the circadian alerting signal drops away and the accumulated homeostatic pressure is suddenly unopposed, opening the sleep gate. The model explains ordinary phenomena directly: the post-lunch dip, the second-wind of the evening alerting zone, and the deep rebound of slow-wave sleep after a night of deprivation, when Process S is abnormally high.

GOOD TO REMEMBER

- **Two-process model (the principle):** sleep timing = *Process S* (homeostatic pressure, building with time awake, adenosine-mediated) opposed by *Process C* (circadian alerting, driven by the suprachiasmatic nucleus). Sleep starts when the circadian alerting signal falls and unmasks accumulated homeostatic drive.

11.7 The ascending arousal system and the sleep-wake flip-flop switch

The wake side. Wakefulness is actively maintained by the **ascending arousal system**, a set of projections rising from the upper brainstem to the thalamus, hypothalamus and cortex (New Oxford Textbook). One arm is cholinergic (pedunculopontine and laterodorsal tegmental nuclei) driving the thalamus; the other is a monoaminergic and peptidergic fan, noradrenaline from the locus coeruleus, serotonin from the raphe, dopamine from the ventral periaqueductal grey, histamine from the tuberomammillary nucleus, and orexin from the lateral hypothalamus. These wake-promoting cells fire fastest in waking, slow in NREM and fall nearly silent in REM.

The sleep side and the switch. Sleep is imposed by the ventrolateral preoptic nucleus (VLPO), which inhibits the whole arousal system through GABA and galanin. Because the arousal system inhibits the VLPO in turn, the two sides are mutually antagonistic, and this reciprocal inhibition behaves as a bistable flip-flop switch (the sleep switch): the brain is pushed firmly into wake or firmly into sleep with fast transitions and little time in between (the accompanying figure). The stabiliser of this switch is orexin (also called hypocretin), the lateral-hypothalamic peptide that reinforces the wake side and prevents unwanted flips. Loss of the orexin neurons destabilises the

switch and is the lesion of narcolepsy with cataplexy, which is why hypocretin and the flip-flop model are examined together.

TRAP **Over-reading normal age-related change as insomnia.** Healthy ageing brings reduced slow-wave sleep, more N1, earlier waking and lighter, more fragmented sleep. Read against the young-adult template these look pathological, but they are normal architecture for the age, not a disorder needing a hypnotic.

GOOD TO REMEMBER

- **Flip-flop switch (the mechanism):** reciprocal inhibition between the *ascending arousal system* (wake) and the *VLPO* (sleep) creates a bistable switch with sharp transitions; *orexin/hypocretin* stabilises it. Orexin-neuron loss destabilises the switch and produces narcolepsy with cataplexy.

11.8 The neurotransmitters of wake and sleep

Wake-promoting versus sleep-promoting. The chemistry maps onto the switch. Wake is promoted by acetylcholine, noradrenaline, serotonin, dopamine, histamine and orexin; sleep is promoted by GABA and galanin from the VLPO, by adenosine as the homeostatic signal, and by melatonin as the circadian darkness cue. REM is special: acetylcholine is highly active in REM as in waking, while the monoamines (noradrenaline and serotonin) go nearly silent, the reciprocal-interaction pattern behind REM generation (Kaufman). This is why anticholinergic and serotonergic antidepressants suppress and delay REM, and why antihistamines cause drowsiness.

STATE	PROMOTING TRANSMITTERS
Wakefulness	Acetylcholine, noradrenaline, serotonin, dopamine, histamine, orexin
NREM sleep	**GABA and galanin (VLPO); adenosine (homeostatic); reduced monoamines**
REM sleep	**Acetylcholine high; noradrenaline and serotonin nearly silent**

Wake and sleep neurochemistry; the REM row (cholinergic on, aminergic off) is the reciprocal-interaction pattern and the reason REM-suppressing drugs are aminergic/anticholinergic.

MNEMONIC

WAKE = A HANDO

Acetylcholine, **H**istamine, **A**drenergic (noradrenaline), **N**ot-quite (serotonin/5-HT), **D**opamine, **O**rexin: the six wake-promoting transmitters of the ascending arousal system. The deep hypnotic and wake-promoting pharmacology (melatonin, ramelteon, the dual orexin receptor antagonists, the z-drugs and the benzodiazepines) is developed in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes.

11.9 Polysomnography: the montage and sleep staging

The three core channels. Polysomnography (the overnight sleep study) scores sleep from a montage whose three defining channels are the EEG (brain rhythm, for staging), the EOG or electro-oculogram (eye movement, to catch the rolling eyes of drowsiness and the rapid eye

movements of REM), and the chin EMG or electromyogram (muscle tone, which falls to silence in REM atonia) (Kaufman). Around this core sit the physiological channels: ECG, nasal and oral airflow, thoracic and abdominal respiratory effort, pulse oximetry, a snore microphone, and an anterior tibialis EMG for leg movements. Sleep is scored in thirty-second epochs, and the sequence of epochs becomes the hypnogram.

What it is for, and its relatives. Polysomnography is indicated where the diagnosis turns on physiology rather than history: breathing-related sleep disorders, periodic limb movement disorder, REM sleep behaviour disorder and suspected narcolepsy (DSM-5-TR). Its daytime companion is the multiple sleep latency test (MSLT), which measures how quickly a person falls asleep across a series of scheduled naps and whether REM appears in them; the MSLT is positive for narcolepsy at a mean sleep latency of eight minutes or less with sleep-onset REM periods in two or more naps (DSM-5-TR, verified). Routine insomnia does not need polysomnography and is diagnosed clinically.

GOOD TO REMEMBER

- **Polysomnography montage (the essentials):** the three core channels are *EEG, EOG and EMG* (brain, eyes, muscle), scored in 30-second epochs; airflow, effort and oximetry are added for breathing disorders. The daytime *MSLT* quantifies sleepiness and traps sleep-onset REM (positive: mean sleep latency of 8 minutes or less plus REM in 2 or more naps).

11.10 The derived indices: the AHI and the periodic-limb-movement index

The apnoea-hypopnea index. Two numbers scored off the study run through the rest of the band. The apnoea-hypopnea index (AHI) counts apnoeas plus hypopneas per hour of sleep and grades the severity of obstructive sleep apnoea; an event is a breathing reduction of at least ten seconds (DSM-5-TR). The diagnostic threshold is five or more obstructive events per hour with symptoms (or fifteen or more without), and severity is banded as mild, moderate or severe. In the verified DSM-5-TR specifier the bands are an AHI under fifteen (mild), fifteen to thirty (moderate) and over thirty (severe); the clinical sleep-medicine convention labels an AHI of five to fifteen as mild, so the exact lower band edge depends on the scheme used and is flagged below.

The periodic-limb-movement index. The periodic limb movement index (PLMI) counts periodic limb movements per hour of sleep and is the polysomnographic sign of periodic limb movement disorder, which overlaps heavily with restless legs syndrome (about forty per cent of narcolepsy patients also show it). Its abnormal threshold in adults is conventionally taken as more than fifteen movements per hour, but the precise cut-off is scheme-dependent and is flagged rather than fixed here.

SEVERITY BAND	AHI (EVENTS PER HOUR)
Diagnostic threshold (with symptoms)	5 or more
Mild	under 15 (clinical convention: 5 to 15)
Moderate	**15 to 30**
Severe	**over 30**

Obstructive sleep apnoea severity by AHI (DSM-5-TR specifier, verified); the mild-band lower edge differs between DSM-5-TR (under 15) and the clinical convention (5 to 15).

20 to 25	90	>30	8
REM SHARE OF THE NIGHT (% OF TOTAL SLEEP TIME)	NORMAL REM LATENCY AND NREM-REM CYCLE (MINUTES)	SEVERE OBSTRUCTIVE SLEEP APNOEA AHI (EVENTS PER HOUR)	MSLT POSITIVE MEAN SLEEP LATENCY (MINUTES OR LESS)

11.11 The Indian frame

Physiology in a real clinic. The examinable physiology is universal, but its use in Indian practice has two edges. Sleep disorders are under-recognised and under-investigated: a full **polysomnography** lab sits mostly in tertiary and metropolitan centres, so the front-line diagnosis of insomnia and of ordinary sleepiness leans on a careful history, a sleep diary and validated questionnaires rather than the study itself, and the study is reserved for the physiological questions (apnoea, narcolepsy, the movement disorders) that history cannot settle.

The two practice pitfalls. The first is the routine prescription of a benzodiazepine for chronic insomnia, still common in Indian practice, when the normal-physiology teaching (that chronic insomnia is a conditioned, hyperarousal problem, not a hypnotic-deficiency state) argues for behavioural first-line care, developed in the insomnia and CBT-I notes. The second is over-reading normal, age-related architecture (lighter, shorter, more fragmented sleep with less slow-wave sleep) as a disease in the older patient. Knowing the healthy template is what protects an older person from an unnecessary long-term hypnotic.

INDIA

Two habits are worth naming. Polysomnography is concentrated in tertiary and metro sleep labs, so most sleep complaints in India are worked up clinically first, with the study reserved for suspected apnoea, narcolepsy or a movement disorder; and the reflex of a benzodiazepine for every sleepless night is over-used, when the physiology says chronic insomnia is a hyperarousal problem better met with sleep-hygiene and behavioural care. Good sleep hygiene, a regular rise time, light exposure, and cutting the late-evening screen and caffeine, is itself an application of the two-process model, strengthening the circadian signal and clearing homeostatic pressure honestly rather than pharmacologically.

HOLD THIS

Normal adult sleep cycles NREM to REM about every **90 minutes** across 4 to 5 cycles, with REM at **20 to 25%** of the night and a first REM period (normal REM latency) at about **90 minutes**; N2 is defined by spindles and K-complexes, N3 by delta, and REM by a wake-like EEG with atonia. Sleep is timed by the two-process model (homeostatic Process S versus circadian Process C) and switched by the arousal-system-versus-VLPO flip-flop that orexin stabilises, and it is measured by polysomnography (EEG, EOG, EMG) whose AHI grades apnoea (severe over 30 events per hour).

12 · Insomnia disorder: assessment and pharmacological management

Insomnia disorder is dissatisfaction with sleep quantity or quality, with difficulty initiating sleep, difficulty maintaining sleep or early-morning waking, that persists despite an adequate

opportunity to sleep and carries daytime consequences. It is the commonest sleep complaint the psychiatrist meets, and the examinable heart of it is a hybrid: first you must recognise insomnia disorder as a diagnosis in its own right and separate it cleanly from the circadian, breathing and movement disorders that mimic it, and then you must know that its treatment is led not by a tablet but by a psychological therapy.

Why it matters, and how this note is framed. Two anchors carry the topic. First, the modern nosology treats insomnia as an independent, treatable condition rather than a symptom secondary to something else, split into a **chronic insomnia** form (three months or longer) and a short-term form, and screened with the seven-item Insomnia Severity Index. Second, the whole of **pharmacological management of insomnia** sits downstream of one rule, that cognitive behavioural therapy for insomnia is first-line for chronic insomnia and a **hypnotic** is not. This is a management topic, so the drug half is built from the verified guideline rows for insomnia, leading with the British Association for Psychopharmacology position (BAP 2019) and then the Indian, NICE and VA/DoD guidance; every first-line named there is verified and is not contradicted here, and any dose or cut-off the parsed library could not confirm is flagged rather than invented.

INSOMNIA SEVERITY INDEX (TYPESET, NOT REPRODUCED)	VERIFIED STRUCTURE AND SEVERITY BANDS
Instrument	The Insomnia Severity Index, a brief self-report measure of perceived insomnia severity over the last two weeks (Morin, 1993), widely used to screen and to track response
Items	7 items, each scored 0 to 4, total range 0 to 28: the severity of sleep-onset difficulty, of sleep-maintenance difficulty and of early-morning waking; satisfaction with the current sleep pattern; interference with daytime functioning; how noticeable the impairment is to others; and the level of worry or distress about the sleep problem
Severity bands	**0 to 7 no clinically significant insomnia; 8 to 14 subthreshold insomnia; 15 to 21 clinical insomnia, moderate; 22 to 28 clinical insomnia, severe**
Use	a change of about 6 or more points marks a clinically meaningful response; it complements, and does not replace, the sleep history and the sleep diary

Insomnia Severity Index: typeset structure and verified bands; the form is copyright and its distribution is permission-sensitive, so it is presented here in typeset form rather than reproduced (Morin CM. Insomnia: Psychological Assessment and Management. New York: Guilford Press; 1993). For the free, non-commercial resident edition only.

Fig 17.10 The Insomnia Severity Index (ISI). A brief seven-item self-report of how severe the insomnia has been over the last two weeks: the severity of getting to sleep, staying asleep and waking too early, satisfaction with sleep, the daytime interference, how noticeable it is to others, and the distress it causes, each rated 0 to 4 for a total of 0 to 28. The bands run 0 to 7 no clinically significant insomnia, 8 to 14 subthreshold, 15 to 21 moderate clinical insomnia and 22 to 28 severe, and a fall of about six points or more marks a meaningful response to treatment. It is a screen and an outcome measure, not a substitute for the sleep history and the sleep diary.

12.1 What insomnia disorder is: the definition, and the shift to a diagnosis in its own right

The definition. The primary element is *dissatisfaction with sleep quantity or quality*, accompanied by at least one of difficulty initiating sleep, difficulty maintaining sleep (frequent awakenings or trouble returning to sleep) or early-morning waking with inability to return to sleep, occurring despite an adequate opportunity and adequate circumstances for sleep, and producing daytime consequences (fatigue, impaired attention or mood disturbance) (Kaplan and Sadock CTP 2024). The clause that adequate opportunity exists is what separates the disorder from simple sleep deprivation: the person is in bed with the chance to sleep and still cannot.

The paradigm shift. Where older systems called insomnia a symptom secondary to some underlying illness and told the clinician to treat only the cause, current thinking treats it as a possible independent condition and reframes the older secondary insomnias as *comorbid*, to be managed in their own right; nonrestorative sleep has moved out to hypersomnolence (Kaplan

and Sadock CTP 2024). The exam point is that treating the depression does not reliably fix the insomnia, so insomnia is targeted directly.

> **PEARL**
> Insomnia is no longer a secondary symptom to be ignored until its cause is fixed. It is a diagnosis in its own right and is treated directly, in parallel with any comorbid depression, anxiety or pain, not after it.

12.2 The DSM-5-TR and ICD-11 criteria, and the chronic-versus-short-term split

The eight criteria. DSM-5-TR evaluates insomnia against eight points: how it harms sleep, how it affects the following wakefulness, its frequency, its chronicity, whether it coexists with another sleep disorder, with medication or substance use, or with another psychiatric, neurological or medical condition, and, critically, that the difficulty occurs notwithstanding an adequate opportunity to sleep (Kaplan and Sadock CTP 2024). The two quantitative thresholds are the ones examiners test: the disturbance must occur at least three nights per week and be present for at least three months.

The chronic-versus-short-term distinction. All three systems now converge on the same divide. ICD-11, which moves the sleep-wake disorders out of the mental-disorders chapter into a dedicated sleep-wake chapter, separates chronic insomnia disorder (symptoms three or more nights per week for three months or longer) from short-term insomnia disorder (the same picture lasting under three months, usually with an identifiable stressor). The AASM classification (ICSD-3) draws the identical chronic-insomnia-disorder versus short-term-insomnia-disorder line (Kaplan and Sadock CTP 2024). The threshold matters because it decides the treatment lever: short-term insomnia is where a brief hypnotic has its legitimate place, whereas chronic insomnia is where the psychological therapy leads.

CRITERION	REQUIREMENT FOR INSOMNIA DISORDER
Core complaint	**Dissatisfaction with sleep quantity or quality**
Symptom (one or more)	Difficulty initiating sleep; difficulty maintaining sleep; early-morning waking with inability to return to sleep
Daytime consequence	Clinically significant distress or impairment (fatigue, attention, mood, function)
Frequency	**At least three nights per week**
Duration (chronic)	**Present for at least three months (short-term insomnia if under three months)**
Adequate opportunity	Occurs despite adequate opportunity and circumstances for sleep
Not better explained by	Another sleep-wake disorder, a substance, or a coexisting mental or medical disorder that fully accounts for it

DSM-5-TR insomnia disorder criteria; the load-bearing numbers are the frequency (three or more nights per week) and the duration (three months) that define the chronic form.

GOOD TO REMEMBER

- **Insomnia disorder (defining criterion):** dissatisfaction with sleep quantity or quality with difficulty initiating or maintaining sleep or early-morning waking, *despite adequate opportunity to sleep* and with daytime consequences; the diagnostic thresholds are at least three nights per week for at least three months, and that three-month mark is what separates chronic insomnia (psychological therapy leads) from short-term insomnia (a brief hypnotic has a place).

12.3 Assessment: the sleep history and the sleep diary

The sleep history. A sleep history should be a short but routine part of every psychiatric consultation, because a limited number of things go wrong with sleep and most sleep disorders can be diagnosed by clinical history alone (New Oxford Textbook of Psychiatry). The complaint reduces to sleeping too little, sleeping too much, sleeping at the wrong time of day, or things that go bump in the night, and a collateral history from the bed partner is often what reveals the snoring, the kicking or the abnormal nocturnal behaviour the patient cannot report. The history maps the day in full: the bedtime routine and environment, sleep-onset latency, awakenings and their causes, final waking time, daytime napping and function, and the substances, caffeine, alcohol, nicotine and stimulant medications, that erode sleep.

The sleep diary. Where the history is ambiguous, a prospective **sleep** diary kept over one to two weeks records bed and rise times, estimated latency, awakenings and daytime naps, exposing the mismatch between perceived and actual sleep and revealing a circadian pattern the single consultation misses; actigraphy extends this objectively where needed. Polysomnography is *not* routine for uncomplicated insomnia and is reserved for suspected sleep apnoea, narcolepsy or a periodic-limb-movement disorder (Kaplan and Sadock CTP 2024).

GOOD TO REMEMBER

- **Assessment (the first step):** take a routine *sleep history* (with a collateral account from the bed partner) and, where unclear, a one-to-two-week prospective sleep diary; most insomnia is diagnosed on history alone, and polysomnography is not routine, reserved for suspected obstructive sleep apnoea, narcolepsy or periodic limb movements.

12.4 The differential: the sleep-wake disorders that mimic insomnia

What must be excluded. Before insomnia disorder is settled, the sleep-wake mimics are cleared. A *circadian rhythm sleep-wake disorder* (delayed or advanced sleep phase, shift-work or jet-lag type) presents as insomnia only because the person is trying to sleep at the wrong biological time, and the tell is that sleep is normal when timed to the patient's own preferred schedule. A *breathing-related sleep disorder*, chiefly obstructive sleep apnoea, presents with un-refreshing sleep, snoring and witnessed apnoeas, and is screened with STOP-BANG. A *movement disorder*, restless legs syndrome or periodic limb movement disorder, delays or fragments sleep through an urge to move or repetitive kicking. Each is developed in its own note; the point here is that a hypnotic prescribed for what is actually apnoea or a phase disorder is both useless and, in apnoea, dangerous.

The comorbid causes. Insomnia is driven by comorbid psychiatric illness (depression, anxiety, mania, post-traumatic stress and substance use) and by medical disease (chronic pain, nocturia, cardiorespiratory disease, and endocrine disorders such as thyroid dysfunction). These are managed in parallel with the insomnia, not instead of it. The psychiatric relevance of these medical sleep disturbances is developed in the Somatic-symptom, sexual, impulse-control disorders and suicide notes and the Consultation-liaison, geriatric and transcultural psychiatry notes.

MIMIC OR DRIVER	THE DISCRIMINATING CLUE
Circadian rhythm sleep-wake disorder	**Sleep is normal in quantity and quality when allowed at the patient's own preferred timing**
Obstructive sleep apnoea (breathing-related)	Snoring, witnessed apnoeas, un-refreshing sleep, daytime sleepiness; screen with STOP-BANG
Restless legs / periodic limb movement	Evening urge to move the legs, relieved by movement; repetitive nocturnal kicking on collateral history
Comorbid psychiatric (depression, anxiety, mania)	**Insomnia tracks the mood or anxiety syndrome but is treated in its own right, not deferred**
Medical and substance causes	Pain, nocturia, cardiorespiratory or thyroid disease; caffeine, alcohol, nicotine, stimulants

The insomnia differential; the circadian and breathing-related disorders are the two that a hypnotic will fail, so both must be excluded before treating for insomnia disorder.

MNEMONIC

CIRCADIAN, BREATHE, MOVE, MOOD, MED

Before diagnosing insomnia disorder, clear the mimics: **Circadian** rhythm disorder (wrong-time sleep), **Breathe** (obstructive sleep apnoea), **Move** (restless legs / periodic limb movement), **Mood** (depression, anxiety, mania), and **Med**ical or substance causes. The five buckets a sleep history must exclude.

12.5 The Insomnia Severity Index and its severity bands

What the ISI is. The Insomnia Severity Index (ISI) is a seven-item self-report tool that captures the patient's own perception of their insomnia, its symptoms, its daytime effects, and how distressed or concerned they are by it. Each item is scored from zero to four, giving a maximum of twenty-eight, and a score of **10 or higher** identifies insomnia with high sensitivity and specificity as a screening threshold (Kaplan and Sadock CTP 2024). The VA/DoD guidance names the ISI (or the Athens Insomnia Scale) as the validated instrument to use in anyone presenting with a sleep complaint (VA/DoD 2025). This topic carries the ISI form on the accompanying scale plate; the daytime-sleepiness counterpart, the Epworth Sleepiness Scale, belongs to the hypersomnolence and narcolepsy assessment and is cross-referenced there.

The severity bands. The total is banded into four severity strata, verified against the max-of-twenty-eight scoring: 0 to 7 no clinically significant insomnia, 8 to 14 subthreshold insomnia, **15**

to 21 clinical insomnia of moderate severity, and 22 to 28 clinical insomnia, severe. These bands are what let the ISI double as an outcome measure: a fall of several points across treatment is the standard marker of response.

ISI TOTAL (SCORE)	SEVERITY BAND
0 to 7	No clinically significant insomnia
8 to 14	Subthreshold insomnia
15 to 21	**Clinical insomnia, moderate severity**
22 to 28	**Clinical insomnia, severe**

ISI severity bands (seven items, zero to four each, maximum twenty-eight); the screening cut-off of ten or higher and the moderate band of fifteen to twenty-one are the two most examinable numbers.

≥10	15 to 21	3	1 to 6
ISI SCREENING CUT-OFF FOR INSOMNIA (SCORE)	ISI MODERATE CLINICAL INSOMNIA BAND (SCORE)	CHRONIC INSOMNIA DURATION THRESHOLD (MONTHS)	LOW-DOSE DOXEPIN FOR INSOMNIA (MG PER DAY)

GOOD TO REMEMBER

- **Insomnia Severity Index (the value):** seven items, each scored zero to four, maximum twenty-eight; a score of ten or higher screens positive with high sensitivity and specificity, and the clinical bands are 15 to 21 (moderate) and 22 to 28 (severe), with 0 to 7 no significant insomnia and 8 to 14 subthreshold; it doubles as the outcome measure across treatment.

12.6 The management rule: CBT-I is first-line for chronic insomnia, a hypnotic is not

The one rule. For **chronic insomnia**, cognitive behavioural therapy for insomnia (CBT-I), delivered as a multicomponent package that includes sleep restriction and stimulus control, is the first-line treatment, offered before drug treatment (BAP 2019; NICE 2023). BAP notes that face-to-face and digital CBT-I are both efficacious, so a shortage of therapists is not a reason to default straight to a tablet. The Indian Psychiatric Society CPG makes CBT-I the mainstay of chronic insomnia, delivered as an individualised package of sleep education, sleep hygiene, cognitive restructuring, stimulus control, sleep restriction and relaxation (IPS 2017), and VA/DoD explicitly prefers CBT-I over pharmacotherapy as first-line (VA/DoD 2025). The component detail of CBT-I is carried in its own note; here it is the anchor that pharmacology hangs off.

Where the drug fits. Pharmacology enters only where CBT-I fails, is unavailable, or the patient cannot engage with it, and even then it is short-term for chronic insomnia rather than an indefinite prescription (BAP 2019; IPS 2017). A crucial negative: BAP and VA/DoD both say antipsychotics such as quetiapine and olanzapine are *not* to be used as first-line for insomnia, and VA/DoD advises against benzodiazepines, diphenhydramine and trazodone for chronic insomnia.

RULE **CBT-I first, the tablet second.** Cognitive behavioural therapy for insomnia (with sleep restriction and stimulus control) is first-line for chronic insomnia; a hypnotic is not first-line and is a short-term measure for when CBT-I fails, is unavailable, or cannot be engaged with.

GOOD TO REMEMBER

- **First-line management (the principle):** CBT-I is first-line for chronic insomnia and is offered before any drug (BAP 2019, IPS 2017, NICE 2023, VA/DoD 2025); a hypnotic is second-line and short-term, and antipsychotics (quetiapine, olanzapine) are explicitly not first-line for insomnia.

12.7 Pharmacological management: the z-drugs and matching half-life to the pattern

When a hypnotic is used. When pharmacology is indicated, the workhorse short-term agents are the GABA positive allosteric modulators, the benzodiazepines and the z-drug hypnotics (zolpidem, zopiclone, eszopiclone, zaleplon) (BAP 2019). BAP frames the choice by kinetics: pick a short-acting agent for sleep-onset insomnia and a slightly longer-acting one for sleep-maintenance insomnia. NICE keeps this pragmatic, noting no compelling efficacy difference between zolpidem, zopiclone and the shorter-acting benzodiazepines, so the lowest-cost agent is chosen, prescribed short-term and strictly within the licensed indication, and a second one is not tried if the first has failed (NICE 2004).

Match the drug to the problem. The **pharmacological management of insomnia** is therefore a kinetics exercise: a short half-life for the patient who cannot fall asleep, a slightly longer one for the patient who wakes and cannot return. The deep hypnotic pharmacology, the mechanism at the GABA-A receptor, the half-life classification, the dependence liability and the taper, is developed in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes.

WORKED EXAMPLE

A patient who lies awake for two hours at the start of the night but sleeps through once asleep has sleep-onset insomnia, so a short-acting agent (for example zolpidem, sold in India as Zolfresh, or melatonin) fits. A patient who falls asleep readily but wakes at three in the morning and cannot return has sleep-maintenance insomnia, so a slightly longer-acting agent (for example zopiclone, or very low-dose doxepin for the late-night awakening) fits. Match the half-life to the pattern.

AGENT OR CLASS	PLACE IN INSOMNIA MANAGEMENT	GUIDELINE ANCHOR
CBT-I (with sleep restriction, stimulus control)	**First-line for chronic insomnia, before any drug**	BAP 2019; IPS 2017; NICE 2023; VA/DoD 2025
Z-drugs (zolpidem, zopiclone, eszopiclone, zaleplon)	**Short-term hypnotic; match half-life to onset vs maintenance**	BAP 2019; NICE 2004
Benzodiazepines (GABA-PAM)	Short-term only; avoided for chronic insomnia (dependence)	BAP 2019; VA/DoD 2025 (against, chronic)
Prolonged-release melatonin	Consider in adults over 55 for onset latency and quality	BAP 2019; IPS 2017
Low-dose doxepin (1 to 6 mg per day)	Selective antihistamine hypnotic, useful for late-night awakenings	BAP 2019

AGENT OR CLASS	PLACE IN INSOMNIA MANAGEMENT	GUIDELINE ANCHOR
Orexin antagonists (daridorexant, suvorexant, lemborexant)	**For long-term insomnia only after CBT-I fails or is unavailable**	NICE 2023; VA/DoD 2025
Sedating antidepressants (trazodone, mirtazapine)	Only when a comorbid mood disorder warrants; weak insomnia evidence	BAP 2019; IPS 2017
Antipsychotics (quetiapine, olanzapine)	Not first-line for insomnia; avoided	BAP 2019; VA/DoD 2025 (against)

The pharmacological ladder for insomnia; CBT-I sits above every drug, the z-drugs are the short-term workhorse matched by half-life, and antipsychotics are explicitly not first-line.

GOOD TO REMEMBER

- **Z-drug hypnotics (the value):** zolpidem, zopiclone, eszopiclone and zaleplon are short-term agents chosen by kinetics, short-acting for sleep-onset insomnia and slightly longer-acting for sleep-maintenance insomnia (BAP 2019); NICE finds no compelling efficacy difference, so pick the lowest-cost agent, prescribe short-term within licence, and do not try a second z-drug if the first has failed (NICE 2004).

12.8 Melatonin, the older adult, and the newer agents

Melatonin and the over-55 patient. Melatonin (in India, Meloset) is a weak hypnotic in its own right but a useful chronobiotic and sleep-promoter, and its licensed niche is the older adult: BAP and IPS both recommend prolonged-release melatonin in patients over 55 years to improve sleep-onset latency and sleep quality, at the licensed 2 mg prolonged-release dose taken before bedtime (BAP 2019; IPS 2017). Its favourable safety and absence of dependence make it the preferred first drug in the elderly, where z-drugs carry falls and confusion risk. The melatonin-receptor agonists ramelteon and agomelatine sit alongside it as chronobiotic options (IPS 2017).

The newer agents. The dual orexin receptor antagonists (daridorexant, suvorexant, lemborexant) block the wake-promoting orexin system and are positioned for long-term insomnia, but only after CBT-I has failed, is unsuitable or is unavailable; if daridorexant does not help enough it is stopped after three months, and if continued it is reviewed regularly (NICE 2023; VA/DoD 2025). Very low-dose doxepin (1 to 6 mg per day), a selective H1 antihistamine, is effective particularly for late-night awakenings (BAP 2019). The receptor pharmacology of melatonin, ramelteon, the orexin antagonists and the z-drugs is carried in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes, and the sleep neurotransmitter and ascending-arousal systems in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and the Functional Neuroanatomy and Neurophysiology notes.

GOOD TO REMEMBER

- **Melatonin (the value):** a weak hypnotic but a useful chronobiotic; its licensed place is prolonged-release melatonin (2 mg) in the adult over 55 to improve sleep-onset latency and quality (BAP 2019, IPS 2017), preferred over a z-drug in the elderly for its safety and lack of dependence; the orexin antagonists (daridorexant) are reserved for long-term insomnia after CBT-I fails.

12.9 Discontinuation, the benzodiazepine trap, and the Indian frame

The taper. Hypnotics are used only as long as clinically indicated, and when they are stopped they are tapered slowly with concurrent CBT-I to improve the outcome and reduce rebound insomnia (BAP 2019). Because the z-drug and benzodiazepine dependence and the withdrawal taper are the deep story, the mechanism and the graded reduction are cross-referenced to the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes. The single most consequential caution stays here: do not start what you cannot stop, and do not run a hypnotic long-term for chronic insomnia when CBT-I is the treatment.

Sleep hygiene is not enough on its own. Sleep hygiene education is a component of CBT-I, but as a stand-alone treatment it is not effective for chronic insomnia and should not be offered alone (VA/DoD 2025). This is the quiet trap of the busy clinic: handing over a sleep-hygiene leaflet and calling it treatment.

TRAP **A long-term hypnotic (or a lone sleep-hygiene leaflet) instead of CBT-I.** Starting an indefinite z-drug or benzodiazepine for chronic insomnia, or offering sleep hygiene as a stand-alone, both substitute for the first-line treatment; CBT-I is what changes the trajectory, and the hypnotic is short-term only.

INDIA

The genuine Indian device here is *benzodiazepine over-use for insomnia*. With CBT-I therapists scarce and hypnotics cheap and easily obtained, long-term benzodiazepine and z-drug prescribing for chronic insomnia is widespread, and clonazepam and alprazolam are routinely used as sleeping tablets and drift into dependence. The corrective is not exotic: treat chronic insomnia with CBT-I as first-line (face-to-face or digital, both work), keep any hypnotic short-term and within licence, prefer prolonged-release melatonin in the older adult, and do not offer a sleep-hygiene leaflet as if it were the whole treatment. Correct sleep-hygiene practice is a component of CBT-I, not a substitute for it.

HOLD THIS

Insomnia disorder is dissatisfaction with sleep despite adequate opportunity, at least three nights per week for three months for the chronic form; screen with the ISI (positive at ten or higher, moderate band 15 to 21), clear the circadian, breathing and movement mimics, and treat chronic insomnia with CBT-I first-line, keeping z-drugs and other hypnotics short-term, kinetics-matched, and tapered, with prolonged-release melatonin for the over-55s and antipsychotics off the first line.

13 · Cognitive behaviour therapy for insomnia (CBT-I)

Cognitive behaviour therapy for insomnia is a structured, multicomponent psychological treatment that re-teaches the sleep system what the bed is for, compresses the night down to real sleep, and dismantles the worry that keeps the patient awake. It is the single most examinable fact in the whole sleep-treatment map, because the modern guidelines have moved the first move in chronic insomnia off the prescription pad and onto this therapy: CBT-I is first-line for chronic insomnia and a hypnotic is not.

Why it matters, and how this note is framed. This is a management topic, so the plan is built from the verified insomnia guideline rows, led by the British Association for Psychopharmacology position (BAP 2019) and then the Indian, NICE and VA/DoD guidance; every first-line named there is verified and is not contradicted here. The examinable spine is that CBT-I is a *package* of five components, that its two active behavioural ingredients are **sleep restriction** and **stimulus control**, that **sleep hygiene** is taught as necessary but not sufficient, and that the whole thing outlasts a tablet. The wider CBT technique and the general psychotherapy frame are developed in the Psychotherapies, clinical assessment, MSE and nosology notes; the deep hypnotic pharmacology that sits downstream of a CBT-I failure is carried in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes. The CBT-I components map is set out in the accompanying figure.

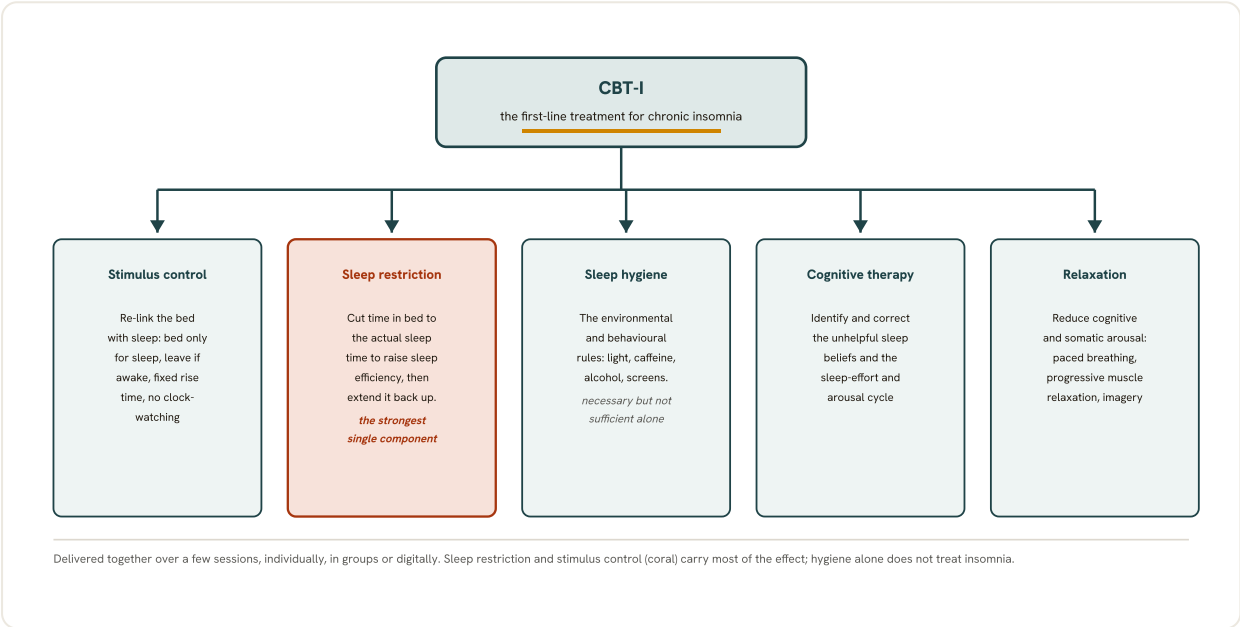


Fig 17.11 The components of cognitive behaviour therapy for insomnia. CBT-I, not a hypnotic, is the first-line treatment for chronic insomnia, and it is a package of five components. Stimulus control re-associates the bed with sleep; sleep restriction, the single most powerful element, curtails time in bed to the actual sleep time so that sleep consolidates and efficiency rises, then extends it back up; sleep hygiene sets the environmental and behavioural conditions but does not by itself treat insomnia; cognitive therapy corrects the unhelpful sleep beliefs and the effort-and-arousal cycle that keep a poor sleeper awake; and relaxation lowers the cognitive and somatic arousal. The wider cognitive behaviour therapy technique is developed in the Psychotherapies, clinical assessment, MSE and nosology notes.

13.1 What CBT-I is: a multicomponent package, not a single technique

The package. CBT-I begins with a careful clinical interview that maps the insomnia's aetiology, chronicity, severity and comorbidity, after which a treatment plan is assembled from relevant components: universal sleep hygiene, stimulus control therapy, sleep restriction therapy, relaxation therapies and biofeedback, cognitive therapy, and occasionally paradoxical intention (Kaplan and Sadock CTP 2024). It is delivered as an individualised multicomponent programme of sleep education, sleep hygiene, cognitive restructuring, stimulus control, sleep restriction and relaxation (IPS 2017). The point examiners test is that no single element is the treatment; the package works because it addresses the several variables that jointly perpetuate insomnia.

The two engines and the three supports. Not all components carry equal weight. The two behavioural interventions with the strongest independent evidence, and the two BAP names explicitly when it defines CBT-I, are sleep restriction and stimulus control (BAP 2019). Sleep hygiene, cognitive therapy and relaxation are the supporting components; sleep hygiene in particular is not a treatment on its own. Holding that hierarchy is what separates a real CBT-I referral from handing over a sleep-hygiene leaflet.

MNEMONIC

2 ENGINES + 3 SUPPORTS

The two behavioural **engines** of CBT-I are **sleep restriction** and **stimulus control** (the components BAP names when it defines the therapy). The three **supports** are **sleep hygiene**, **cognitive therapy** and **relaxation**. Five components, one package; the engines drive it, the supports steady it.

13.2 Stimulus control: re-associate the bed with sleep

The idea. Stimulus control therapy, a deconditioning paradigm developed by Richard Bootzin at the University of Arizona, aims to break the learned link between the bed and wakeful frustration and to rebuild the association between going to bed and falling asleep quickly (Kaplan and Sadock CTP 2024). The chronic insomniac has, in effect, conditioned the bedroom into a cue for lying awake; stimulus control undoes that conditioning through a small set of rules that must be followed consistently.

The rules. Go to bed only when sleepy. Use the bed for sleep only, so no television, reading, eating or phone in bed. If sleep does not come after a short while, get up (without watching the clock), go to another room, do something non-arousing, and return only when sleepy again, repeating this as often as needed. Rise at the same fixed time every morning regardless of how the night went, and do not nap. Results may take a few weeks to a month to appear, so the patient is warned not to abandon the method early.

GOOD TO REMEMBER

- **Stimulus control (the principle):** re-associate the bed with rapid sleep onset by four rules, bed only when sleepy, bed for sleep only, out of bed to another room if not asleep (return when sleepy, do not clock-watch), and a fixed rise time every morning with no napping; the effect builds over a few weeks, not overnight (Bootzin; BAP 2019).

13.3 Sleep restriction: curtail time in bed to consolidate sleep, then titrate up

The idea. Sleep restriction therapy, developed by Arthur Spielman, raises sleep efficiency, the proportion of time in bed actually spent asleep, by cutting back the time the patient lies in bed to match the time they truly sleep (Kaplan and Sadock CTP 2024). Compressing time in bed maximises homeostatic sleep drive and consolidates fragmented sleep; the mild sleep deprivation it induces is the therapeutic lever.

The titration. If a patient sleeps only about five hours of a scheduled eight in bed, time in bed is reduced towards the sleep time, but never set below roughly **four to five hours** per night, and the

patient is warned about the daytime sleepiness this deliberately provokes. Daytime sleep is avoided, though an older adult may take a short nap. Sleep efficiency is then monitored, and when it reaches **85%** averaged over **five nights**, time in bed is lengthened by **15 minutes**; the schedule is stepped up in this way until adequate sleep is reached, producing a gradual, steady fall in nocturnal wakefulness.

WORKED EXAMPLE

A patient records eight hours in bed but only about five asleep, a sleep efficiency near sixty-two per cent. Time in bed is set to around five and a half hours (not below the four-to-five-hour floor) with a fixed rise time. Over the following week the sleep the patient does get becomes solid and continuous; once efficiency averages 85% or more across five nights, time in bed is extended by fifteen minutes, and the process repeats until the patient is sleeping enough with little time awake in bed.

GOOD TO REMEMBER

- **Sleep restriction (the value):** curtail time in bed to the actual sleep time to raise sleep efficiency (time asleep as a proportion of time in bed), holding a floor of about four to five hours; when efficiency reaches 85% over five nights, add 15 minutes to time in bed and titrate up (Spielman; BAP 2019).

13.4 Sleep hygiene: the rules, taught as necessary but not sufficient

What it is. Sleep hygiene education targets the modifiable environmental and behavioural factors that erode sleep: a regular schedule, avoiding caffeine, nicotine and alcohol near bedtime, limiting daytime napping, keeping the bedroom dark, quiet and cool, and not exercising or eating heavily too close to sleep (Kaplan and Sadock CTP 2024). Because these are entrenched lifestyle habits, only one or two items are tackled at a time so the patient is not overwhelmed.

Why it is not enough on its own. The load-bearing exam point is that sleep hygiene education alone does not appear to improve chronic insomnia, and VA/DoD explicitly advises against using it as a stand-alone treatment for chronic insomnia disorder (VA/DoD 2025). It is a genuine component of the package and a reasonable universal measure, but calling a sleep-hygiene handout "treatment" is the quiet error of the busy clinic.

TRAP **Sleep hygiene is not CBT-I.** Handing over a sleep-hygiene leaflet and calling it done is not treatment; sleep hygiene alone does not improve chronic insomnia and must sit inside the full multicomponent package (VA/DoD 2025).

GOOD TO REMEMBER

- **Sleep hygiene (the caution):** the environmental and behavioural rules (regular schedule, no caffeine/nicotine/alcohol near bedtime, limit naps, cool dark quiet room, tackle one or two habits at a time) are necessary but not sufficient, and are not effective as a stand-alone treatment for chronic insomnia (VA/DoD 2025).

13.5 Cognitive therapy for insomnia: correct the beliefs and the sleep-effort cycle

What it targets. Cognitive therapy, adapted for insomnia (the cognitive therapy insomnia component of the package), targets the negative emotional response to an appraisal of the sleep situation, because that emotional arousal is what perpetuates the insomnia (Kaplan and Sadock CTP 2024). Patients hold maladaptive sleep-related beliefs, catastrophising ("there must be something wrong with me if I cannot fall asleep in forty minutes") and unrealistic expectations ("if I do not get eight hours the day is ruined"), which feed a self-defeating *sleep-effort and hyperarousal cycle*: the harder they try to sleep, the more aroused and awake they become.

How it works. The method is the standard cognitive sequence applied to sleep: first identify the dysfunctional sleep-related cognitions, then challenge their validity, then substitute more adaptive and realistic thoughts, which lowers the arousal that was keeping the patient awake. This dovetails with paradoxical intention, where the patient is asked to stop trying to sleep, removing the very sleep effort that fuels the arousal. The wider cognitive technique is developed in the Psychotherapies, clinical assessment, MSE and nosology notes.

GOOD TO REMEMBER

- **Cognitive therapy for insomnia (the principle):** identify, challenge and substitute the unhelpful sleep-related beliefs (catastrophising, rigid eight-hour expectations) that drive the sleep-effort and hyperarousal cycle; lowering that arousal is the mechanism, and paradoxical intention (stop trying to sleep) works the same lever (Kaplan and Sadock CTP 2024).

13.6 Relaxation: lower the somatic and cognitive arousal at bedtime

The techniques. Relaxation methods reduce the physiological and mental arousal that blocks sleep onset: progressive muscle relaxation (deliberately tensing a muscle group for a few seconds then releasing it for longer, working from head to feet, and noticing the contrast), guided imagery of a restful scene, slow abdominal breathing, self-hypnosis, and biofeedback of a physiological marker such as forehead muscle tension (Kaplan and Sadock CTP 2024). Progressive muscle relaxation suits the patient whose insomnia is driven by bodily tension.

How they are used. The crucial teaching point is that a relaxation technique must be over-learned and mastered in the daytime, away from bed, over several weeks before it is applied at bedtime, so that by the time it is used to fall asleep the skill is automatic and does not itself become associated with the failure to sleep. Relaxation combines readily with sleep hygiene and stimulus control and doubles as a distraction from the ruminations that fuel insomnia.

GOOD TO REMEMBER

- **Relaxation (the value):** progressive muscle relaxation, guided imagery, abdominal breathing and biofeedback lower the arousal that blocks sleep onset; they must be over-learned in the daytime, away from the bed, before being applied at bedtime so the skill is automatic and never linked to sleeplessness (Kaplan and Sadock CTP 2024).

13.7 The five components at a glance

The map. The table below sets the five components against what each one does and its core instruction; the two engines are marked, and it mirrors the CBT-I components map in the

accompanying figure. Paradoxical intention is added as the occasional sixth technique that shares the cognitive component's target.

COMPONENT	WHAT IT DOES	THE CORE INSTRUCTION
Stimulus control (engine)	**Re-associates the bed with rapid sleep onset (deconditioning)**	Bed only when sleepy; bed for sleep only; out of bed if awake; fixed rise time; no naps
Sleep restriction (engine)	**Consolidates sleep and raises sleep efficiency via mild sleep debt**	Cut time in bed to sleep time (floor about four to five hours); titrate up 15 min at 85% efficiency
Sleep hygiene (support)	Removes environmental and behavioural sleep-eroders	Regular schedule, no caffeine/nicotine/alcohol near bed, limit naps; one or two habits at a time
Cognitive therapy (support)	Corrects dysfunctional sleep beliefs and the arousal cycle	Identify, challenge and substitute catastrophic and rigid sleep thoughts
Relaxation (support)	Lowers somatic and cognitive arousal at bedtime	Master PMR, imagery or breathing in the daytime, then apply at bed
Paradoxical intention (occasional)	Removes the sleep effort that feeds hyperarousal	Stop trying to sleep; give up the effort to fall asleep

The CBT-I components; sleep restriction and stimulus control are the two behavioural engines, sleep hygiene, cognitive therapy and relaxation the supports, and sleep hygiene alone is not a treatment.

13.8 The evidence base: durable where a tablet is not

What the evidence shows. Studies repeatedly show significant, sustained improvement in sleep with CBT-I: shorter sleep-onset latency, fewer and briefer awakenings, and less time awake in bed, with no demonstrated adverse effects (Kaplan and Sadock CTP 2024). Its short-term benefit is broadly similar to that of hypnotic medication, but the decisive difference is durability, the gains persist long after treatment ends, even **36 months** out, whereas insomnia frequently returns when a hypnotic is stopped, sometimes with rebound insomnia.

The trade-off. The costs are that CBT-I takes longer to work than a tablet, needs an actively participating and motivated patient, and depends on trained therapists who are often scarce, which is exactly why the digital route matters. The desperate patient wants a quick fix; the clinician's task is to hold the line that the therapy that takes a few weeks is the one that lasts.

PEARL

CBT-I and a hypnotic look similar at the finish of a short course, but they diverge afterwards: stop the drug and the insomnia usually comes back, sometimes worse (rebound), whereas the CBT-I gains hold for years. Durability, not speed, is the reason CBT-I leads.

13.9 Delivery: individual, group, and digital CBT-I

The formats. CBT-I can be delivered one to one, in groups, or digitally with no in-person visit, and BAP is explicit that face-to-face and digital CBT-I (dCBT-I) are both efficacious, so the patient can be offered a choice among evidence-based options and a shortage of therapists is not a reason to default to a tablet (BAP 2019). Digital and app-based programmes extend reach where trained clinicians are few.

The brief variant. A condensed form, brief behavioural treatment for insomnia (BBT-I), distils the behavioural core (chiefly sleep restriction and stimulus control) into a shorter, more deliverable package, and VA/DoD lists it as a reasonable option for chronic insomnia disorder (VA/DoD 2025). The message across formats is the same: the components travel, whether delivered by a therapist, an app or a brief protocol.

GOOD TO REMEMBER

- **Delivery (the value):** CBT-I works individually, in groups and digitally, with face-to-face and digital CBT-I both efficacious (BAP 2019); brief behavioural treatment for insomnia (BBT-I) is a shorter behavioural-core option (VA/DoD 2025), so scarcity of therapists is not a reason to skip straight to a hypnotic.

13.10 First-line status, where the drug fits, and the Indian frame

The one rule. CBT-I, delivered as the multicomponent package including sleep restriction and stimulus control, is the first-line chronic insomnia treatment, offered before any drug (BAP 2019; NICE 2023). The Indian Psychiatric Society CPG makes CBT-I the mainstay of chronic insomnia (IPS 2017), and VA/DoD gives it a strong recommendation and explicitly prefers it over pharmacotherapy (VA/DoD 2025). Pharmacology enters only where CBT-I fails, is unavailable, or the patient cannot engage with it, and when a hypnotic is later discontinued it is tapered slowly with concurrent CBT-I to improve the outcome (BAP 2019). The deep hypnotic pharmacology is carried in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes.

The Indian frame. IPS 2017 sets CBT-I as the mainstay, but the practice reality is a shortage of clinicians trained to deliver it, so the default in much Indian practice slides towards a benzodiazepine or z-drug prescription and a sleep-hygiene handout, precisely the two moves the evidence cautions against as stand-alone treatment. Indian textbooks teach the sleep-hygiene rules, regular daytime exercise (not in the evening), minimising daytime naps, avoiding heavy meals and fluids before bed, and avoiding caffeine and alcohol as a sleep aid, but these are the necessary-but-not-sufficient support, not the therapy. The digital-CBT-I route is the realistic way to close the access gap.

RULE **CBT-I first, the tablet second.** Cognitive behaviour therapy for insomnia, with sleep restriction and stimulus control at its core, is first-line for chronic insomnia and is offered before any drug; a hypnotic is a short-term second-line measure for when CBT-I fails, is unavailable, or cannot be engaged with (BAP 2019, IPS 2017, NICE 2023, VA/DoD 2025).

TRAP **Do not start what you cannot stop.** Reaching for a long-term hypnotic in chronic insomnia when CBT-I is the treatment trades a durable fix for dependence and rebound; the tablet is short-term, and even then it is tapered with concurrent CBT-I.

INDIA

IPS 2017 names CBT-I the mainstay of chronic insomnia, yet trained CBT-I therapists are scarce across Indian services, so practice too often defaults to a benzodiazepine or z-drug plus a sleep-hygiene leaflet, the two moves the evidence flags as insufficient on their own. Digital CBT-I is the pragmatic way to widen access; the benzodiazepine habit is the pattern to unlearn.

85%	15	36
SLEEP-EFFICIENCY TARGET TO TITRATE TIME IN BED UP	TIME-IN-BED STEP-UP INCREMENT (MINUTES)	CBT-I BENEFIT SUSTAINED POST-TREATMENT (MONTHS)

HOLD THIS

CBT-I is a five-component package, sleep restriction and stimulus control the two engines, sleep hygiene, cognitive therapy and relaxation the supports, and it is first-line for chronic insomnia, offered before any drug because its gains outlast a hypnotic.

14 · Narcolepsy

Narcolepsy is a chronic disorder of the sleep-wake boundary in which the machinery of rapid-eye-movement sleep, its irresistible sleepiness and its muscle atonia and dreaming, intrudes into wakefulness. The examinable heart of it is a symptom cluster, a mechanism and a test: the **narcolepsy tetrad**, the loss of the hypothalamic orexin (hypocretin) neurons, and the multiple sleep latency test. It is a favourite of examiners precisely because it hides so well in psychiatric clinics, wearing the face of a treatment-resistant depression, of laziness, or of a seizure disorder, so that the patient who has been irresistibly sleepy since adolescence is treated for everything except the disorder they actually have.

Why it matters, and how this note is framed. This is a hybrid topic. The diagnostic half asks you to know the tetrad and its pentad extension, that cataplexy is the pathognomonic feature, the orexin loss and its HLA and autoimmune associations, the split into type 1 and type 2, the differential that traps the psychiatrist, and that the diagnosis is sealed on the mslt with its two verified numbers plus a low cerebrospinal-fluid orexin. The management half asks you to know the wake-promoting agents for the daytime sleepiness, sodium oxybate for cataplexy and the broken night, and the older antidepressants that suppress cataplexy, led by the sleep-medicine practice standard and with the Indian availability made explicit. Two structures accompany this topic and are flagged for drawing: the orexin sleep-switch and the tetrad schematic. Because narcolepsy sits outside the guideline database used for the eating and insomnia drugs, its criteria and doses are grounded in the parsed textbooks and the sleep classification, and any recommendation the library could not confirm is flagged rather than invented.

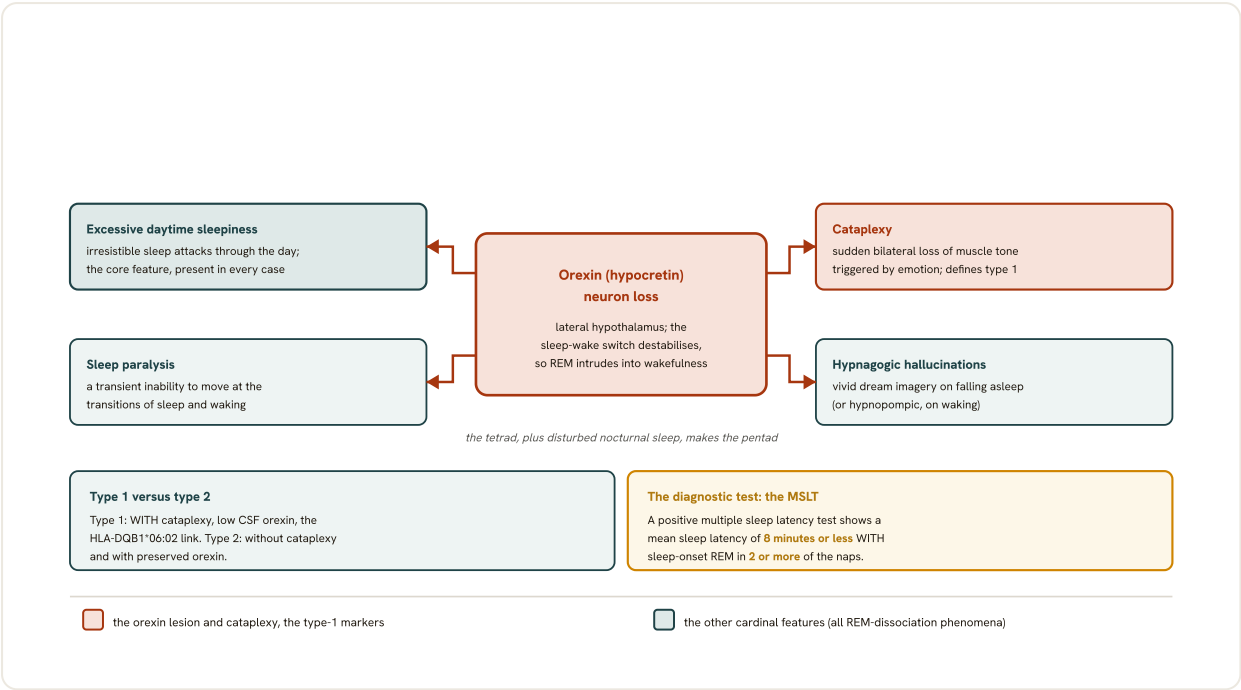


Fig 17.12 Narcolepsy: the orexin loss and the tetrad. The lesion is the loss of the orexin (hypocretin) neurons of the lateral hypothalamus, the peptide that stabilises the sleep-wake flip-flop switch, so the switch becomes unstable and the phenomena of REM sleep intrude into wakefulness. That produces the cardinal tetrad: excessive daytime sleepiness with irresistible sleep attacks (the core feature, present in every case), cataplexy (a sudden bilateral loss of muscle tone triggered by emotion, which is REM atonia breaking through and which defines type 1), sleep paralysis, and hypnagogic or hypnopompic hallucinations, with disturbed nocturnal sleep completing a pentad. Type 1 narcolepsy has cataplexy, a low cerebrospinal-fluid orexin and the HLA-DQB1*06:02 association; type 2 lacks cataplexy and has preserved orexin. The diagnosis is confirmed on the multiple sleep latency test by a mean sleep latency of eight minutes or less with sleep-onset REM periods in two or more naps. The wake-promoting and anti-cataplectic pharmacology is named in the topic and its detail cross-referenced to the anxiolytic and hypnotic pharmacology notes.

14.1 The tetrad, and the pentad

The four cardinal symptoms. For decades narcolepsy was defined by a tetrad (Kaplan and Sadock CTP 2024): irresistible **excessive daytime sleepiness** with sleep attacks, cataplexy, **sleep paralysis**, and **hypnagogic hallucinations** at sleep onset (or hypnopompic on waking). Excessive sleepiness is the constant and usually the presenting complaint: an overwhelming, un-resistible urge to sleep that breaks through in the middle of a meal, a conversation or a task, with brief naps that are characteristically refreshing (unlike the un-refreshing naps of idiopathic hypersomnia). The other three are the REM-intrusion phenomena, the fragments of dream sleep leaking into wakefulness.

The pentad. Disturbed, fragmented nocturnal sleep is the fifth feature, which is why the paradox of narcolepsy is a patient who is desperately sleepy by day yet sleeps badly at night. The examinable trap embedded here is that only two of the four classic symptoms, the sleepiness and the cataplexy, are reasonably specific; sleep paralysis and hypnagogic hallucinations are nonspecific and occur in isolation in the general population, so they support but never make the diagnosis.

MNEMONIC

CHESS

Cataplexy; **H**ypnagogic (and hypnopompic) hallucinations; **E**xcessive daytime sleepiness (with sleep attacks); **S**leep paralysis; disturbed nocturnal **S**leep (the fifth, pentad, feature). Sleepiness is the constant; cataplexy is the specific one.

Sleep attack
An irresistible, overwhelming urge to sleep breaking through into wakefulness, with a brief and typically refreshing nap.

Cataplexy
Sudden bilateral loss of skeletal muscle tone triggered by strong emotion (classically laughter), with consciousness preserved.

Sleep paralysis
Transient inability to move or speak at sleep onset or on waking; the REM atonia persisting into wakefulness.

Hypnagogic hallucination
Vivid, often frightening dream-like perception at sleep onset (hypnopompic if on waking); dream imagery intruding into wake.

GOOD TO REMEMBER

- **Narcolepsy tetrad (the defining cluster):** excessive daytime sleepiness with irresistible sleep attacks, cataplexy, sleep paralysis and hypnagogic or hypnopompic hallucinations, with disturbed nocturnal sleep as the fifth (pentad) feature; the sleepiness is the constant and cataplexy is the specific member, while sleep paralysis and hypnagogic hallucinations are nonspecific and occur in isolation in healthy people.

14.2 Cataplexy: the pathognomonic feature

What it is. Cataplexy is the sudden loss of muscle tone, with continuing full or partial consciousness, precipitated by strong emotion and most commonly by laughter (Kaplan and Sadock CTP 2024). It ranges from the barely perceptible, a head nod, a sagging jaw, a slurring of speech or buckling knees, to a total collapse to the floor, and episodes last from a few seconds to a couple of minutes. It is bilateral, the patient is aware throughout, and reflexes are abolished during the attack, which is the neurological point that separates it from a psychogenic drop. In children, or in the first few months of onset, cataplexy can look atypical: spontaneous grimacing, jaw-opening with tongue thrusting, or a global hypotonia without a clear emotional trigger.

Why it matters. Cataplexy is the one feature specific enough to clinch the diagnosis and defines type 1 disease; it is REM-sleep atonia (the same paralysis that normally protects us from acting out dreams) discharging into wakefulness. It occurs in a majority of narcolepsy patients and is the strongest clinical marker of the orexin deficiency, which is why demonstrating cataplexy, like demonstrating a low cerebrospinal-fluid orexin, is enough to place the patient in type 1 without further testing.

PEARL

Ask specifically what happens when the patient laughs hard, is startled, or gets angry. The pathognomonic history is knees buckling or the head dropping at the punchline of a joke, with the patient fully aware and unable to move for a few seconds. That single question separates narcolepsy from every other cause of daytime sleepiness.

TRAP **Reading cataplexy or a sleep attack as a seizure.** An emotion-triggered fall with preserved awareness and abolished reflexes is cataplexy, not an atonic seizure, and repeated daytime "absences" that are really sleep attacks earn antiepileptics for years before the sleep history is finally taken.

14.3 The pathophysiology: loss of the orexin (hypocretin) neurons

The orexin system. A small population of neurons in the **lateral hypothalamus** makes the peptide neurotransmitter hypocretin, discovered independently by two groups and so carrying two names: hypocretin (for its hypothalamic location) and orexin (from the Greek *orexis*, appetite). These neurons normally excite the brainstem and hypothalamic arousal centres and hold wakefulness stable, stabilising the switch between the wake and sleep states; their peptides are orexin A and B (hypocretin 1 and 2). The accompanying figure sets this orexin sleep-switch against the tetrad so the leak of REM phenomena into wakefulness can be read off the failing switch.

The lesion. Narcolepsy with cataplexy is caused by the selective loss of these hypocretin-producing neurons, so the orexin signal that clamps the sleep-wake boundary is gone and REM sleep and its atonia intrude into the day (Kaplan and Sadock CTP 2024; Kaufman). The near-total loss (up to ninety per cent of the orexin neurons) is why the cerebrospinal-fluid orexin falls so low. The leading account of the lesion is autoimmune: the strong HLA-DQB1*06:02 association, the onset that often follows an infection, and the near-universal orexin loss in cataplectic disease all point to an immune-mediated destruction of the orexin neurons.

The HLA association. Narcolepsy with cataplexy is very tightly linked to the major-histocompatibility allele HLA-DQB1*06:02 on chromosome 6 (Kaufman). The examinable subtlety is that despite this tight association the allele is neither necessary nor sufficient: it is common in the healthy population, so it supports but cannot confirm the diagnosis, and its main use is as a screening or supportive test rather than a diagnostic one.

GOOD TO REMEMBER

- **Orexin loss (the mechanism):** narcolepsy type 1 is the selective loss of the lateral-hypothalamic orexin (hypocretin) neurons that normally stabilise wakefulness, most likely autoimmune, marked by the HLA-DQB1*06:02 association and a low or absent cerebrospinal-fluid orexin; the allele is neither necessary nor sufficient, so it screens but never seals the diagnosis.

14.4 Type 1 versus type 2

The split. The classification (ICSD-3; DSM-5-TR 2022) divides narcolepsy by the orexin lesion. **Type 1** (narcolepsy with cataplexy, or hypocretin deficiency) is the classic orexin-deficient

disease: cataplexy is present and, or, the cerebrospinal-fluid orexin is low; this is the form with the tight HLA link and the autoimmune story. **Type 2** (narcolepsy without cataplexy and without demonstrated hypocretin deficiency) has the daytime sleepiness and the MSLT findings but no cataplexy and a normal or unmeasured orexin; it is a more heterogeneous, less well-understood group, and a proportion later declare cataplexy and reclassify as type 1.

The load-bearing rule. Either cataplexy or a low cerebrospinal-fluid orexin is sufficient to call it type 1, which is why the bedside question about emotion-triggered weakness carries as much diagnostic weight as a lumbar puncture. Both types still require the objective sleepiness on the MSLT; the type distinction is about the orexin lesion, not about the sleepiness.

FEATURE	TYPE 1 (WITH CATAPLEXY OR LOW OREXIN)	TYPE 2 (WITHOUT EITHER)
Cataplexy	**Present (or low CSF orexin)**	Absent
CSF orexin (hypocretin-1)	**Low or absent (under 110 pg per mL)**	Normal or not measured
HLA-DQB1*06:02	Strongly associated	Less strongly associated
MSLT (sleepiness plus SOREMPs)	Required	Required
Underlying lesion	Orexin-neuron loss (autoimmune)	Heterogeneous, orexin often intact

Type 1 versus type 2 narcolepsy; either cataplexy or a low cerebrospinal-fluid orexin defines type 1, both types share the objective MSLT sleepiness, and some type 2 patients later declare cataplexy and reclassify.

GOOD TO REMEMBER

- **Type 1 versus type 2 (the discriminator):** type 1 narcolepsy is defined by cataplexy or a low cerebrospinal-fluid orexin (under 110 pg per mL) and carries the HLA-DQB1*06:02 and autoimmune story; type 2 has the sleepiness and the MSLT findings but no cataplexy and a normal or unmeasured orexin; both require objective MSLT sleepiness, so the type is about the orexin lesion, not the sleepiness.

14.5 The differential: the masquerades that trap the psychiatrist

The sleep-medicine differential. **Idiopathic hypersomnia** is the closest mimic: genuine excessive daytime sleepiness, but with long, un-refreshing naps and sleep drunkenness, no cataplexy, and an MSLT that shows a short mean sleep latency without the two sleep-onset REM periods and without orexin deficiency. Chronic insufficient sleep (behaviourally induced sleep deprivation), the commonest cause of daytime sleepiness of all, is excluded by a sleep diary or actigraphy and by the sleepiness resolving when sleep is extended; obstructive sleep apnoea is excluded on the preceding-night polysomnogram.

The psychiatric masquerades. Two errors are the examinable ones. The first is the **treatment-resistant depression** masquerade: the young adult with pervasive daytime sleepiness, low energy, poor concentration and secondary low mood is labelled depressed, and antidepressant after antidepressant is stacked while the untreated narcolepsy drives the fatigue (and, worse,

several antidepressants blunt REM and mask the cataplexy that would have made the diagnosis). The second is the **epilepsy** masquerade: cataplectic drops and sleep attacks are mistaken for atonic or absence seizures, and the patient collects antiepileptics and a normal electroencephalogram for years. The corrective in both is the same, take a sleep history and ask about emotion-triggered weakness.

MIMIC	DISCRIMINATOR FROM NARCOLEPSY
Idiopathic hypersomnia	**Long un-refreshing naps, no cataplexy, MSLT without 2 SOREMPs, normal orexin**
Chronic insufficient sleep	Short habitual sleep; resolves when sleep is extended (diary or actigraphy)
Obstructive sleep apnoea	Snoring and witnessed apnoeas; excluded on preceding-night polysomnogram
Treatment-resistant depression	**Sleepiness and fatigue precede or exceed the mood; ask for cataplexy**
Epilepsy (atonic or absence)	**Cataplexy has an emotional trigger, preserved awareness and a normal EEG**

The narcolepsy differential; idiopathic hypersomnia is the closest sleep-medicine mimic, while the depression and epilepsy masquerades are the errors that keep the psychiatrist from the diagnosis for years.

RULE **Ask for cataplexy before you escalate.** In a young adult with pervasive daytime sleepiness that outweighs the mood, ask about emotion-triggered weakness and take a sleep history before labelling a "treatment-resistant depression" or an epilepsy, because narcolepsy is the diagnosis those two masquerades hide.

14.6 Diagnosis: the MSLT and the low cerebrospinal-fluid orexin

The confirmatory tests. The diagnosis is built on an overnight polysomnogram followed the next morning by the multiple sleep latency test (MSLT), five short scheduled nap opportunities across the day that quantify how fast the patient falls asleep and whether REM sleep appears abnormally early (Kaufman; Tasman Psychiatry). The overnight study serves two purposes: it excludes another cause of the sleepiness (apnoea, poor prior-night sleep) and it can itself catch an abnormally short REM latency.

The two MSLT numbers. The MSLT criterion for narcolepsy is a mean sleep latency of eight minutes or less *and* two or more sleep-onset REM periods (SOREMPs) across the naps (Kaufman; DSM-5-TR 2022). A short REM latency of fifteen minutes or less on the preceding-night polysomnogram can count as one of the two required SOREMPs. These are the load-bearing figures: the short latency proves the pathological sleepiness, and the two SOREMPs prove the REM-intrusion that is the signature of narcolepsy (normal REM latency is about ninety to a hundred minutes, so REM within a nap is grossly abnormal).

The orexin test. The most specific single finding in narcolepsy with cataplexy is a low or absent cerebrospinal-fluid orexin (hypocretin-1), conventionally under 110 pg per mL, while the serum level stays normal (Kaufman). It is diagnostic of type 1 but is not routinely available in most

clinical settings, so in practice cataplexy plus the MSLT carries the diagnosis and the lumbar puncture is reserved for the difficult case.

≤8	≥2	<110	200 to 400
MSLT MEAN SLEEP LATENCY (MINUTES)	SLEEP-ONSET REM PERIODS ON MSLT (COUNT)	CSF OREXIN CUT-OFF, TYPE 1 (PG PER ML)	MODAFINIL DOSE IN NARCOLEPSY (MG PER DAY)

TEST	DIAGNOSTIC FINDING
MSLT mean sleep latency	**8 minutes or less**
MSLT sleep-onset REM periods	**2 or more across the naps**
Preceding-night PSG REM latency	15 minutes or less can count as one SOREMP
CSF orexin (hypocretin-1)	**Low or absent (under 110 pg per mL); defines type 1**

The diagnostic thresholds for narcolepsy; the MSLT needs a mean sleep latency of eight minutes or less plus two or more sleep-onset REM periods, and a low cerebrospinal-fluid orexin is the most specific but least available test.

GOOD TO REMEMBER

- **Diagnosis (the confirmatory step):** an overnight polysomnogram followed by the MSLT, which is positive at a mean sleep latency of eight minutes or less *and* two or more sleep-onset REM periods (a preceding-night REM latency of fifteen minutes or less can serve as one SOREMP); a cerebrospinal-fluid orexin under 110 pg per mL is the most specific finding and defines type 1 but is rarely available.

14.7 Management: the wake-promoting agents for daytime sleepiness

The practice-standard position. Narcolepsy is not curable, so treatment targets the two problems separately: the excessive daytime sleepiness and the cataplexy. The sleep-medicine practice standard (the American Academy of Sleep Medicine clinical practice guideline, and the sleep-medicine texts) places the wake-promoting agents first for the daytime sleepiness, with scheduled short naps and firm sleep hygiene as the non-drug backbone alongside them. Because narcolepsy is not covered by the day's guideline supplement, the drug detail here is grounded in the parsed prescribing texts, and the exact strength-of-recommendation grading of the AASM 2021 guideline is flagged for confirmation against the primary source rather than reproduced.

The wake-promoting drugs. Modafinil (in India, Modalert or Provake) is the first-line agent for the excessive daytime sleepiness of narcolepsy, a wakefulness-promoting dopamine-transporter inhibitor that is not classed as a psychostimulant, given at 200 to 400 mg per day, and it improves the sleepiness but does *not* benefit cataplexy (Kaplan and Sadock CTP 2024). Its longer-acting R-enantiomer armodafinil is an alternative. Two newer agents extend the class: solriamfetol, a norepinephrine-dopamine reuptake inhibitor, and pitolisant, a histamine H3-receptor antagonist and inverse agonist that raises brain histamine and, unusually for a wake-promoter, also reduces cataplexy (Stahl). The traditional psychostimulants (methylphenidate, dexamphetamine) remain a second line for residual sleepiness, with their tolerance and dependence liability.

GOOD TO REMEMBER

- **Wake-promoting agents (the value):** modafinil (Indian brands Modalert or Provake), a dopamine-transporter inhibitor at 200 to 400 mg per day, is first-line for the excessive daytime sleepiness of narcolepsy but does not touch cataplexy; armodafinil, solriamfetol and pitolisant extend the class, pitolisant (an H3 antagonist) uniquely also reducing cataplexy, with the amphetamines held as a dependence-prone second line.

14.8 Sodium oxybate for cataplexy, and the anticataplectic antidepressants

Sodium oxybate. Sodium oxybate (the sodium salt of gamma-hydroxybutyrate, GHB) is the most effective single treatment for cataplexy and is the one agent that also consolidates the broken night and improves the daytime sleepiness, taken in divided doses across the night because it enhances slow-wave sleep (Kaufman; Tasman Psychiatry; Stahl). It also blunts sleep paralysis and the hypnagogic and hypnopompic hallucinations. Its liability is its identity: GHB is a drug of abuse (the "date-rape drug"), so it is a tightly controlled substance dispensed through restricted programmes, and it must never be combined with alcohol or other central-nervous-system depressants.

The older anticataplectic drugs. Before sodium oxybate and pitolisant, cataplexy was suppressed with REM-suppressing antidepressants, and these remain a practical option: an SSRI or an SNRI (venlafaxine), or the tricyclic clomipramine (also imipramine or protriptyline). They work by suppressing REM sleep and its atonia, and abrupt withdrawal can cause a rebound of cataplexy (status cataplecticus), so they are tapered rather than stopped. They do little for the daytime sleepiness, which is why cataplexy and sleepiness are usually treated with two different drugs.

WORKED EXAMPLE

A woman in her twenties has been irresistibly sleepy since her mid-teens and has failed three antidepressants for a presumed depression. Asked directly, she describes her knees buckling whenever she laughs hard, fully aware throughout. An overnight polysomnogram excludes apnoea, and the next-morning MSLT shows a mean sleep latency of five minutes with three sleep-onset REM periods. The diagnosis is narcolepsy type 1. She is started on modafinil (Modalert) for the sleepiness, and because the cataplexy is disabling and her nights are fragmented, sodium oxybate is added where available; where it is not, venlafaxine is used for the cataplexy instead.

GOOD TO REMEMBER

- **Cataplexy treatment (the value):** sodium oxybate (GHB) is the most effective drug for cataplexy and the only one that also consolidates the broken night and improves daytime sleepiness, but it is an abuse-liable controlled substance never combined with alcohol; the older option is a REM-suppressing antidepressant (an SSRI/SNRI or clomipramine), tapered rather than stopped to avoid rebound cataplexy.

14.9 The Indian picture: drug availability and the missed diagnosis

What is available, and what is not. The genuine Indian device in narcolepsy is drug availability. Modafinil is widely and cheaply available in India as Modalert, Provake and other brands, and

armodafinil is available too, so the first-line treatment of the daytime sleepiness is entirely practical. The problem is the rest of the ladder: sodium oxybate is not marketed in India (it is a controlled substance dispensed only through restricted programmes abroad), and the newer agents pitolisant and solriamfetol are not routinely available either. The practical consequence is that Indian cataplexy is usually managed not with sodium oxybate but with an SSRI, an SNRI or clomipramine, the older anticataplectic antidepressants, which is exactly the substitution the worked example makes.

The under-recognition. Narcolepsy is under-diagnosed in India for the same reasons the eating disorders are: sleep laboratories and the MSLT are scarce and out-of-pocket, cerebrospinal-fluid orexin testing is essentially unavailable, and the young adult who has been sleepy since adolescence is far more likely to be told to sleep more, try harder, or take an antidepressant than to be sent for a sleep study. The cheap corrective is clinical, ask every chronically sleepy young patient about emotion-triggered weakness, because cataplexy alone can carry the diagnosis to treatment even where the confirmatory tests cannot be had.

INDIA

Modafinil (Modalert, Provake) and armodafinil are freely available and make first-line treatment of the daytime sleepiness straightforward, but sodium oxybate, pitolisant and solriamfetol are not marketed in India, so cataplexy is managed with the older anticataplectic antidepressants (an SSRI or SNRI, or clomipramine) instead. Layered on this is under-recognition: MSLT-capable sleep labs are scarce and orexin assay is essentially unavailable, so the sleepy adolescent is treated for laziness or depression for years. The corrective costs nothing, ask about knees buckling at a joke, because cataplexy alone places the patient in type 1 and gets them treated.

HOLD THIS

Narcolepsy is REM sleep intruding into wakefulness from loss of the hypothalamic orexin (hypocretin) neurons: the tetrad is excessive daytime sleepiness with sleep attacks, cataplexy, sleep paralysis and hypnagogic hallucinations (disturbed nocturnal sleep the pentad fifth), cataplexy plus a low CSF orexin (under 110 pg per mL) defines type 1, and it is confirmed on the MSLT at a mean sleep latency of eight minutes or less with two or more sleep-onset REM periods; treat the sleepiness with modafinil (Modalert or Provake) and the cataplexy with sodium oxybate or, in India, an SSRI/SNRI or clomipramine.

15 · Obstructive sleep apnoea and its psychiatric relevance

Obstructive sleep apnoea is a breathing-related sleep disorder in which the upper airway repeatedly collapses during sleep, so that ventilation stops or falls, the blood oxygen dips, and the brain briefly rouses to reopen the airway, hundreds of times a night. It is included here not as respiratory trivia but because it is the medical disorder the psychiatrist most reliably misses: it masquerades as depression, as cognitive impairment, and as a stubborn **treatment-resistant depression**, and the man snoring in the waiting room with a collar-size neck and a low mood is more often carrying obstructive sleep apnoea (OSA) than a pure mood disorder.

Why it matters, and how this note is framed. This is a hybrid topic. The diagnostic half asks you to know the pathophysiology (the airway collapse, the apnoea and hypopnoea, the oxygen desaturation, the arousal and the sleep fragmentation), the clinical picture, the **apnoea-hypopnoea index** and its verified severity bands, and that the diagnosis is sealed on polysomnography. The management half asks you to know that continuous positive airway pressure is the mainstay, with weight, positional, oral-appliance and surgical options behind it, and to screen at the bedside with STOP-BANG and its verified risk bands. Two figures accompany this topic and are flagged for drawing: the apnoea-hypopnoea and oxygen-desaturation trace, and the STOP-BANG scale plate. Because this disorder sits outside the guideline database used for the eating and insomnia drugs, its numbers are grounded in the parsed textbooks and a verified primary source, and any figure the library could not confirm is flagged rather than invented.

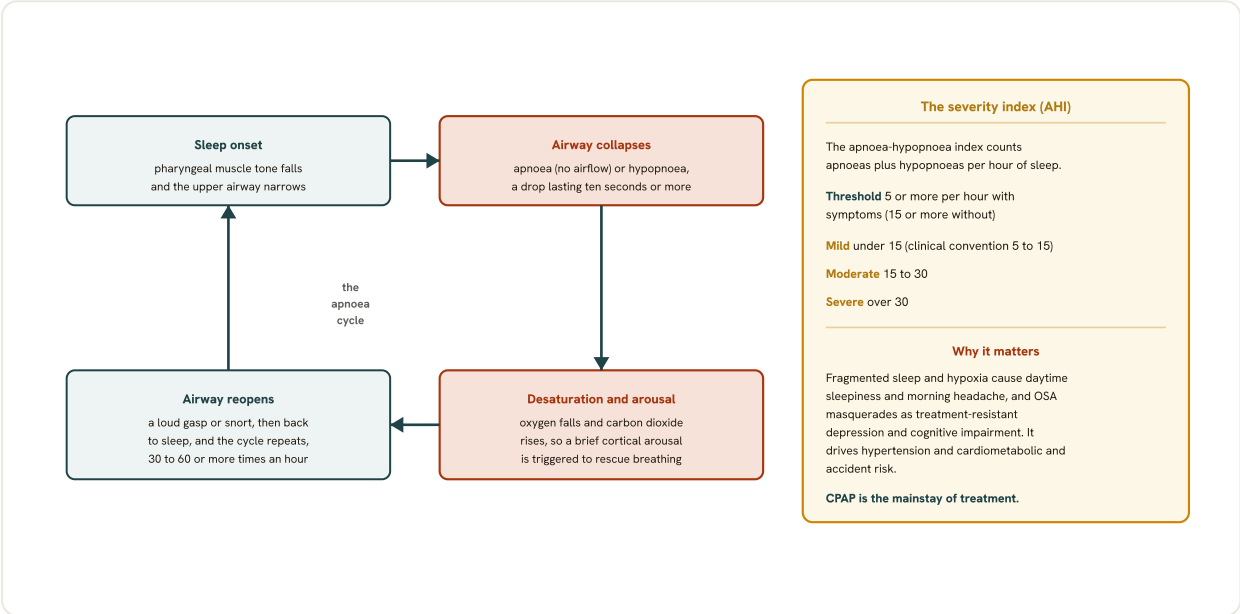


Fig 17.13 Obstructive sleep apnoea: the apnoea-hypopnoea cycle. In sleep the pharyngeal muscle tone falls and, in a susceptible airway, the upper airway collapses, so airflow stops (apnoea) or is sharply reduced (hypopnoea) for ten seconds or more. Oxygen falls and carbon dioxide rises until a brief cortical arousal restores muscle tone and the airway reopens with the characteristic loud gasp or snort, whereupon the person returns to sleep and the whole cycle repeats, thirty to sixty or more times an hour. The result is a night shredded into fragments with repetitive hypoxia. Severity is graded by the apnoea-hypopnoea index, the number of events per hour, diagnostic at five or more with symptoms and banded mild, moderate (fifteen to thirty) and severe (over thirty), with the lower edge of the mild band differing between the DSM-5-TR specifier and the clinical convention. The importance for psychiatry is that the daytime sleepiness and cognitive dulling masquerade as treatment-resistant depression, so it is a diagnosis to exclude; continuous positive airway pressure is the mainstay of treatment.

STOP-BANG, THE OSA SCREEN (REPRODUCED)	SCORE ONE POINT FOR EACH "YES"
S noring	Do you snore loudly (louder than talking, or loud enough to be heard through a closed door)?
T iredness	Do you often feel tired, fatigued or sleepy during the daytime?
O bserved	Has anyone observed you stop breathing during your sleep?
P ressure	Do you have, or are you being treated for, high blood pressure?
B MI	Body mass index more than 35 kg per square metre?
A ge	Age over 50 years?
N eck	Neck circumference greater than 40 cm?
G ender	Male?
Risk bands	**0 to 2 low risk; 3 to 4 intermediate risk; 5 to 8 high risk of moderate-to-severe obstructive sleep apnoea**

STOP-BANG: reproduced from Chung F, Yegneswaran B, Liao P, et al. Anesthesiology. 2008;108:812-821. A widely used, freely available OSA screen; for the free, non-commercial resident edition only.

Fig 17.14 The STOP-BANG obstructive sleep apnoea screen. An eight-item yes-or-no screen whose name is its mnemonic: Snoring, Tiredness, Observed apnoea and Pressure (blood pressure), then BMI over 35, Age over 50, Neck over 40 cm and male Gender. One point is scored for each yes, and the total stratifies risk as low (0 to 2), intermediate (3 to 4) or high (5 to 8) for moderate-to-severe obstructive sleep apnoea, so a high score prompts referral for sleep study. It is quick and sensitive, which is exactly what a psychiatric clinic needs to catch the sleep apnoea hiding behind a picture of treatment-resistant depression or daytime fatigue.

15.1 The pathophysiology: repetitive upper-airway collapse, apnoea and hypopnoea, desaturation and arousal

The mechanism. During sleep the muscles that hold the pharynx open lose tone, and in the vulnerable airway (a crowded, narrow or fat-loaded pharynx behind the tongue and soft palate) the negative pressure of inspiration sucks the walls shut despite continued respiratory effort. A total collapse for **ten seconds** or longer is an *apnoea*; a partial collapse that reduces airflow for ten seconds or longer is a *hypopnoea* (Kaplan and Sadock CTP 2024). The obstruction is what distinguishes it from central apnoea, where effort itself ceases: in the obstructive event the chest and abdomen keep straining against a shut airway.

The cascade. Each obstructed breath produces a fall in blood oxygen, an **oxygen desaturation**, and the rising carbon dioxide and effort trigger a brief cortical arousal that restores airway tone, often ended by a loud snort or gasp, after which the person falls back asleep and the cycle repeats. The consequence is twofold: intermittent nocturnal hypoxaemia, and a sleep so fragmented by micro-arousals that it never consolidates, which is why the patient sleeps a full night yet wakes unrefreshed and is sleepy throughout the day. The accompanying figure sets the airflow trace, the

effort trace and the falling oxygen saturation against one another so the apnoea, the hypopnoea and the arousal can be read off a single polysomnographic strip.

Apnoea

Cessation of airflow for ten seconds or longer during sleep (obstructive when respiratory effort continues against a collapsed airway).

Hypopnoea

A reduction in airflow for ten seconds or longer, scored when it produces a defined oxygen desaturation or a cortical arousal.

Oxygen desaturation

The dip in blood oxygen saturation each obstructed breath produces; a hypopnoea is conventionally scored at a fall of a few percent or more.

Arousal and fragmentation

The brief cortical waking that reopens the airway; repeated hundreds of times, it shatters sleep continuity and drives the daytime sleepiness.

> **PEARL**
>
> The daytime sleepiness of obstructive sleep apnoea is not from too little sleep but from sleep that is repeatedly broken. The patient may spend eight hours in bed and still be pathologically sleepy, because every obstructed breath buys an arousal and no stretch of sleep is ever allowed to deepen and consolidate.

15.2 The clinical picture and the risk factors

What the patient and the bed partner report. The cardinal triad is loud habitual **snoring**, witnessed apnoeas, and excessive daytime sleepiness. The snoring of obstructive sleep apnoea is characteristically loud enough to be heard outside the bedroom door, the pauses are long, typically twenty to thirty seconds rather than a few, and each is broken by a snort or a start (New Oxford Textbook of Psychiatry). The bed partner is the key informant, because the patient is asleep for the apnoeas and the snorting and often denies both. Add un-refreshing sleep, a dry mouth, a morning headache, nocturia, irritability and impaired concentration, and, in the psychiatrist's chair, low mood and cognitive slowing.

Who is at risk. The dominant risk factor is obesity, and specifically central and upper-body fat that loads the pharynx, so a large neck circumference is a better bedside marker than weight alone. Male sex, older age, a retrognathic or micrognathic jaw and other craniofacial crowding of the airway, tonsillar hypertrophy, and alcohol or sedatives (which relax the airway further) all raise the risk. The examinable point is that the sleepy, snoring, thick-necked, hypertensive middle-aged man is the archetype, and that in India a lean patient with craniofacial crowding can carry it without the obesity that would prompt the thought.

DOMAIN	FEATURE
Nocturnal	**Loud habitual snoring, witnessed apnoeas, snorting or gasping arousals, choking**
Nocturnal (other)	Restless un-refreshing sleep, nocturia, dry mouth, sweating
Daytime	**Excessive daytime sleepiness, morning headache, poor concentration, low mood, irritability**
Risk factors	Obesity, large neck circumference, male sex, older age, craniofacial or retrognathic crowding, alcohol and sedatives

The clinical picture of obstructive sleep apnoea; snoring, witnessed apnoeas and daytime sleepiness are the triad, and the neck circumference is the single most useful bedside risk marker.

15.3 The apnoea-hypopnoea index and its severity bands

What the index is. The apnoea-hypopnoea index (AHI) is the number of apnoeas plus hypopnoeas per hour of sleep, and it is the number that both diagnoses the disorder and grades its severity (Kaplan and Sadock CTP 2024). A related index, the oxygen desaturation index, counts the desaturation dips per hour and tracks the hypoxic burden. The AHI is what every treatment decision and every examination question hangs off.

The verified severity bands. An AHI **under five per hour** is normal. Five to fifteen is mild, **fifteen to thirty** is moderate, and **above thirty** is severe (the AASM and ICSD-3 clinical bands). The DSM-5-TR severity specifier for obstructive sleep apnoea hypopnoea writes the same ceiling: mild is an AHI less than fifteen, moderate is fifteen to thirty, and severe is greater than thirty, its mild band starting at the diagnostic floor of five (DSM-5-TR 2022; Kaplan and Sadock CTP 2024). The moderate and severe thresholds are the load-bearing numbers, because they are where continuous positive airway pressure becomes the clear treatment of choice.

AHI (EVENTS PER HOUR)	SEVERITY BAND
Under 5	Normal (no obstructive sleep apnoea)
5 to 15	Mild
15 to 30	**Moderate**
Greater than 30	**Severe**

AHI severity bands (apnoeas plus hypopnoeas per hour of sleep); DSM-5-TR labels the mild band as an AHI under fifteen because diagnosis requires at least five events, and the moderate (15 to 30) and severe (over 30) cut-offs are identical across the classifications.

10	15 to 30	>30	5 to 8
MINIMUM APNOEA OR HYPOPNOEA EVENT (SECONDS)	AHI MODERATE BAND (EVENTS PER HOUR)	AHI SEVERE-OSA THRESHOLD (EVENTS PER HOUR)	STOP-BANG HIGH-RISK BAND (SCORE)

GOOD TO REMEMBER

- **Obstructive sleep apnoea (defining criterion):** repetitive obstructive apnoeas and hypopnoeas (airflow stopping or falling for ten seconds or longer despite continued effort) quantified as the apnoea-hypopnoea index; the disorder is graded normal (AHI under 5), mild (5 to 15), moderate (15 to 30) and severe (over 30), and DSM-5-TR writes mild as an AHI under fifteen with the diagnostic floor at five.

15.4 Diagnosis by polysomnography

The confirmatory test. The diagnosis is made on polysomnography, the overnight sleep study that records airflow, respiratory effort, oxygen saturation, the electroencephalogram, eye movements and muscle tone, from which the apnoeas, hypopnoeas and arousals are counted and the AHI computed; a validated home sleep apnoea test can substitute in the appropriately selected patient (Kaplan and Sadock CTP 2024). Polysomnography is not routine for uncomplicated insomnia, but it is exactly what suspected obstructive sleep apnoea earns.

The diagnostic thresholds. In the absence of symptoms an AHI of fifteen or more (predominantly obstructive events) establishes the diagnosis; with relevant symptoms, an AHI of five or more suffices (Kaplan and Sadock CTP 2024). The symptoms and comorbidities that license the lower threshold are the psychiatrically loaded ones: daytime sleepiness, witnessed apnoeas, gasping or habitual snoring, and hypertension, a mood disorder, cognitive dysfunction, coronary disease, stroke, heart failure, atrial fibrillation or type 2 diabetes. Note that a coexisting mood disorder is itself listed among the conditions that lower the diagnostic bar, which is the nosology quietly telling you that depression and apnoea travel together.

SETTING	AHI REQUIRED (EVENTS PER HOUR)
No symptoms or comorbidity	15 or more, predominantly obstructive
With symptoms or relevant comorbidity	5 or more, predominantly obstructive

Polysomnographic diagnostic thresholds for obstructive sleep apnoea; a mood disorder and cognitive dysfunction are among the comorbidities that lower the bar to an AHI of five.

GOOD TO REMEMBER

- **Diagnosis (the confirmatory step):** obstructive sleep apnoea is confirmed on polysomnography (or a validated home sleep apnoea test), diagnostic at an AHI of fifteen or more without symptoms or five or more with symptoms or relevant comorbidity; a coexisting mood disorder is one of the comorbidities that licenses the lower five-per-hour threshold.

15.5 The STOP-BANG screen and its verified risk bands

What STOP-BANG is. STOP-BANG is an eight-item yes/no bedside screen for the risk of obstructive sleep apnoea, developed to flag the patients who need a sleep study (Tasman Psychiatry). Each positive item scores one point, giving a total out of eight. The mnemonic itself carries the four symptom questions and the four demographic-and-examination items, which is why it is so examinable. This topic carries the STOP-BANG form on the accompanying scale plate; the Epworth Sleepiness Scale, the eight-item self-rating of daytime sleepiness (scored out

of twenty-four, sleepiness above ten), quantifies the sleepiness that STOP-BANG's first items ask about and is cross-referenced with the hypersomnolence and narcolepsy assessment.

The verified risk bands. The total stratifies risk into three bands: zero to two is low risk, three to four is intermediate risk, and **five to eight** is high risk of obstructive sleep apnoea. These item cut-offs and risk bands are taken from the primary STOP-BANG literature (Chung and colleagues), because the parsed textbooks name the instrument and its general risk factors but do not print the banded scoring; the exact bands are therefore flagged as source-verified rather than textbook-derived.

MNEMONIC

STOP-BANG

Snoring (loud); **T**iredness or daytime sleepiness; **O**bserved apnoeas; high blood **P**ressure; **B**MI over 35 (kg per m squared); **A**ge over 50 years; **N**eck circumference over 40 cm; male **G**ender. One point each, out of eight; three or more is a positive screen worth a sleep study, five or more is high risk.

STOP-BANG ITEM	POSITIVE IF
Snoring	Loud, heard through a closed door
Tiredness	Excessive daytime sleepiness or fatigue
Observed apnoea	**Bed partner has witnessed you stop breathing**
Pressure	Hypertension (treated or untreated)
BMI	Over 35 (kg per m squared)
Age	Over 50 years
Neck	**Circumference over 40 cm**
Gender	Male

The eight STOP-BANG items (Chung and colleagues); each yes scores one point out of eight, with three or more flagging a patient for polysomnography.

STOP-BANG TOTAL (SCORE)	RISK OF OBSTRUCTIVE SLEEP APNOEA
0 to 2	Low risk
3 to 4	Intermediate risk
5 to 8	**High risk**

STOP-BANG risk bands; five or more of eight is high risk and should prompt a sleep study, and the screen is less sensitive in women and older patients.

GOOD TO REMEMBER

- **STOP-BANG (the value):** eight yes/no items (Snoring, Tiredness, Observed apnoea, Pressure, BMI over 35, Age over 50, Neck over 40 cm, male Gender), one point each out of eight; 0 to 2 is low risk, 3 to 4 intermediate and 5 to 8 high risk of obstructive sleep apnoea, so three or more warrants a sleep study; less sensitive in women and the elderly.

15.6 The psychiatric relevance: the depression and cognitive masquerade, the treatment-resistant-depression trap, and the cardiometabolic risk

The masquerade. The **psychiatric relevance** of obstructive sleep apnoea is that its daytime face, fatigue, low mood, anhedonia, poor concentration, memory complaints and irritability, is indistinguishable at a glance from a depressive episode or an early neurocognitive disorder. Obstructive sleep apnoea is independently associated with depressed mood, an association stronger in women than in men (Tasman Psychiatry), and the intermittent nocturnal hypoxaemia and fragmented sleep produce genuine deficits of attention, executive function and memory that can be mistaken for a dementia. It sits, alongside thyroid disease and vitamin deficiency, on the list of reversible medical conditions to exclude before a depression or a cognitive decline is accepted as primary (Companion to Psychiatric Studies).

The treatment-resistant-depression trap. The consequential error is to keep switching and stacking antidepressants in a depression that will not lift, when the fatigue, the un-refreshing sleep and the concentration loss are being driven by an untreated apnoea. Untreated obstructive sleep apnoea blunts antidepressant response, and the sleepy, snoring, obese, hypertensive depressive who is called treatment-resistant should be screened for it before the regimen is escalated again. The cardiometabolic tail sharpens the stakes: obstructive sleep apnoea drives hypertension, atrial fibrillation and other nocturnal dysrhythmias, heart failure, myocardial infarction and stroke, and carries insulin and leptin resistance, so the sleepiness is also a cardiovascular warning, and the daytime sleepiness itself causes motor-vehicle and workplace accidents.

RULE **Screen before you escalate.** Before a fatigued, poorly concentrating "treatment-resistant" depression is escalated again, screen the sleepy, snoring, thick-necked, hypertensive patient for obstructive sleep apnoea with STOP-BANG; a mood disorder is itself a comorbidity that lowers the diagnostic threshold.

WORKED EXAMPLE

A man in his fifties is referred with a depression that has failed three antidepressants. He is overweight, hypertensive, and complains of no energy and no focus. His wife, asked directly, says he snores loudly and she has watched him stop breathing and gasp awake. His STOP-BANG is six of eight (snoring, tiredness, observed apnoea, pressure, neck over 40 cm, male). The next step is not a fourth antidepressant but polysomnography; the AHI is thirty-four, severe, and continuous positive airway pressure lifts both the sleepiness and much of the mood.

15.7 Management: continuous positive airway pressure is the mainstay

The one treatment. Continuous positive airway pressure (CPAP) is the gold standard and most effective treatment for obstructive sleep apnoea (Kaplan and Sadock CTP 2024; Stahl). A blower delivers air through a nasal or oronasal mask at a titrated positive pressure that acts as a pneumatic splint, holding the collapsing pharynx open; it abolishes the apnoeas, lifts the oxygen desaturation, restores sleep continuity, and improves daytime sleepiness, cognition and cardiovascular outcomes, and even the most severe apnoea is usually controlled once the pressure

is set correctly. Variants exist for the patient who cannot exhale against a fixed pressure (bi-level, BPAP) or who needs an adapting pressure (auto-titrating, APAP), but the principle is one.

The one real problem is adherence. The therapeutic challenge is not efficacy but nightly use, and the striking psychiatric point is that depression is a key predictor of poor CPAP compliance (Kaplan and Sadock CTP 2024), so the untreated mood disorder and the untreated apnoea sabotage each other, and treating the depression helps the patient wear the mask. Wake-promoting agents, modafinil (in India, Modalert or Provake), armodafinil and solriamfetol, are licensed only for the residual sleepiness that persists in a minority of otherwise well-treated, adherent patients; they do nothing for the airway obstruction itself and are never a substitute for CPAP.

GOOD TO REMEMBER

- **Continuous positive airway pressure (the value):** CPAP is the mainstay and gold-standard treatment for obstructive sleep apnoea, splinting the airway open to abolish apnoeas, correct the oxygen desaturation and restore sleep; its one real limitation is adherence, and depression is a key predictor of poor compliance, so a wake-promoting agent (modafinil) treats only residual sleepiness and never replaces CPAP.

15.8 The weight, positional, oral-appliance and surgical options

The options behind CPAP. Weight loss genuinely reduces the AHI and is recommended for every overweight patient, though it is slow and unreliable and cannot be relied on alone. A mandibular-advancement oral appliance, which holds the jaw and tongue forward, is a reasonable alternative in mild-to-moderate disease or for the patient who cannot tolerate CPAP. Positional therapy (preventing supine sleep with a wedge, a back-worn bumper or an alarm) helps the patient whose apnoea is confined to lying on the back. Surgery is reserved for the patient with a correctable anatomical obstruction who has failed or declined CPAP: uvulopalatopharyngoplasty benefits perhaps a third to a half of selected patients, maxillomandibular advancement suits retrognathic anatomy, and a hypoglossal nerve stimulator (the implanted "pacemaker" that protrudes the tongue) is the newer option, with tracheostomy the historical last resort.

Alcohol and sedatives. A quiet but examinable adjunct is to remove what worsens the airway: alcohol in the evening and sedative-hypnotics both relax the pharyngeal muscles and deepen the desaturations, so they are avoided, and this is precisely where the disorder collides with everyday Indian prescribing.

OPTION	PLACE IN MANAGEMENT
CPAP (and BPAP, APAP)	**Mainstay and gold standard for moderate-to-severe disease**
Weight loss	Recommended for every overweight patient; adjunct, not sole therapy
Mandibular-advancement oral appliance	Alternative in mild-to-moderate disease or CPAP intolerance
Positional therapy	For supine-predominant apnoea
Surgery (UPPP, maxillomandibular, hypoglossal stimulator)	**Selected anatomical obstruction after CPAP fails or is declined**
Avoid alcohol and sedatives	They relax the airway and worsen desaturation

The management ladder for obstructive sleep apnoea; CPAP leads, the other options fit selected patients, and evening alcohol and sedatives are removed because they worsen the airway.

GOOD TO REMEMBER

- **The options behind CPAP (the value):** weight loss lowers the AHI in every overweight patient but is adjunct, not sole therapy; a mandibular-advancement oral appliance is the alternative in mild-to-moderate disease or CPAP intolerance; positional therapy suits supine-predominant apnoea; surgery (uvulopalatopharyngoplasty, maxillomandibular advancement, hypoglossal nerve stimulator) is reserved for a correctable anatomical obstruction after CPAP fails or is declined; and evening alcohol and sedative-hypnotics are stopped because they relax the airway and deepen the oxygen desaturation.

TRAP **A hypnotic for the "insomniac" who actually has apnoea.** Prescribing a benzodiazepine or Z-drug to a snoring, sleepy patient whose real problem is obstructive sleep apnoea is useless and dangerous: the sedative relaxes the airway further, deepens the oxygen desaturation, and worsens the disorder you failed to diagnose.

INDIA

The genuine Indian device here is under-recognition compounded by the benzodiazepine reflex. Obstructive sleep apnoea is common and badly under-diagnosed, sleep laboratories are scarce and CPAP machines are a real out-of-pocket cost, so the snoring, sleepy, thick-necked patient is too often handed a benzodiazepine or Z-drug for "insomnia", the very drug class that relaxes the airway and worsens the apnoea. Two correctives are cheap and exam-worthy: use STOP-BANG at the bedside to catch the high-risk patient before reaching for a hypnotic, and do not treat presumed insomnia in a loud snorer with a sedative until apnoea has been excluded. The lean patient with craniofacial crowding, who lacks the obesity that would prompt the thought, is the one most often missed.

HOLD THIS

Obstructive sleep apnoea is repetitive upper-airway collapse causing apnoeas and hypopnoeas (airflow gone for ten seconds or longer), oxygen desaturation and arousal, graded by the apnoea-hypopnoea index (mild 5 to 15, moderate 15 to 30, severe over 30) and confirmed on polysomnography; it masquerades as depression, cognitive impairment and treatment-resistant depression, so screen the sleepy snorer with STOP-BANG (high risk 5 to 8 of 8), and treat with CPAP as the mainstay, never a hypnotic.

16 · Parasomnias: NREM and REM including RBD

A parasomnia is an unwanted physical or experiential event that intrudes into sleep or the transitions in and out of it: not a disorder of *how much* a person sleeps but of *what happens* while they do. Kaplan and Sadock frame the whole class as a series of **state-boundary violations**, one of the three basic states (wakefulness, NREM sleep, REM sleep) leaking into another. That single idea organises the entire topic. When wakeful motor behaviour erupts out of deep NREM sleep you get the **disorders of arousal**; when the paralysis of REM sleep fails and the sleeper acts out the dream you get REM sleep behaviour disorder; when REM atonia persists into waking you get sleep paralysis.



Fig 17.15 Parasomnias map onto sleep state: confusional arousals, sleepwalking and sleep terrors arise from NREM sleep, often earlier in the night, while nightmares and REM sleep behaviour disorder arise from REM sleep, often later.

Why it matters, and how this note is framed. This is a teaching-the-diagnosis topic, and the examinable spine is the split between two families: the NREM parasomnia disorders of arousal (confusional arousal, sleepwalking and sleep terror) that rise from slow-wave sleep in the first third of the night in amnestic, hard-to-rouse children, and the REM parasomnias (nightmare disorder, sleep paralysis and RBD) that belong to the dream-rich second half of the night. The one point the examiner will not let you miss, and the reason this topic outgrows its size, is that RBD is not a benign curiosity of an old man's bedroom but the strongest clinical prodrome of a synucleinopathy, cross-referenced to the Dementias and neurocognitive disorders notes and the Neurology foundations for psychiatrists notes. Two traps are set for you: reading a dream-enacting RBD as a simple nightmare (and missing the neurodegenerative risk), and reading a sleepwalking or sleep-terror event as a nocturnal seizure. The accompanying figure sets the two families against the hypnogram so the timing tells you the family.

16.1 Two families, read off the sleep stage

The organising split. Every parasomnia in the syllabus falls into one of two boxes defined by the sleep state it erupts from (Kaplan and Sadock CTP 2024). The **NREM disorders of arousal** are momentary wakeful behaviours breaking out of slow-wave (deep NREM, stage N3) sleep, so they cluster in the first third of the night when N3 is richest, and the sleeper is caught between sleep and wake with reduced awareness and dense amnesia. The **REM parasomnias** belong to REM sleep, which dominates the last third of the night, and they carry the signature of dreaming: vivid recall, and in RBD the motor enactment of the dream because the atonia has failed.

Why the timing is diagnostic. The stage a parasomnia comes from is not a detail, it is the discriminator. A frightening nocturnal event early in the night in an amnestic child who cannot be roused is almost certainly a disorder of arousal; the same story late in the night in an older man who wakes and describes fighting off an attacker is RBD until proven otherwise. Learn the two families as a pair and most single-best-answer questions on parasomnias answer themselves.

> **PEARL**
>
> Ask two questions of any nocturnal event: *when in the night* and *does the patient remember it*. First third of the night with amnesia points to a NREM disorder of arousal; last third with full dream recall (and enactment) points to a REM parasomnia. Time and recall sort the two families before you reach for a sleep study.

16.2 The NREM disorders of arousal: the shared signature

The common phenotype. The three NREM parasomnias share one pathophysiology, an incomplete arousal from slow-wave sleep, and therefore one clinical signature (DSM-5-TR 2022; Kaplan and Sadock CTP 2024). The DSM-5-TR criterion A is recurrent episodes of incomplete awakening from sleep, usually during the **first third of the major sleep episode**, with either sleepwalking or sleep-terror behaviour; the eyes are typically open, the events last one to ten minutes, there is **no or little dream imagery** recalled (criterion B), and there is **amnesia** for the episode (criterion C). The person is difficult to rouse, and if woken is confused and disoriented before full recovery.

The demographic and the triggers. These are disorders of childhood: prevalence peaks young and they usually remit spontaneously after adolescence, they run in families, and they are provoked by anything that deepens or fragments slow-wave sleep, above all sleep deprivation, but also fever, a full bladder, noise, and CNS-depressant use or withdrawal. Persistence into or new onset in adult life is less benign and raises the question of a comorbid disorder (obstructive sleep apnoea in particular) or an underlying stressor. Confusional arousals are the mild end of this same continuum, sleepwalking the middle, sleep terrors the florid extreme.

FEATURE	VALUE IN THE NREM DISORDERS OF AROUSAL
Sleep stage of origin	**Slow-wave (deep NREM, N3) sleep**
Timing in the night	**First third of the major sleep episode**
Episode duration	1 to 10 minutes (occasionally longer)

FEATURE	VALUE IN THE NREM DISORDERS OF AROUSAL
Eyes	Typically open
Dream recall	**No or little imagery recalled**
Memory for the event	**Amnesia**
Rousability	Difficult to rouse; confused if woken
Age and family history	Childhood peak, remits after adolescence, familial

The shared signature of the NREM disorders of arousal; deep-NREM origin, first-third timing, amnesia and no dream recall are what separate the whole family from the REM parasomnias.

RULE **Timing plus amnesia diagnoses the family.** A nocturnal event out of the first third of the night, in a child who is hard to rouse and has no memory of it and recalls no dream, is a NREM disorder of arousal, no sleep study needed to make that call.

GOOD TO REMEMBER

- **NREM disorders of arousal (the defining criterion):** recurrent incomplete awakenings from slow-wave (deep NREM) sleep in the first third of the night, with the eyes typically open, no or little dream imagery recalled and amnesia for the event (DSM-5-TR criteria A to C); peak in childhood, remit after adolescence, run in families, and are provoked by sleep deprivation, fever and CNS depressants.

16.3 Confusional arousals

The mild end. A confusional arousal (ICSD-3; Kaplan and Sadock CTP 2024) is the gentlest disorder of arousal: the sleeper, usually a young child, partially wakes and sits up confused, may mumble or look about, but characteristically lies back down and resumes sleep without leaving the bed and without the autonomic storm of a sleep terror. It is thought to sit on a continuum with sleepwalking and sleep terrors, sharing their slow-wave origin and their amnesia. In adults an equivalent is the disoriented, sometimes belligerent partial waking on being roused from deep sleep (classically sleep drunkenness or morning confusion), and it can be exacerbated by sedatives and sleep deprivation.

GOOD TO REMEMBER

- **Confusional arousal (the defining criterion):** a partial awakening from slow-wave sleep with confusion but *without* ambulation and without the intense fear and autonomic surge of a sleep terror; the mildest of the disorders of arousal, common in young children, on a continuum with sleepwalking and sleep terrors, and amnesic like the rest of the family.

16.4 Sleepwalking (somnambulism)

What it is. Sleepwalking, or **somnambulism**, is arising from bed and ambulating without fully awakening, out of slow-wave sleep, characteristically toward the end of the first or second slow-wave episode (Kaplan and Sadock CTP 2024). The DSM-5-TR requires repeated episodes of rising and walking with a blank, staring face, relative unresponsiveness, and great difficulty being awakened. Behaviour ranges from sitting up and fumbling to complex semi-purposeful sequences; the sleepwalker can often navigate the environment yet may interact with it

dangerously (stepping through an upstairs window, walking into a road), and injury and even acts of violence occur. It is very common in children, with peak prevalence between four and eight years of age, and rare and more clinically significant in adults, where it is familial and often secondary to another sleep disorder such as apnoea.

The management principle in one line. Do not grab, shake or shout at a sleepwalker; in their confused state they may believe they are being attacked and lash out. Guide them gently back to bed. Two clinical variants are subsumed here as the sleepwalking type: sleep-related eating (nocturnal eating with amnesia and weight gain) and sleep-related sexual behaviour (**sexsomnia**), which the DSM-5-TR classes as a NREM arousal disorder, not a REM phenomenon.

GOOD TO REMEMBER

- **Sleepwalking (the defining criterion):** repeated episodes of rising from bed and walking during slow-wave sleep with a blank stare, unresponsiveness and difficulty being awakened, and amnesia afterwards (DSM-5-TR); childhood peak four to eight years, familial, provoked by sleep deprivation; sleep-related eating and sexsomnia are its specifiers, and it is managed by gently returning the walker to bed, never by forcibly waking them.

16.5 Sleep terrors (pavor nocturnus)

What it is. A sleep terror is a sudden arousal from slow-wave sleep with intense fear, often opening with a piercing scream, in a child who sits up unresponsive, inconsolable, with florid autonomic arousal (mydriasis, tachycardia, rapid breathing, sweating) and who is amnesic for the event afterwards (DSM-5-TR 2022; Kaplan and Sadock CTP 2024). Unlike a nightmare there is no unfolding dream narrative, at most a single fragmentary frightening image, and the child cannot be comforted during the episode and does not remember it in the morning. Also called **pavor nocturnus** or night terror, it is familial, provoked by sleep deprivation, fever and CNS-depressant withdrawal, and psychopathology is seldom associated in children (though a history of trauma or psychiatric problems is more often comorbid when it presents in adults).

The two things it is confused with. A sleep terror is confused with a nightmare (a REM event with full recall, from the second half of the night, no autonomic storm and the child is easily consoled and remembers it) and, more dangerously, with a nocturnal seizure. For children whose sleep terrors are frequent and distressing, scheduled awakenings shortly before the usual time of the event can pre-empt them (Rutter).

COMMON TRAP

The screaming, thrashing, inconsolable child who is amnesic in the morning is a sleep terror, a NREM parasomnia, not a nightmare and not necessarily an epileptic event, but seizure sits at the top of the differential for *any* stereotyped nocturnal behaviour. The discriminators: a sleep terror varies in content and is provoked by sleep deprivation and fever, whereas nocturnal seizures tend to repeat the same stereotyped semiology and are captured on the polysomnogram's EEG leads. When in doubt, the study that settles it is a polysomnogram with seizure montage.

GOOD TO REMEMBER

- **Sleep terror (the defining criterion):** abrupt arousal from slow-wave sleep with a panicky scream, intense fear and marked autonomic arousal, inconsolable during the event, no or only a fragmentary image recalled, and amnesia afterwards (DSM-5-TR); distinguished from a nightmare (REM, full recall, consolable) and from a nocturnal seizure (stereotyped, EEG-positive) which is the discriminator that must not be missed.

16.6 The REM parasomnias: nightmare disorder and sleep paralysis

Nightmare disorder. Nightmares are frightening, elaborate dreams that arise in REM sleep and therefore in the last third of the night, growing more terrifying until they awaken the dreamer, who comes fully awake and **remembers the dream in detail** (Kaplan and Sadock CTP 2024). That full recall and rapid return to alert orientation is the single feature that separates a nightmare from a sleep terror. Nightmares are common in children aged three to six and rare in adults, and become nightmare disorder when they are frequent and distressing enough to breed a fear of sleeping. Post-traumatic nightmares are a special case; the evidence-supported drug there is prazosin, a central alpha-1 antagonist, for PTSD-related nightmares.

Sleep paralysis. Isolated sleep paralysis is the persistence of REM atonia into the wake transition: for seconds to a couple of minutes at sleep onset or on waking the person is conscious and aware of the surroundings but unable to move or speak, often with a frightening sense of a presence in the room (Kaplan and Sadock CTP 2024). It is common and usually benign in isolation, but recurrent sleep paralysis with hypnagogic hallucinations should prompt a thought about narcolepsy, cross-referenced to the sleep neurotransmitter systems in the Functional Neuroanatomy and Neurophysiology notes.

GOOD TO REMEMBER

- **Nightmare disorder (the defining criterion):** repeated frightening, well-remembered dreams arising from REM sleep in the second half of the night, with rapid full awakening and detailed recall (the opposite of the amnestic, autonomic sleep terror), causing distress or fear of sleep; sleep paralysis is REM atonia intruding into waking, benign in isolation but a pointer to narcolepsy when it recurs with hypnagogic hallucinations.

16.7 REM sleep behaviour disorder: the atonia fails and the dream is enacted

The mechanism. During normal REM sleep the perilocus-coeruleus nuclei impose atonia (flaccid quadriparesis and areflexia) so that the vivid dreaming brain cannot move the body (Kaufman; Kaplan and Sadock CTP 2024). In **RBD** that atonia fails, intermittently or completely, and the sleeper enacts the dream: punching, kicking, leaping, running, shouting and screaming, frequently injuring themselves or the bed partner. Because it is a REM phenomenon it belongs to the last half of the night, the eyes are closed, and when woken the patient is quickly alert and can recount the dream, which characteristically involved defending against or fleeing an attack. The contrast with sleepwalking is instructive: a sleepwalker may calmly open a window and step out, whereas a person with RBD, acting on the dream sensorium rather than the real room, would dive through it believing it a lake.

Who gets it. RBD is overwhelmingly a disorder of **older men (usually over 65 years)** (Kaufman). It may be idiopathic, drug-induced (many antidepressants, the SSRIs, SNRIs such as venlafaxine, tricyclics and MAOIs, can precipitate or unmask it by allowing muscle activity during REM), or, most importantly for the examiner, the harbinger of a neurodegenerative disease.

FEATURE	NREM DISORDER OF AROUSAL	RBD (REM PARASOMNIA)
Sleep stage	Slow-wave (deep NREM, N3)	**REM sleep**
Time of night	First third	**Last half**
Typical age and sex	Children, either sex	**Men over 65 years**
Eyes	Typically open	Closed
Dream recall	None or a fragment; amnesic	**Recalls the dream; alert on waking**
Behaviour	Ambulation, navigates the real room	**Dream enactment, acts on the dream**
Ominous association	Benign; remits	**Prodrome of a synucleinopathy**

The load-bearing comparison; the NREM disorders of arousal and RBD differ on stage, timing, age, eyes, recall and, decisively, on what they portend.

GOOD TO REMEMBER

- **RBD (the defining criterion):** loss of the normal REM-sleep atonia so that the patient enacts the dream (punching, kicking, leaping, shouting) with the eyes closed in the last half of the night, is quickly alert on waking and recalls a dream of being attacked; typically a man over 65, in contrast to the amnestic, eyes-open, first-third NREM disorders of arousal.

16.8 The critical point: RBD is a prodrome of a synucleinopathy

The link that makes this topic examinable. RBD is now regarded as the single strongest clinical prodrome of the **synucleinopathies**, the neurodegenerative diseases in which alpha-synuclein aggregates: Parkinson's disease, dementia with Lewy bodies and multiple system atrophy (Kaufman; Tasman Psychiatry). The dream-enactment often precedes the motor or cognitive disease by years, so an older man with new RBD is carrying a warning of neurodegeneration well before the tremor, the parkinsonism or the fluctuating cognition and visual hallucinations appear. The relationship is close and specific: RBD develops in the course of Parkinson's disease in roughly 30 to 50 per cent of cases and in dementia with Lewy bodies in 50 to 80 per cent, and conversely a synucleinopathy declares itself in as many as half of RBD patients within three to ten years of the sleep disorder (longer follow-up pushes the conversion figure higher still). The point is cross-referenced to the Dementias and neurocognitive disorders notes and the Neurology foundations for psychiatrists notes.

The discriminating subtlety. This specificity is diagnostic gold. RBD tracks with the *synucleinopathies* and only rarely complicates the tauopathies such as Alzheimer's disease and frontotemporal dementia (Kaufman). So dream enactment in a patient with an evolving dementia

is itself a pointer toward Lewy body disease rather than Alzheimer's. It is diagnostically weighty enough that when RBD is comorbid with a known synucleinopathy the DSM-5-TR does not even require polysomnographic confirmation of the REM sleep.

MNEMONIC

RBD warns of PDM

Parkinson's disease, **D**ementia with Lewy bodies, **M**ultiple system atrophy: the three synucleinopathies RBD heralds. If you see dream enactment in an older man, think alpha-synuclein and watch for parkinsonism and fluctuating cognition, not for the tau of Alzheimer's disease.

TRAP **Filing RBD under nightmare disorder.** An older man who "acts out his nightmares" is not having a nightmare disorder (which has no motor enactment and no neurodegenerative risk); he has RBD, and calling it a nightmare buries the single most important thing about him, that he is showing a prodrome of a synucleinopathy years before the neurology declares itself.

1 to 10	≈50	>65	1
NREM AROUSAL EPISODE LENGTH (MINUTES)	RBD PHENOCONVERTING WITHIN 3 TO 10 YEARS (PER CENT)	TYPICAL RBD ONSET AGE (YEARS)	CLONAZEPAM BEDTIME DOSE IN RBD (MG)

16.9 Safety first, then the drugs: managing the parasomnias

Safety is the shared first step. Across both families the first intervention is not a drug but the bedroom: because the injury risk is real in sleepwalking and considerable in RBD, the environment is made safe (locking windows and doors, removing sharp or breakable objects, moving the mattress low, and for RBD the bed partner often sleeping separately) (Kaplan and Sadock CTP 2024; Kaufman). For the NREM disorders of arousal the mainstay is reassurance of the family, protecting slow-wave sleep by **avoiding sleep deprivation**, treating the provokers (obstructive sleep apnoea, fever, a full bladder, offending sedatives), and, for a child with frequent sleep terrors, scheduled awakenings; drugs are seldom needed and are reserved for severe, injurious or highly disruptive cases, where a bedtime benzodiazepine (clonazepam) or an antidepressant may be used.

The pharmacology of RBD. RBD, by contrast, usually does need a drug because of the injury risk, and here two agents carry the topic (Kaufman). Clonazepam at a low bedtime dose (the parsed texts quote 1 mg at night, in practice titrated in the 0.5 to 2 mg range) reduces or abolishes the episodes so reliably that a good response supports the diagnosis. High-dose melatonin at night is the other mainstay and is often preferred first, particularly in the very patients who have RBD, older people and those with parkinsonism or dementia, where clonazepam's sedation, confusion and fall risk are least welcome. Both agents, and the wider question of the benzodiazepines, the z-drugs and melatonin, belong to the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes; a further step is to review and, where possible, stop any antidepressant that may be unmasking the RBD.

RULE **Secure the bedroom before you reach for a prescription.** In every parasomnia the first-line intervention is environmental safety and, for the NREM disorders of arousal, protecting sleep and removing triggers; medication (clonazepam or melatonin) is for RBD and for the severe, injurious NREM case, not the routine one.

INDIA

The genuine Indian problem in parasomnias is on the RBD side. Polysomnography and the sleep laboratories that would confirm the loss of REM atonia are scarce and out-of-pocket, so an older man's dream enactment is far more likely to be dismissed as "just nightmares" than recognised, and the neurodegenerative warning it carries is lost. Layered on this is India's liberal use of benzodiazepines: clonazepam is among the most freely prescribed drugs in the country, which cuts two ways, it means an effective RBD treatment is cheap and available, but it also means a benign childhood NREM parasomnia that needed only reassurance and a safe bedroom can end up medicated with a benzodiazepine it never required. Sleep hygiene, and specifically protecting sleep against the deprivation that provokes the disorders of arousal, is the cheapest and most under-used intervention of all.

GOOD TO REMEMBER

- **Management (the value):** environmental safety and trigger removal come first in every parasomnia; the NREM disorders of arousal need reassurance, protected sleep and (for children with sleep terrors) scheduled awakenings rather than drugs, while RBD is treated pharmacologically with clonazepam (about 1 mg at bedtime) or high-dose melatonin (often preferred in the elderly and in those with parkinsonism to avoid clonazepam's falls and sedation), alongside stopping any antidepressant that may be unmasking it.

HOLD THIS

Read a parasomnia off the sleep stage: NREM disorders of arousal (confusional arousal, sleepwalking, sleep terror) rise from slow-wave sleep in the first third of the night in amnestic, hard-to-rouse, eyes-open children who recall no dream and are managed with safety and reassurance; REM parasomnias belong to the dream-rich second half, and REM sleep behaviour disorder (lost REM atonia, dream enactment, eyes closed, dream recalled, men over 65) is the one that matters most because it is a prodrome of a synucleinopathy (Parkinson's disease, dementia with Lewy bodies, multiple system atrophy), phenoconverting in up to half of patients within three to ten years, and is treated with clonazepam (about 1 mg at night) or high-dose melatonin.

17 · Circadian rhythm sleep-wake disorders

A **circadian rhythm sleep-wake disorder** is a persistent mismatch between the endogenous circadian clock and the sleep-wake schedule the person wants or is required to keep. The clock itself, the suprachiasmatic nucleus, is intact and keeps near-perfect time; the fault is one of *alignment*, so the patient sleeps well but at the wrong hour of the twenty-four. That single idea is the examinable heart of the group, and it is also the diagnostic discriminator: when a person with one of these disorders is allowed to sleep on their own preferred schedule, the quantity and quality of sleep are normal.

Why it matters, and how this note is framed. The circadian disorders are the mimic that a hypnotic will fail, so recognising them cleanly saves the patient a pointless sleeping tablet, and their management is a small, elegant piece of physiology rather than a drug ladder: light therapy and melatonin are timed against the phase-response curve to push the clock the right way. This is a management topic, so the treatment half leads with the British Association for Psychopharmacology position (BAP 2019), whose consensus statement explicitly covers circadian rhythm disorders, and then states what the sleep-medicine guideline recommends per type; the specific per-type light-and-melatonin timings and doses are not in the verified drug supplement, so they are grounded on the American Academy of Sleep Medicine clinical practice guideline (AASM 2015, Auger et al.) and Kaplan and Sadock and flagged as such. The one rule to carry throughout is the direction: advance the clock with morning light, delay it with evening light, and treat melatonin as the mirror image.

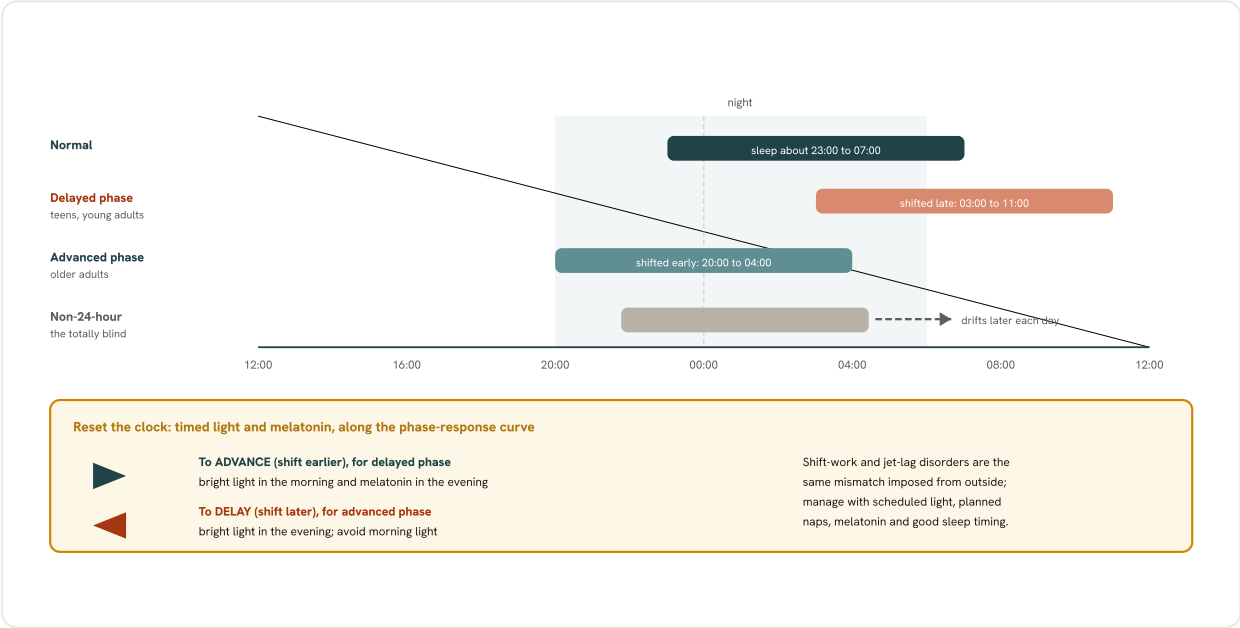


Fig 17.16 The circadian rhythm sleep-wake disorders. Each is a mismatch between the internal circadian clock and the desired or required sleep-wake schedule. In delayed sleep-wake phase disorder, common in adolescents, the whole sleep window is shifted late, so the person cannot fall asleep or wake at conventional times; in advanced sleep-wake phase disorder, seen in older adults, it is shifted early, with evening sleepiness and pre-dawn waking; in non-24-hour disorder, typical of the totally blind who lack light entrainment, the clock drifts a little later each day; and shift-work and jet-lag disorders are the same misalignment imposed from outside. Management resets the clock along the phase-response curve: morning bright light and evening melatonin advance the clock (for the delayed type), while evening light delays it (for the advanced type), supported by scheduled light, planned naps and consistent sleep timing.

17.1 The concept: a clock that keeps good time but points the wrong way

The shared mechanism. Every disorder in this collection shares one aetiology: desynchrony between the internal circadian pacemaker and the desired sleep-wake cycle (Kaplan and Sadock CTP 2024). The pacemaker sits in the suprachiasmatic nucleus, oscillates with a period of about twenty-four hours, and its output tracks the daily swing in core body temperature. The mismatch can arise three ways, an improper phase relationship between the clock and the schedule (the phase is shifted early or late), travel across time zones, or an intrinsic fault in the rhythm itself (the clock free-runs or is flattened).

The discriminator from insomnia. The tell that separates a circadian disorder from insomnia disorder is that sleep is normal in amount and quality when it is timed to the patient's own biological schedule; the delayed-phase adolescent who cannot fall asleep at a socially normal hour sleeps perfectly well if left to sleep late (Kaplan and Sadock CTP 2024). Insomnia persists whenever the person tries to sleep; a circadian disorder resolves the moment the schedule is allowed to follow the clock.

PEARL

Ask the single screening question: "when you are on holiday and can sleep and wake whenever you like, is your sleep normal?" A yes points to a circadian rhythm sleep-wake disorder, not insomnia. The clock is not broken, it is simply set to the wrong time.

17.2 The diagnostic criteria, the subtypes, and the duration specifiers

The three criteria. To diagnose a circadian rhythm sleep-wake disorder there must be (a) an alteration of, or a misalignment between, the endogenous circadian rhythm and the required sleep-wake schedule, (b) sleep disruption producing insomnia, excessive daytime sleepiness, or both, and (c) resulting distress or social, occupational or other functional impairment (DSM-5-TR; Kaplan and Sadock CTP 2024). ICD-11 moves the whole sleep-wake group out of the mental-disorders chapter into its own dedicated chapter, reflecting that the pathophysiology is a body-clock problem rather than a primary psychiatric one.

The subtypes and the specifiers. DSM-5-TR codes six subtypes: delayed sleep-wake phase type, advanced sleep-wake phase type, irregular sleep-wake type, non-24-hour sleep-wake type, shift work type, and unspecified type. The jet lag type is listed in the sleep-medicine classification (ICSD-3) but was *not* carried into DSM-5-TR, a favourite examiner point. Each is further specified by course: episodic (symptoms one month or more but under three months), persistent (three months or longer), or recurrent (two or more episodes within a one-year period) (Kaplan and Sadock CTP 2024).

ELEMENT	REQUIREMENT FOR A CIRCADIAN RHYTHM SLEEP-WAKE DISORDER
Core mechanism	**Alteration of, or misalignment between, the endogenous circadian rhythm and the required sleep-wake schedule**
Sleep disruption	Insomnia, excessive daytime sleepiness, or both
Consequence	Clinically significant distress or functional impairment
Discriminator	**Sleep is normal in amount and quality when timed to the patient's own preferred schedule**
Subtypes (DSM-5-TR)	Delayed phase, advanced phase, irregular, non-24-hour, shift work, unspecified (jet lag is ICSD-3, not DSM-5-TR)
Course specifier	Episodic (one to under three months), persistent (three months or longer), recurrent (two or more episodes in a year)

The circadian rhythm sleep-wake disorder criteria; the load-bearing points are the misalignment mechanism, the normal-sleep-on-own-schedule discriminator, and the persistent-versus-episodic three-month line.

GOOD TO REMEMBER

- **Circadian rhythm sleep-wake disorder (defining criterion):** a persistent misalignment between the endogenous circadian clock and the required sleep-wake schedule that produces insomnia or excessive sleepiness plus impairment, with the discriminating feature that sleep is *normal when timed to the patient's own preferred schedule*; DSM-5-TR codes six subtypes and specifies persistent when three months or longer, and jet lag sits in ICSD-3 but not DSM-5-TR.

17.3 Delayed sleep-wake phase type: the adolescent night owl

The picture. In the **delayed sleep-wake phase** type the biological clock runs slower than twenty-four hours or is set later than the desired schedule, producing a phase delay in the sleepiness-alertness cycle. These patients are alert late into the evening, fall asleep only in the small hours (habitual onset around two to six in the morning) and wake late (around ten in the morning to one in the afternoon), and are the classic "night owls" (Kaplan and Sadock CTP 2024). It is the commonest of the intrinsic circadian disorders, affecting roughly two percent of the population, and is overrepresented in adolescents and young adults because puberty-related changes in sleep homeostasis push the clock later just as inflexible school and college timings demand an early start (New Oxford Textbook of Psychiatry). Forced to a conventional schedule they present as sleep-onset insomnia with morning grogginess; left to their own timing they sleep normally.

GOOD TO REMEMBER

- **Delayed sleep-wake phase type (the criterion):** a stable, later-than-desired sleep window (onset around two to six in the morning) with normal sleep on the patient's own schedule; the population is the adolescent and young adult night owl, prevalence about two percent, and management advances the clock with morning light plus early-evening melatonin.

17.4 Advanced sleep-wake phase type: the early-rising older adult

The picture. The **advanced sleep-wake phase** type is the mirror: the clock is set earlier, so the patient becomes sleepy in the early evening (sleep onset around six to nine in the evening) and wakes several hours before they wish to (around two to five in the morning), unable to return to sleep (New Oxford Textbook of Psychiatry). The complaint is therefore early-morning waking and an inability to stay awake for evening social life. Prevalence rises with age, and an age-related phase advance, a shortened endogenous circadian period, and increased retinal sensitivity to morning light are the proposed mechanisms. A familial advanced-phase form shows autosomal dominant inheritance, classically a PER2 gene mutation causing hypophosphorylation of the PER2 protein, and a missense mutation in casein kinase I (Kaplan and Sadock CTP 2024).

GOOD TO REMEMBER

- **Advanced sleep-wake phase type (the criterion):** an earlier-than-desired sleep window (onset around six to nine in the evening, waking around two to five in the morning) presenting as early-morning waking; the population is the older adult, the familial form is autosomal dominant with a PER2 mutation, and management delays the clock with timed evening bright light.

17.5 Non-24-hour and irregular sleep-wake types: the blind and the neurologically impaired

Non-24-hour type. Here the pacemaker has a cycle length different from twenty-four hours and, crucially, is not reset each morning, so it free-runs and drifts steadily out of phase with the environment (Kaplan and Sadock CTP 2024). It is the disorder of the *totally blind*, in whom the loss of light input to the suprachiasmatic nucleus removes the daily photic reset. Sleep-onset insomnia and daytime sleepiness worsen progressively until clock and environment are furthest apart, then briefly normalise as they realign, giving the characteristic cycling that earned the older name periodic insomnia and periodic excessive sleepiness.

Irregular sleep-wake type. In the irregular type the circadian rhythm is absent or pathologically diminished, so sleep is scattered into three or more short episodes across the twenty-four hours with no consolidated night; the total sleep amount is normal but its temporal organisation is lost (Kaplan and Sadock CTP 2024). It is seen with neurodegeneration and dementia and with neurodevelopmental disorder, where the driving oscillator and the daily zeitgebers are both weak. Long daytime naps alternate with inappropriate nocturnal wakefulness, and daily function is significantly impaired.

GOOD TO REMEMBER

- **Non-24-hour type (the criterion):** a free-running clock not reset each morning, the disorder of the *totally blind*, giving cyclically worsening then briefly normalising insomnia and sleepiness; managed with timed melatonin or the melatonin agonist tasimelteon.
- **Irregular sleep-wake type (the criterion):** an absent or flattened rhythm with *three or more* fragmented sleep bouts across the day and no consolidated night (total sleep normal), typical of dementia and neurodevelopmental disorder; managed with morning bright light and a structured daily routine.

17.6 Shift work and jet lag types: the extrinsic, socially imposed disorders

Shift work type. This is diagnosed by the history of recent **shift work**: the person must sleep and stay awake against their circadian rhythm, giving insomnia when they try to sleep by day and excessive sleepiness when they must work by night, with profound cumulative sleep deprivation (Kaplan and Sadock CTP 2024). The natural low point of the sleep-wake rhythm falls at about three to five in the morning, which is precisely when transport and industrial accidents cluster, so the disorder is a safety issue as much as a sleep complaint. Weekend reversion to a day schedule keeps the underlying rhythm stubbornly unshifted.

Jet lag type. Rapid travel across several time zones induces a transient misalignment: eastward travel requires a phase advance and westward travel a phase delay (Kaplan and Sadock CTP 2024). Eastward flights are harder to adjust to (and harder still for "owls") because advancing the clock is intrinsically difficult. Healthy people re-entrain at roughly one to two time zones per day, so an eight-hour translocation takes about four or more days to settle. Jet lag disorder is classified in ICSD-3 but, again, is not a DSM-5-TR subtype.

GOOD TO REMEMBER

- **Shift work type (the criterion):** insomnia and sleepiness driven by a work schedule that opposes the circadian rhythm (recent shift-work history is the anchor), with the circadian nadir and accident window at about three to five in the morning; managed with planned napping, timed melatonin and modafinil for the sleepiness.
- **Jet lag type (the criterion):** transient misalignment after crossing multiple time zones, eastward travel needing a phase advance (harder) and westward a phase delay, re-entraining at about one to two zones per day; an ICSD-3 entity absent from DSM-5-TR.

17.7 Assessment: the sleep diary, actigraphy, and the phase markers

The two workhorse tools. The diagnosis is largely clinical, confirmed by a prospective **sleep** diary kept over one to two weeks, which exposes the stable early or late timing that a single consultation misses, supplemented by actigraphy, a wrist accelerometer that objectively logs the rest-activity pattern over the same period (Kaplan and Sadock CTP 2024; New Oxford Textbook of Psychiatry). Together they show that the sleep is normal in structure but consistently mistimed.

The phase markers that let you time treatment. To give light and melatonin correctly the clinician must estimate the patient's circadian phase, and the two most robust markers are the core body temperature nadir and the dim light melatonin onset (DLMO), the rise in endogenous melatonin measured under dim light (New Oxford Textbook of Psychiatry). As a rule of thumb the temperature nadir falls about two hours before habitual waking, and the DLMO begins about two to three hours before habitual sleep onset. These are not academic: light and melatonin shift the clock in opposite directions on either side of these markers, so mis-estimating the phase means pushing the clock the wrong way.

Zeitgeber

An external time cue that entrains the clock; light is the most powerful.

Phase advance

Shifting the sleep-wake cycle *earlier* (the fix for delayed phase).

Phase delay

Shifting the sleep-wake cycle *later* (the fix for advanced phase).

DLMO

Dim light melatonin onset, the endogenous melatonin rise about two to three hours before habitual sleep onset; a key phase marker.

Core temperature nadir

The lowest point of core body temperature, about two hours before habitual waking; the pivot of the light phase-response curve.

GOOD TO REMEMBER

- **Assessment (the first step):** a one-to-two-week prospective sleep diary plus actigraphy establishes the mistimed-but-normal pattern; the dim light melatonin onset (about two to three hours before habitual sleep onset) and the core body temperature nadir (about two hours before waking) are the two phase markers used to time light and melatonin correctly.

17.8 Management: the phase-response curve, and timed light therapy

The governing rule. The clock is reset each day chiefly by bright light acting as the dominant zeitgeber, and the *timing* of light decides the direction of the shift. Referenced to the core body temperature nadir, light given *after* the nadir advances the clock, while light given *before* the nadir delays it (Kaplan and Sadock CTP 2024). Translated to the clinic this is the one thing to memorise: morning bright light advances the clock and treats the delayed-phase patient, and evening bright light delays the clock and treats the advanced-phase patient (New Oxford Textbook of Psychiatry). Therapeutic intensity is roughly two thousand five hundred to ten thousand lux, and the blue spectrum is the most potent ingredient.

What the guidelines say, by type. BAP 2019 endorses appropriately timed light and melatonin for the circadian disorders as the core approach (BAP 2019). The sleep-medicine guideline is type-specific: it supports timed evening bright light for advanced sleep-wake phase disorder; for delayed sleep-wake phase disorder in adults it could not recommend light as a stand-alone on current evidence quality, though it endorses it combined with behavioural measures in children and adolescents; and for the irregular type in older adults with dementia it supports morning bright light while advising against sleep-promoting medication (AASM 2015). The types, populations and first-line levers are set out in the figure alongside and the table below.

RULE **Morning light advances, evening light delays.** Timed bright light is the primary tool; give it in the morning to phase-advance a delayed clock and in the evening to phase-delay an advanced clock. Relative to the core temperature nadir: light after the nadir advances, light before it delays.

MNEMONIC

AM ADVANCES, PM POSTPONES

AM light **A**dvances the clock (earlier sleep, treats delayed phase); **P**M light **P**ostpones it (later sleep, treats advanced phase). Melatonin is the mirror image, so flip the timing for the tablet.

SUBTYPE	TYPICAL POPULATION	SLEEP-WAKE PATTERN	FIRST-LINE MANAGEMENT (PER PHASE-RESPONSE CURVE)
Delayed sleep-wake phase	**Adolescents, young adults ("night owls")**	Onset around 2 to 6 in the morning, wake around 10 in the morning to 1 in the afternoon	**Advance: morning bright light plus early-evening melatonin (0.5 to 3 mg)**
Advanced sleep-wake phase	Older adults; autosomal dominant familial form (PER2)	Onset around 6 to 9 in the evening, wake around 2 to 5 in the morning	**Delay: timed evening bright light**
Non-24-hour	The totally blind	Sleep drifts progressively later, cycling insomnia and sleepiness	Timed melatonin, or the melatonin agonist tasimelteon
Irregular sleep-wake	Dementia, neurodevelopmental disorder	Three or more fragmented sleep bouts, no consolidated night	Morning bright light plus a structured routine and daytime activity
Shift work	Night and rotating-shift workers	Daytime insomnia, night-time sleepiness; nadir 3 to 5 in the morning	Planned napping, timed melatonin, modafinil for sleepiness
Jet lag (ICSD-3)	Multi-time-zone travellers	Transient misalignment; eastward is the harder advance	Timed light and melatonin toward destination time; adapts about 1 to 2 zones per day

The six circadian subtypes with population and first-line management; the pattern to hold is that delayed phase is advanced (morning light, evening melatonin) and advanced phase is delayed (evening light).

2	2500 to 10000	0.5 to 3	1.5 to 6.5
DELAYED SLEEP-WAKE PHASE PREVALENCE (%)	THERAPEUTIC BRIGHT-LIGHT INTENSITY (LUX)	MELATONIN DOSE, DELAYED PHASE (MG)	MELATONIN TIMING BEFORE BEDTIME (HOURS)

GOOD TO REMEMBER

- **Light therapy (the value):** timed bright light (about two thousand five hundred to ten thousand lux, blue spectrum most potent) is the primary lever; *morning light advances* the clock for delayed phase and *evening light delays* it for advanced phase (relative to the core temperature nadir, after the nadir advances and before it delays); BAP 2019 endorses timed light, and AASM 2015 supports evening light for advanced phase and morning light for the irregular type in dementia.

17.9 Management: timed melatonin, modafinil, chronotherapy, and the Indian frame

Melatonin, the mirror of light. Melatonin (in India, Meloset) is the internal signal of darkness: endogenous levels rise at dusk and stay high until dawn, and bright light suppresses them (Kaplan and Sadock CTP 2024). Its phase-response curve is roughly the mirror image of light's, so *evening* melatonin advances the clock while *morning* melatonin delays it. For delayed sleep-wake phase disorder, small doses (0.5 to 3 mg) taken about one and a half to six and a half hours

before habitual bedtime, that is before the dim light melatonin onset, reliably advance the clock; earlier timing within that window works best (New Oxford Textbook of Psychiatry). Combined with morning bright light, this is the standard advance package for the delayed-phase adolescent, and the sleep-medicine guideline recommends timed melatonin for delayed phase across adults, children and adolescents (AASM 2015). For the non-24-hour disorder of the totally blind, timed melatonin, or the melatonin agonist tasimelteon, re-entrains the free-running clock; tasimelteon is licensed for this abroad but is not marketed in India, so only the generic is named here.

Modafinil and chronotherapy. For the excessive sleepiness of shift work type, the wake-promoter modafinil (in India, Modalert or Provake) is approved to treat the sleepiness, alongside planned napping and melatonin (Kaplan and Sadock CTP 2024). Chronotherapy, progressively phase-delaying bedtime by two to three hours each night until the clock reaches the desired schedule, exploits the natural human tendency to drift later and so is easier than forcing an advance, but it is cumbersome, disrupts a week of school or work, and has been largely overshadowed by light and melatonin. The receptor pharmacology of melatonin, ramelteon and the hypnotics is developed in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes, and the ascending-arousal and sleep neurotransmitter systems in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and the Functional Neuroanatomy and Neurophysiology notes.

WORKED EXAMPLE

A seventeen-year-old cannot fall asleep before three in the morning, sleeps soundly until noon at weekends, but is failing college for chronic lateness and morning grogginess. This is delayed sleep-wake phase disorder, and the clock needs advancing. The plan advances it from both ends: bright light (or simply bright morning sunlight) on waking to phase-advance, and low-dose melatonin (0.5 to 3 mg) in the early evening, before the dim light melatonin onset, to advance from the other side, with the wake time then held steady. A hypnotic would be the wrong tool entirely.

TRAP **A hypnotic for a clock problem, or the timing reversed.** Prescribing a sleeping tablet for what is a circadian misalignment treats the symptom and not the cause, and giving light or melatonin at the wrong time pushes the clock the wrong way; the patient who sleeps normally on their own schedule needs the clock re-timed, not sedated.

INDIA

The genuine Indian device here is *shift work type*. India's large IT, business-process-outsourcing and healthcare workforces run night and rotating shifts, often serving Western time zones, so shift-work disorder is common and under-recognised, dismissed as ordinary tiredness. Two practical Indian realities shape management: melatonin (Meloset) is inexpensive and available over the counter, so timed low-dose melatonin is easy to deploy, while formal light boxes are scarce, which makes free, abundant morning sunlight the most accessible phototherapy for advancing a delayed clock. The trap to avoid is the widespread habit of using benzodiazepines to force sleep at the wrong biological hour, which sedates without re-timing and drifts into dependence; the fix is scheduling, timed light and melatonin, not a hypnotic.

HOLD THIS

A circadian rhythm sleep-wake disorder is a clock that keeps good time but points the wrong way, so sleep is normal on the patient's own schedule; recognise it, phase it with a sleep diary, actigraphy and the melatonin and temperature markers, then re-time the clock with the phase-response curve, morning light advances and evening light delays, with melatonin as the mirror (evening melatonin advances), modafinil for shift-work sleepiness, and never a hypnotic for what is a timing problem.

18 · Restless legs syndrome and PLMD

Two movement disorders of the night, one waking and one asleep. **Restless legs syndrome** (restless legs syndrome, RLS, historically Ekbom syndrome) and **periodic limb movement disorder** (periodic limb movement disorder, PLMD) are the two sleep-related movement disorders an examiner expects you to separate cleanly. RLS is a *waking* clinical diagnosis: a sensory urge to move the legs that comes on at rest and in the evening and eases with movement, diagnosed from the history alone. PLMD is an *asleep* polysomnographic diagnosis: repetitive stereotyped leg jerks recorded on the sleep study that fragment sleep and cause daytime sleepiness. They overlap heavily but are not the same thing, and the discrimination is the whole examinable point.

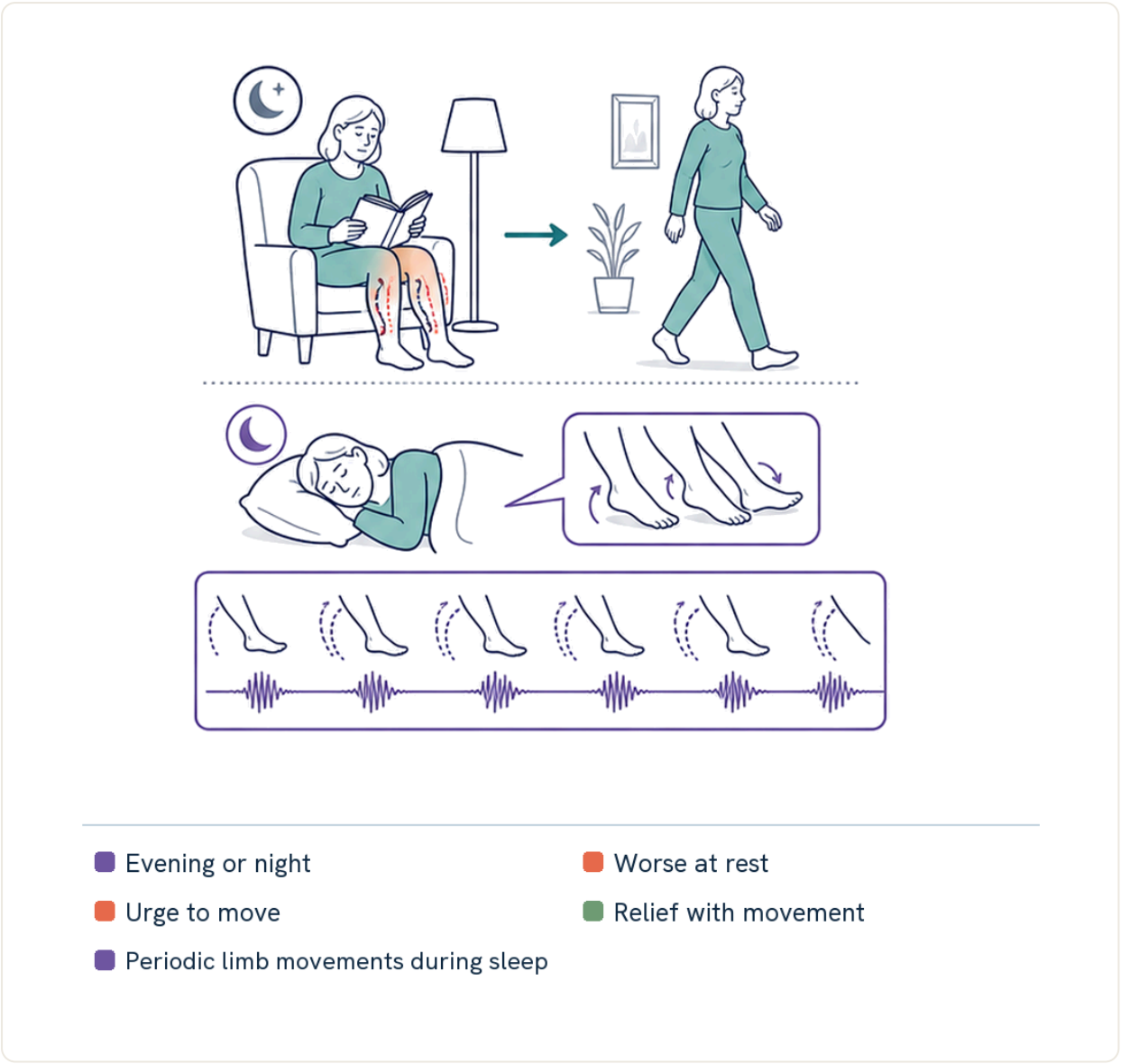


Fig 17.17 Restless legs syndrome is an urge to move with unpleasant sensations, worse at rest and in the evening and relieved by movement. Periodic limb movements are stereotyped recurrent movements during sleep.

Why the pair matters. Both are common, both rise with age, both are easily missed or mislabelled, and both have a specific, cheap first move that the viva rewards: check the ferritin. RLS is under-recognised, frequently dismissed as cramp or anxiety or a peripheral neuropathy, and its treatment carries a signature drug trap (augmentation) that is worth a mark on its own. The **dopaminergic** systems and iron stores that underlie RLS are laid out further in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and the Functional Neuroanatomy and Neurophysiology notes; this note owns the diagnosis, the discrimination and the guideline-anchored management.

18.1 Restless legs syndrome: the sensory urge and the four essential questions

The clinical picture. RLS is a sleep-related movement disorder defined by an urge to move the legs, usually accompanied or caused by an uncomfortable or unpleasant sensation, classically described as a "creepy-crawly", crawling or restless feeling deep in the calves. It comes on during relaxed wakefulness and inactivity, is worse in the evening or at night, and is transiently relieved

by movement such as walking or stretching. The sensation, not the movement, is the engine: the patient moves to relieve the urge.

Four questions, all "yes". The diagnosis is purely clinical, built on four essential features. All four must be present, and other causes of leg discomfort must be excluded first (Kaplan & Sadock, CTP 2024).

ESSENTIAL DIAGNOSTIC FEATURE (ALL FOUR REQUIRED)	URGE CUE
An urge to move the legs, usually with an uncomfortable or unpleasant leg sensation	**U**: Urge
The urge begins or worsens during rest or inactivity (sitting, lying down)	**R**: Rest worsens
The urge is partially or wholly relieved by movement, for as long as movement continues	**G**: Gets better on moving
The urge is worse in the evening or at night, or occurs only then	**E**: Evening/night

The four essential clinical criteria for restless legs syndrome; the diagnosis needs all four and is made on history alone, with no role for polysomnography (Kaplan & Sadock, CTP 2024; the accompanying scale plate typesets the Cambridge-Hopkins diagnostic questionnaire).

MNEMONIC

URGE

Urge to move (with an unpleasant sensation), worse on **R**est/inactivity, **G**ets better with movement, worse in the **E**vening or at night. Four features, all four needed. Structured questionnaires (the Cambridge-Hopkins diagnostic questionnaire, the RLS Diagnostic Index) map onto exactly these.

RULE **RLS is a bedside diagnosis, not a sleep-lab one.** All four URGE features present, mimics excluded, and you have restless legs syndrome; polysomnography has no role in diagnosing RLS itself.

GOOD TO REMEMBER

- **Restless legs syndrome (the syndrome):** an urge to move the legs with an uncomfortable sensation that (1) worsens at rest, (2) is relieved by movement, and (3) is worse in the evening or at night; all four features are required, mimics (neuropathy, cramps, arthritis, vascular insufficiency, positional discomfort) are excluded, and the diagnosis is clinical with no polysomnography needed.

18.2 Ferritin, iron and the comorbidities

Iron is the reversible cause you must not miss. The pathophysiology of RLS involves both central and peripheral abnormalities, with iron stores and **dopaminergic** transmission both implicated (low brain iron impairs dopamine synthesis). So every patient gets a serum ferritin: supplemental iron is recommended when the ferritin is **≤75 mcg per L**, because correcting the iron deficiency frequently reduces both the paraesthesiae and the movements (Kaplan & Sadock,

CTP 2024; Kaufman's Clinical Neurology). Ferritin is an acute-phase reactant, so a "low-normal" value can still reflect true depletion.

The company RLS keeps. Secondary RLS clusters with iron deficiency, end-stage renal disease (dialysis patients), pregnancy, peripheral neuropathy, diabetes, fibromyalgia, multiple sclerosis and Parkinson disease; the Parkinson and neurodegenerative associations are drawn out further in the Neurology foundations for psychiatrists notes. Prevalence in older adults runs **9% to 20%** and rises with age, and RLS is about twice as common in older women as in older men (Kaplan & Sadock, CTP 2024).

WORKED EXAMPLE

A woman on maintenance haemodialysis complains that every evening her calves feel "crawly" and she has to get up and pace; the feeling settles while she walks and returns the moment she sits. There is no daytime problem. This is textbook secondary RLS on end-stage renal disease. Send a ferritin before reaching for any drug: if it is at or below the threshold, iron replacement may be all she needs.

GOOD TO REMEMBER

- **The ferritin check (the value):** in restless legs syndrome, measure serum ferritin and give supplemental iron when it is **≤75 mcg per L**; low iron stores are the commonest reversible driver, and end-stage renal disease, pregnancy and neuropathy are the other secondary causes to screen for.

18.3 Treatment: dopaminergic and alpha-2-delta agents, and the augmentation trap

Two first-line drug classes. Once iron is corrected and any provoking drug removed, two classes are both considered first-line for RLS and PLMD (Kaplan & Sadock, CTP 2024). The non-ergot **dopaminergic** agonists pramipexole, ropinirole and transdermal rotigotine suppress the sensations and the movements. The **alpha-2-delta** calcium-channel ligands (gabapentin enacarbil, pregabalin and gabapentin) are equally first-line and are often preferred where there is pain, anxiety or a history of impulse-control problems.

Remove the aggravators. Several psychiatric drugs worsen RLS and should be stopped where possible: antidepressants, antipsychotics (neuroleptics) and sedating antihistamines, including the ones hidden in over-the-counter sleep aids and allergy remedies. Sleep deprivation also aggravates it.

Dopaminergic (non-ergot dopamine agonists)

Pramipexole, ropinirole, rotigotine transdermal patch; effective but carry the augmentation risk with long-term use.

Alpha-2-delta ligands

Gabapentin enacarbil, pregabalin, gabapentin; equally first-line, no augmentation, useful when pain or anxiety coexists.

Iron

Replace when ferritin is at or below threshold; can be the only treatment secondary RLS needs.

TRAP **Augmentation.** Long-term **dopaminergic** therapy can paradoxically make RLS worse: symptoms start earlier in the day, become more intense, and spread to the arms and trunk as the dose is pushed up. Do not chase it with more drug; reduce or split the dose, or switch to an alpha-2-delta agent.

GOOD TO REMEMBER

- **RLS pharmacotherapy (the value and the caution):** non-ergot dopamine agonists (pramipexole, ropinirole, rotigotine) and alpha-2-delta ligands (gabapentin enacarbil, pregabalin, gabapentin) are both first-line; the signature complication is dopaminergic augmentation (earlier, more intense, spreading symptoms on rising doses), managed by dose reduction, dose-splitting or a switch away from the dopamine agonist.

18.4 Periodic limb movement disorder: PLMS on polysomnography and the index

The movements, then the disorder. Periodic limb movements in sleep (PLMS) are periodic, repetitive, stereotyped limb movements during sleep, most often a brief upward dorsiflexion of both feet lasting roughly half a second to a few seconds, recurring in trains typically separated by **20 to 40 seconds**, predominantly in NREM sleep and recorded from the anterior tibialis on polysomnography. PLMS are extremely common on their own and are seen in more than **80%** of RLS patients who undergo a sleep study; up to **45%** of community-dwelling adults over 65 have them (Kaplan & Sadock, CTP 2024). The movements alone are not a disorder.

When PLMS becomes PLMD. The burden is quantified by the **periodic-limb-movement index**, the number of periodic limb movements per hour of sleep. Periodic limb movement disorder (PLMD) is diagnosed only when polysomnography-confirmed PLMS are combined with a clinical complaint of disturbed, non-restorative sleep or excessive daytime sleepiness, and other sleep disorders have been excluded. PLMD is explicitly a polysomnographic diagnosis, and it is undefined as a category in DSM-5 (Kaufman's Clinical Neurology); the International Classification of Sleep Disorders, third edition (ICSD-3) places both RLS and PLMD among the sleep-related movement disorders.

GOOD TO REMEMBER

- **Periodic limb movement disorder (the criterion):** periodic limb movements in sleep (PLMS) on polysomnography (stereotyped leg jerks, roughly **20 to 40 seconds** apart, mainly in NREM) quantified by the periodic-limb-movement index, *plus* disturbed sleep or daytime sleepiness, with other sleep disorders excluded; PLMS without any sleep consequence is not PLMD, and PLMD needs the sleep study whereas RLS does not.

18.5 Telling RLS from PLMD (and from the mimics)

One discriminator settles it. Is there a conscious sensory urge? RLS has a waking urge and paraesthesia that drive the movement; PLMS/PLMD are purely sleep movements that arise at regular intervals and are *not* a response to any urge or sensation, of which the patient is usually unaware (the bed partner reports the kicking, or the patient reports only unrefreshing sleep). The figure alongside places the waking urge of RLS against a sleep tracing of rhythmic anterior tibialis contractions.

FEATURE	RESTLESS LEGS SYNDROME (RLS)	PERIODIC LIMB MOVEMENT DISORDER (PLMD)
Core phenomenon	Waking sensory urge to move the legs	Repetitive stereotyped leg jerks in sleep
State when it occurs	Relaxed wakefulness, at rest, evening/night	**Only during sleep (mainly NREM)**
Sensory urge / paraesthesia	**Present and drives the movement**	Absent; movements are not a response to an urge
How diagnosed	Clinical, history alone; the four URGE features	**Polysomnography showing PLMS (plus sleep complaint)**
Patient awareness	Aware of the urge	Usually unaware; bed partner reports the jerks
Overlap	Over 80% have PLMS on the sleep study	Frequently coexists with RLS

Restless legs syndrome versus periodic limb movement disorder; the discriminator is the waking sensory urge (present in RLS, absent in PLMD) and whether polysomnography is required (yes for PLMD, no for RLS) (Kaplan & Sadock, CTP 2024; Kaufman's Clinical Neurology).

75 SERUM FERRITIN IRON-THERAPY THRESHOLD (MCG PER L)	**4** ESSENTIAL RLS QUESTIONS, ALL MUST BE "YES"	**20 to 40** INTER-MOVEMENT INTERVAL IN PLMS (SECONDS)	**>80%** OF RLS PATIENTS SHOW PLMS ON POLYSOMNOGRAPHY

INDIA

Three Indian realities converge here. First, iron deficiency is highly prevalent, so the ferritin check is unusually high-yield and often curative when RLS is secondary to depleted stores, especially in menstruating women and in pregnancy. Second, RLS is widely under-recognised and easily mislabelled as cramp, "gas", anxiety or a peripheral neuropathy, so evening leg restlessness relieved by walking is worth asking about directly. Third, patients presenting with this kind of broken, non-restorative sleep are commonly started on a benzodiazepine for "insomnia", which treats neither the iron deficiency nor the movement disorder and adds a dependence risk; the wider problem of benzodiazepine over-use for insomnia and the safer taper are covered in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes. Check a ferritin before you write a hypnotic.

HOLD THIS

Restless legs syndrome is a clinical, waking diagnosis (urge to move the legs, worse at rest and in the evening, relieved by movement, all four URGE features) whose first move is a ferritin (replace iron if ≤75 mcg per L) and whose first-line drugs are dopaminergic agonists or alpha-2-delta ligands, the dopaminergic ones risking augmentation; PLMD is its polysomnographic cousin, periodic limb movements in sleep plus a sleep complaint, with no waking urge.

Apply and consolidate

19 · Worked cases

Worked cases is where the whole arc pays off. The eating and sleep-wake topics were taught one machine at a time, the criteria on one page and the management on another; the exam presents them fused, as a patient in front of you. This closer drills that fusion through four **vignette**-driven worked examples, each reasoned aloud, so the moves become reflex: an anorexia nervosa case taken through medical-risk assessment, stabilisation and safe refeeding; a bulimia nervosa case read off its purging footprint and its potassium; a chronic-insomnia case that chooses a therapy over a tablet; and a narcolepsy work-up rescued from a mislabelled depression.

How to use this closer. Every case is worked in two disciplined halves, the same split the day was built on. First you *name the syndrome* from its defining criterion and its discriminator, then you *manage it* by the guideline anchor, the one first-line, the one value. The verified numbers, the refeeding rate, the fluoxetine dose, the multiple-sleep-latency thresholds, the scale cut-offs, are carried here exactly as the source topics established them; nothing new is invented, and any figure a source could not confirm was already flagged upstream. The reasoning flow for the four cases is set out in the accompanying figure, and each screening instrument named sits on the accompanying scale plate.

19.1 Reading an eating or sleep case: name the syndrome, then treat it

The two-halves discipline. The commonest way a candidate loses a station is by lunging at treatment before the diagnosis is secure, prescribing a hypnotic for what is actually a phase disorder, or a drug to make an anorexic patient gain weight. The corrective is a fixed order: settle the diagnosis on its criterion and its one discriminator, stage the medical risk, and only then reach for the management ladder. On these notes the discriminators are cheap and verbal, the significantly low weight from restriction, the binge-purge cycle at a normal weight, the sleep complaint despite adequate opportunity, and the emotion-triggered muscle weakness of cataplexy.

What each case tests. The eating cases test whether you can hold a hierarchy, that no drug is first-line in anorexia and that fluoxetine is the one licensed drug in bulimia, and whether you can refeed without killing the patient. The sleep cases test whether you lead chronic insomnia with a therapy rather than a tablet, and whether you can pull a narcolepsy out from behind a treatment-resistant depression. Hold the order and each case answers itself.

> **PEARL**
>
> Diagnose before you treat, and treat by the anchor, not the impulse. In every one of these cases the marks are split evenly between naming the syndrome from its one discriminator and choosing the one first-line move; a candidate who reaches for a drug before the diagnosis is settled loses half the station whatever they prescribe.

19.2 Case one, anorexia nervosa: the vignette and the medical-risk read

The vignette. The presentation is the sickest patient of the four, and the one where the danger is easy to under-read because the bloods can look bland.

> **WORKED EXAMPLE**
>
> **case:** a 19-year-old woman is brought by her family for fainting and six months of amenorrhoea. She eats tiny measured portions and exercises for hours, but attributes the poor intake to "gas and bloating and no appetite" and denies any wish to be thin. She is emaciated with fine downy **lanugo** on the forearms and cold peripheries; the body mass index is 14.6, the pulse 42 with a lying-to-standing blood-pressure drop, the serum potassium 2.9 and the electrocardiogram QTc prolonged.

Naming it, despite the absent fear. This is anorexia nervosa, restricting subtype: a restriction-driven, significantly low weight held by persistent weight-defeating behaviour, with disturbed recognition of the danger. The trap embedded in the vignette is the absent stated fear of fatness, the non-fat-phobic presentation; the diagnosis still stands, because the criterion accepts persistent behaviour that blocks weight gain in place of a voiced fear, and the significantly low weight from restriction is the non-negotiable anchor. By the DSM-5-TR band she is extreme (a body mass index under **15**); ICD-11 calls this significantly low body weight, with dangerously low body weight (the deeper grade) reserved for a body mass index under **14**, just below where she sits.

The medical-risk assessment. Before any feeding, the body is staged: weight, orthostatic blood pressure, pulse, temperature and peripheral circulation, with bloods for full blood count, urea and electrolytes weighted to **potassium**, magnesium and **phosphate**, liver function, glucose, an electrocardiogram for the QTc, and bone density by DEXA if the underweight is prolonged. Her bradycardia, postural drop, hypokalaemia and prolonged QTc place her, on the MARSIPAN risk stratification, in the high-risk zone that mandates emergency medical admission rather than outpatient refeeding. The neuroendocrine axes behind her amenorrhoea and bradycardia (the hypothalamic-pituitary-gonadal, thyroid and adrenal changes of starvation) are developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes.

> **INDIA**
>
> This vignette is deliberately Indian in shape. The **non-fat-phobic** presentation, restriction rationalised as gastrointestinal discomfort or loss of appetite rather than a wish to be thin, is relatively more common in Indian and other Asian patients, and calling such a starving patient "not anorexia" for want of a stated fear is the classic error. Layered on it is under-recognition: eating disorders are widely missed in India and stereotyped as an affluent-urban-female problem, so the severely underweight patient reaches care late and profoundly starved, exactly the one most endangered by refeeding. The corrective is a low threshold to screen (the SCOFF at the bedside) and always to attach a weight, orthostatic vitals, a potassium and an electrocardiogram QTc.

GOOD TO REMEMBER

- **Anorexia nervosa (defining criterion):** restriction of intake driving a *significantly low body weight*, plus a fear of weight gain *or* persistent behaviour that blocks it, plus disturbed body-image or non-recognition of the danger; the defining criterion is the restriction-driven low weight, and the fear need not be voiced, so a non-fat-phobic case: still meets the diagnosis.

19.3 Case one, the management: stabilise, refeed low-and-slow, then the therapy

Correct first, then feed cautiously. Once admitted, the sequence is correct the electrolytes, cover with **thiamine** before or with the first carbohydrate, and crawl the calories up. Feeding begins low, and the two numeric sources disagree about how low: NICE CG32 1.4.8 caps the high-risk start at **10 kcal per kg per day** and uses only **5 kcal per kg per day** in the extreme case such as a body mass index under 14, increasing slowly to meet or exceed full needs within **4 to 7 days**, whereas RCPsych MEED CR233 (2022) starts at **20 kcal per kg per day**, never below the immediate pre-admission intake, and warns against underfeeding; NICE NG69 gives no figure and refers to MEED, so quote the source the question names. Either way, daily phosphate, magnesium, potassium and thiamine supplementation runs alongside. The hallmark to pre-empt is refeeding syndrome, whose biochemical signature is hypophosphataemia.

Watch the phosphate early. Electrolytes are monitored daily through the first week, when the insulin-driven intracellular shift is steepest, and the phosphate trend over the first three days is the earliest warning that the syndrome is developing; a near-normal admission panel does not exclude the risk. Only once she is medically stable does the primary treatment proper begin: weight restoration to a healthy body mass index as the goal, delivered inside a multidisciplinary plan, plus a manualised psychological therapy chosen with her, CBT-ED, MANTRA or SSCM, all first-line and equivalent in adults. Medication treats comorbidity only; the general cognitive-behavioural technique behind CBT-ED is developed in the Psychotherapies, clinical assessment, MSE and nosology notes.

SOURCE AND CLINICAL STATE	STARTING RATE (KCAL PER KG PER DAY)	SUPPLEMENT AND MONITOR
NICE CG32 1.4.8, high risk of refeeding problems	**maximum 10**	Phosphate, magnesium, potassium, thiamine daily; full needs within 4 to 7 days
NICE CG32 1.4.8, extreme (body mass index under 14)	**only 5**	**Slowest start; electrolytes daily, phosphate watched over the first three days**
RCPsych MEED CR233 2022, eating disorders	**start at 20**	Never below the pre-admission intake; build up swiftly, avoid underfeeding

The two numeric refeeding positions for this case, and they disagree: NICE CG32 caps the high-risk start at 10 kcal per kg per day, RCPsych MEED CR233 2022 opens at 20, and NICE NG69 sets no rate and refers to MEED. Quote whichever source the question names; the exact electrolyte thresholds and the full monitoring schedule are owned by the refeeding-syndrome topic and its diagram.

MNEMONIC

CORRECT, COVER, CRAWL

Correct the electrolytes proactively (phosphate, potassium, magnesium); **Cover** with thiamine before or with the first feed; **Crawl** the calories up from a low start. The three prevention moves, applied to this admission in that order.

TRAP **Refeeding too fast, and trusting a bland admission panel.** Piling on calories to correct a dangerously low weight drives phosphate, potassium and magnesium into the cells; the falling phosphate of the opening days precipitates cardiac failure and arrhythmia. Start low, replace electrolytes, give thiamine first, and re-check daily through the first week.

GOOD TO REMEMBER

- **Refeeding syndrome (defining criterion):** the fatal fluid-and-electrolyte cluster of reintroducing feeding into a starved body, defined biochemically by *hypophosphataemia* with falling potassium and magnesium and fluid retention; the discriminator is that serum ions look near-normal until feeding drives them intracellularly.
- **Safe refeeding (the value):** *correct the electrolytes, give thiamine, start slow*, opening at a maximum of 10 kcal per kg per day on NICE CG32 (only 5 if extreme) or at 20 on RCPsych MEED CR233 2022, which warns against underfeeding, quoting whichever the question names, with daily supplementation and electrolytes monitored daily through the first week; the rate is the one variable fully under the clinician's control.
- **Anorexia therapy (the value):** the primary treatment is *weight restoration plus a manualised psychological therapy* (adults: CBT-ED, MANTRA or SSCM, all first-line; young people: family-based treatment), and *no drug is first-line*, medication treats comorbidity only.

19.4 Case two, bulimia nervosa: the binge-purge cycle and the potassium

The vignette, and the diagnosis you make by asking. This case hides in plain sight, because the weight is normal and nothing on inspection announces the disorder.

WORKED EXAMPLE

case: a 22-year-old woman of normal weight (body mass index 22) discloses, only when asked directly, that she binges secretly several evenings a week and then makes herself vomit. On examination there are knuckle calluses (Russell's sign), bilateral parotid fullness and eroded dental enamel; the serum potassium is 3.0 with a borderline-prolonged QTc.

Naming it. This is bulimia nervosa: the recurrent **binge-purge cycle**, binge eating with loss of control plus recurrent inappropriate compensatory behaviour (here self-induced vomiting), with self-evaluation hostage to weight and shape, at a normal or above-normal weight. That normal weight is the whole diagnostic point, and the reason it is missed; the discriminators from its neighbours are that the binges are objective, the purging recurrent, and the weight not significantly low (were it low, the label would become anorexia nervosa, binge-purge type). The frequency-and-duration threshold to state is at least once weekly for **three months** in DSM-5-TR (one month in ICD-11).

Reading the footprint of purging. The body records the vomiting: Russell's sign, parotid swelling and dental erosion are the visible residue, and the biochemistry is a hypochloraemic, hypokalaemic metabolic alkalosis. The two urgent findings that must be actively sought are marked hypokalaemia and a prolonged QTc, because a low potassium drives fatal arrhythmia; her potassium of 3.0 and borderline QTc make the ECG and the electrolyte correction the first, non-negotiable move, normal weight notwithstanding.

PEARL

Bulimia nervosa is the eating disorder you diagnose by *asking*, not by looking. The weight is normal, so the tells are the secret binge-purge cycle on history and Russell's sign, parotid fullness, eroded teeth and a quietly low potassium on examination. Screen with the SCOFF (positive at two), and always attach a potassium and an electrocardiogram.

GOOD TO REMEMBER

- **Bulimia nervosa (defining criterion):** the recurrent *binge-purge cycle*, binge eating with loss of control plus recurrent compensatory behaviour (most often self-induced vomiting) at least once weekly for three months (one month in ICD-11), with self-evaluation unduly influenced by weight and shape; the discriminating fact in this case: is that the weight is *normal or above*, not low, and the potassium and QTc are the emergency to seek.

19.5 Case two, the management: CBT-ED, and fluoxetine at 60 mg per day

Stabilise, then therapy first. The plan is to correct and monitor the potassium and arrange an electrocardiogram, then lead with a psychological therapy, never a drug alone. Under NICE NG69 the adult first step is bulimia-nervosa-focused guided self-help, stepping up to individual **CBT-ED** if that is unacceptable or ineffective; CBT-ED is the best-evidenced treatment and targets the machinery of the cycle directly, installing regular eating and dismantling the compensatory behaviours and the over-evaluation of shape and weight.

The one drug, at the antibinge dose. If a medication is added for the bingeing and purging, the answer is fluoxetine, the medication of choice and the one licensed drug for bulimia nervosa, titrated to **60 mg per day**, a dose *above* its 20 to 40 mg antidepressant range, and effective whether or not the patient is depressed. In India fluoxetine is cheap and widely available (brands Prodep, Fludac, Flunil), given alongside the therapy, not instead of it; its deep pharmacology (the high bulimia dose, the long half-life, the interactions) is carried in the Mood disorders: pharmacotherapy notes. The drug to avoid is the exam trap, bupropion is contraindicated because it lowers the seizure threshold in purging patients.

RULE **Fluoxetine 60 mg per day is THE licensed drug for bulimia.** The one antibulimic dose to memorise is fluoxetine *60 mg per day*, the antibinge dose sitting above the 20 to 40 mg antidepressant range; it is the medication of choice, given *with* a psychological therapy (guided self-help then CBT-ED), never instead of it, and never bupropion.

GOOD TO REMEMBER

- **CBT-ED (the value):** eating-disorder-focused CBT is the *best-evidenced treatment* for bulimia nervosa; NICE NG69 leads with guided self-help stepping up to CBT-ED, a psychological therapy is primary and medication is never the sole treatment.
- **Fluoxetine (the value):** the one value is *60 mg per day*, above the antidepressant dose, as the licensed antibinge drug (works whether or not the patient is depressed), given with the therapy; bupropion is *contraindicated* for its seizure-threshold effect in purging patients.

19.6 Case three, chronic insomnia: choosing CBT-I over a long-term hypnotic

The vignette. The third case is the one where the easy move is the wrong one, and the patient is actively asking for it.

WORKED EXAMPLE

case: a 46-year-old man reports six months of difficulty staying asleep, waking around three in the morning at least four nights a week, unable to return, with daytime fatigue and poor concentration, all despite going to bed with an adequate chance to sleep. His Insomnia Severity Index is 18 (moderate). He has been taking nightly alprazolam obtained from a pharmacy and asks for a stronger dose.

Naming it, after clearing the mimics. This is insomnia disorder, chronic form: dissatisfaction with sleep with difficulty maintaining it, *despite adequate opportunity*, at least three nights a week for at least three months, with daytime consequences. Before settling it, the sleep-wake mimics are cleared, a circadian phase disorder (sleep normal when timed to his own preference), obstructive sleep apnoea (snoring, witnessed apnoeas), and a movement disorder (an evening urge to move the legs); a hypnotic prescribed for apnoea would be useless and, in apnoea, dangerous. His ISI of 18 sits in the moderate clinical band (**15 to 21**), and the screening threshold is **10 or higher**.

The management move that defines the case. The whole station turns on one decision: cognitive behaviour therapy for insomnia (CBT-I), delivered as the multicomponent package with **sleep restriction** and **stimulus control** at its core, is first-line for chronic insomnia and is offered before any drug, because its gains outlast a tablet. The correct plan is to start CBT-I (face-to-face or digital, both efficacious) and to taper his alprazolam slowly with concurrent CBT-I, not to escalate a hypnotic he cannot then stop. The z-drug and benzodiazepine dependence and the withdrawal taper are developed in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes; the ISI form sits on the accompanying scale plate.

INDIA

The genuine Indian device here is *benzodiazepine over-use for insomnia*. With CBT-I therapists scarce and hypnotics cheap and easily obtained over the counter, long-term alprazolam and clonazepam prescribing for chronic insomnia is widespread and drifts into dependence, exactly this patient's trajectory. The corrective is not exotic: lead with CBT-I as first-line (digital where a therapist is out of reach), keep any hypnotic short-term and within licence, prefer prolonged-release melatonin in the older adult, and remember that correct sleep-hygiene practice is a *component* of CBT-I, not a substitute handed over as a leaflet.

RULE **CBT-I first, the tablet second, and do not start what you cannot stop.** Cognitive behaviour therapy for insomnia, with sleep restriction and stimulus control at its core, is first-line for chronic insomnia and precedes any drug; a hypnotic is short-term only, and an existing long-term benzodiazepine is tapered *with* concurrent CBT-I, not escalated.

GOOD TO REMEMBER

- **Insomnia disorder (defining criterion):** dissatisfaction with sleep with difficulty initiating or maintaining it or early waking, *despite adequate opportunity to sleep*, with daytime consequences; the thresholds are at least three nights a week for at least three months for the chronic form, and the mimics (circadian, breathing, movement) are cleared before the label is fixed.
- **CBT-I (the value):** CBT-I is *first-line for chronic insomnia, before any drug* (sleep restriction and stimulus control are its two engines); a hypnotic is not first-line, and a long-term benzodiazepine is tapered with concurrent CBT-I rather than escalated.

19.7 Case four, the narcolepsy work-up: the tetrad and the MSLT

The vignette, hiding behind a diagnosis. The last case is the one the psychiatrist meets already mislabelled, and the whole diagnosis turns on a single question no one has asked.

WORKED EXAMPLE

case: a 21-year-old man has been irresistibly sleepy since his mid-teens and has failed three antidepressants for a presumed "treatment-resistant depression". Asked directly what happens when he laughs hard, he describes his knees buckling and his head dropping while fully aware, lasting a few seconds (cataplexy); he also reports occasional inability to move on waking (sleep paralysis) and vivid dream-like images at sleep onset (hypnagogic hallucinations).

Naming it from the tetrad. The cluster is the **narcolepsy tetrad**: excessive daytime sleepiness with sleep attacks, cataplexy, sleep paralysis and hypnagogic hallucinations (disturbed nocturnal sleep is the fifth, pentad, feature). Sleepiness is the constant and the presenting complaint; cataplexy is the pathognomonic member, the emotion-triggered bilateral loss of muscle tone with preserved awareness, and it is REM-sleep atonia discharging into wakefulness from loss of the hypothalamic orexin (hypocretin) neurons. Cataplexy alone places him in type 1.

Sealing it on the test. The work-up is an overnight polysomnogram (to exclude apnoea) followed by the multiple sleep latency test, and his result is diagnostic: a mean sleep latency of five minutes with three sleep-onset REM periods across the naps. The MSLT criterion is a mean sleep

latency of **eight minutes or less** and **two or more** sleep-onset REM periods; a low cerebrospinal-fluid orexin (under **110 pg per mL**) is the most specific finding and defines type 1 but is rarely available.

TEST	DIAGNOSTIC FINDING IN THIS CASE
MSLT mean sleep latency	**8 minutes or less (his was 5)**
MSLT sleep-onset REM periods	**2 or more across the naps (his was 3)**
CSF orexin (hypocretin-1)	Low or absent (under 110 pg per mL); defines type 1, rarely available

The confirmatory thresholds applied to case four; the MSLT needs a mean sleep latency of eight minutes or less plus two or more sleep-onset REM periods, both of which he exceeds.

MNEMONIC

CHESS

Cataplexy; **H**ypnagogic hallucinations; **E**xcessive daytime sleepiness; **S**leep paralysis; disturbed nocturnal **S**leep (the pentad fifth). In this case: the sleepiness is the constant that got him labelled depressed; the cataplexy is the specific member that makes the diagnosis.

TRAP **Narcolepsy hiding as a treatment-resistant depression (or an epilepsy).** Pervasive daytime sleepiness that outweighs the mood earns antidepressant after antidepressant, and emotion-triggered drops get read as atonic seizures; the corrective is one question, ask about knees buckling at a joke, before escalating either label.

GOOD TO REMEMBER

- **Narcolepsy (defining cluster and confirmatory step):** the tetrad is excessive daytime sleepiness with sleep attacks, cataplexy, sleep paralysis and hypnagogic hallucinations (disturbed nocturnal sleep the pentad fifth), from loss of the orexin (hypocretin) neurons; *cataplexy is the pathognomonic member* and defines type 1, and the diagnosis is sealed on the MSLT at a mean sleep latency of eight minutes or less with two or more sleep-onset REM periods.

19.8 Case four, the management: the wake-promoting agent and sodium oxybate for cataplexy

Treat the two problems separately. Narcolepsy is not curable, so the daytime sleepiness and the cataplexy are targeted with different drugs on the sleep-medicine practice standard, with scheduled short naps and firm sleep hygiene as the non-drug backbone. For his sleepiness, the first-line wake-promoting agent is modafinil (in India, Modalert or Provake), a dopamine-transporter inhibitor at **200 to 400 mg per day** that improves the sleepiness but does *not* touch cataplexy; armodafinil, solriamfetol and pitolisant extend the class.

The cataplexy, and the Indian substitution. For the disabling cataplexy and his fragmented nights, sodium oxybate (the sodium salt of gamma-hydroxybutyrate) is the most effective single agent and the only one that also consolidates the broken night and improves daytime sleepiness, but it is an abuse-liable controlled substance dispensed through restricted programmes and never combined with alcohol. Where it is unavailable, cataplexy is suppressed with a REM-suppressing

antidepressant, an SSRI or SNRI (venlafaxine) or the tricyclic clomipramine, tapered rather than stopped to avoid rebound cataplexy. The sleep neurotransmitter and ascending-arousal systems behind these agents are developed in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and the Functional Neuroanatomy and Neurophysiology notes.

INDIA

The genuine Indian device in narcolepsy is *drug availability*. Modafinil (Modalert, Provake) and armodafinil are freely and cheaply available, so first-line treatment of the daytime sleepiness is entirely practical; but sodium oxybate, pitolisant and solriamfetol are not marketed in India, so cataplexy is usually managed with the older anticataplectic antidepressants (an SSRI or SNRI, or clomipramine) instead, exactly the substitution this case: makes. Under-recognition compounds it: MSLT-capable sleep labs are scarce and orexin assay essentially unavailable, so the sleepy adolescent is treated for laziness or depression for years. The corrective costs nothing, ask every chronically sleepy young patient about emotion-triggered weakness.

GOOD TO REMEMBER

- **Wake-promoting agent (the value):** *modafinil* (Modalert or Provake), a dopamine-transporter inhibitor at 200 to 400 mg per day, is first-line for the excessive daytime sleepiness of narcolepsy but does *not* benefit cataplexy; armodafinil, solriamfetol and pitolisant extend the class.
- **Sodium oxybate (the value):** the most effective single drug for *cataplexy* and the only one that also consolidates the broken night, but an abuse-liable controlled substance never combined with alcohol; where it is unavailable (as in India) cataplexy is managed with a REM-suppressing antidepressant (SSRI or SNRI, or clomipramine), tapered to avoid rebound cataplexy.

19.9 The four cases at a glance, and the through-line

One grid to hold them. Read side by side, the four cases rehearse the day's spine: the eating pair drills that no drug is first-line in anorexia while fluoxetine is the one licensed drug in bulimia, and that refeeding is prevented, not chased; the sleep pair drills that chronic insomnia leads with a therapy and that a narcolepsy is only ever found by asking about cataplexy. The through-line across all four is the same discipline, name the syndrome from its one discriminator, then treat by the anchor.

CASE	WORKING DIAGNOSIS	THE ONE DISCRIMINATOR	THE FIRST MANAGEMENT MOVE
One (case:)	**Anorexia nervosa, restricting**	Significantly low weight from restriction (fear need not be voiced)	Stabilise and refeed low-and-slow (CG32 caps at 10 kcal per kg per day, MEED 2022 opens at 20), then therapy; no drug first-line
Two (case:)	**Bulimia nervosa**	Binge-purge cycle at a *normal* weight; low potassium and Russell's sign	**Correct potassium; CBT-ED, and fluoxetine 60 mg per day if a drug is added**

CASE	WORKING DIAGNOSIS	THE ONE DISCRIMINATOR	THE FIRST MANAGEMENT MOVE
Three (case:)	**Insomnia disorder, chronic**	Sleep complaint despite adequate opportunity, three-plus nights a week for three months	**CBT-I first-line; taper the benzodiazepine, do not escalate a hypnotic**
Four (case:)	**Narcolepsy, type 1**	Cataplexy (emotion-triggered atonia, aware); MSLT sleepiness plus SOREMPs	Modafinil for sleepiness; sodium oxybate (or, in India, an SSRI/SNRI/clomipramine) for cataplexy

The four worked cases side by side; each is settled on one discriminator and opened on one management anchor, the discipline these notes are built to install.

10 or 20 CASE ONE REFEEDING START (KCAL PER KG PER DAY): CG32 CAPS AT 10, MEED 2022 OPENS AT 20	**60** CASE TWO FLUOXETINE DOSE FOR BULIMIA (MG PER DAY)	**≤8** CASE FOUR MSLT MEAN SLEEP LATENCY (MINUTES)	**≥2** CASE FOUR MSLT SLEEP-ONSET REM PERIODS (COUNT)

HOLD THIS

Four cases, one discipline: name the syndrome from its discriminator, then treat by the anchor. Anorexia is restriction-driven low weight (fear need not be voiced), stabilised and refed low-and-slow to pre-empt hypophosphataemia with no drug first-line; bulimia is the binge-purge cycle at a normal weight with a dangerous potassium, treated with CBT-ED and fluoxetine 60 mg per day; chronic insomnia is a sleep complaint despite adequate opportunity, led by CBT-I not a long-term hypnotic; and narcolepsy is the tetrad with cataplexy, sealed on the MSLT (mean sleep latency eight minutes or less with two or more sleep-onset REM periods) and treated with modafinil for sleepiness and sodium oxybate, or in India an SSRI/SNRI or clomipramine, for cataplexy.

20 · Consolidation

The whole eating and sleep-wake block now sits in front of you, and this closing topic is not new content but the machinery that turns reading into recall. The examination does not reward the candidate who has *read* the eating and sleep chapter; it rewards the one who can, cold and under pressure, state the discriminating criterion for each syndrome, name the one first-line move for each management problem, quote the refeeding rate and the scale bands to the number, and recite the narcolepsy tetrad and the AHI cut-offs in a single line. Those retrievals are what this topic drills. The single most robust finding in the science of learning is that **active recall** (pulling an answer out of an empty page) and **retrieval practice** (repeatedly testing yourself rather than re-reading) beat every passive method for durable memory, so the design here is deliberately answer-sparse: prompts first, and the answers held elsewhere in the chapter so you must fetch them.

Why it matters, and what this note owns. This note owns three things: the **mnemonic** that ties the chapter together, paid off from where it was seeded at the anorexia opener; a set of answer-free prompt lists for **active recall** across the eating-disorder discriminators, the refeeding thresholds and the drug anchors, the sleep architecture and the two-process model, the CBT-I

rule, and the narcolepsy tetrad, the AHI bands and the parasomnia-neurodegeneration link; and a whole-chapter **synthesis map** you are meant to **redraw from memory**. It re-derives no criteria, doses or bands of its own; every number quoted here is a pointer back to the topic that verified it. The deep pharmacology behind the drug names lives in the Mood disorders: pharmacotherapy notes (the SSRI at the high bulimia dose) and the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes (the hypnotics, their dependence and the taper); the sleep neurotransmitter systems and the neuroendocrine axes that fail in starvation sit in the Neurochemistry, Neuroendocrinology, Neuroimaging and Basic Psychopharmacology notes and the Functional Neuroanatomy and Neurophysiology notes; the general CBT frame sits in the Psychotherapies, clinical assessment, MSE and nosology notes. The synthesis map that carries the whole block is drawn in the accompanying figure, framed cover-the-branches so it can be used as a retrieval test.

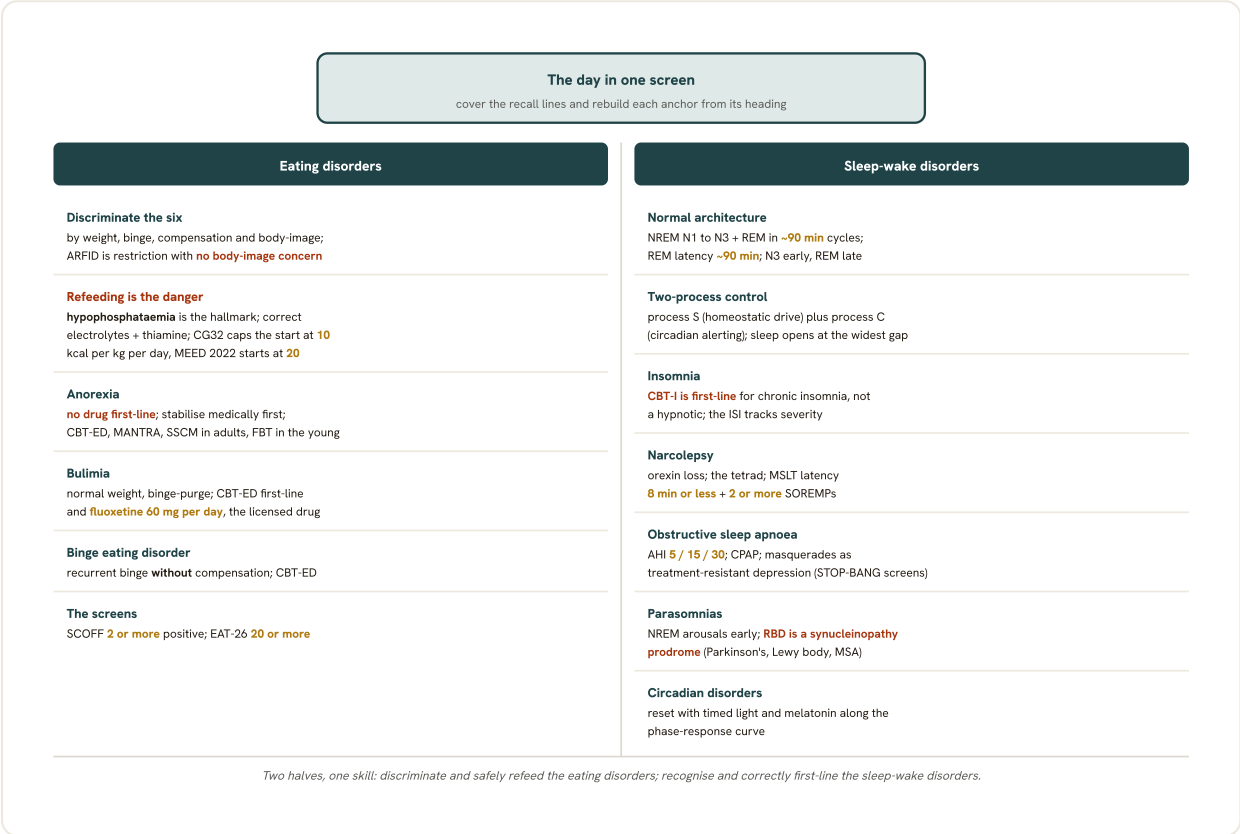


Fig 17.18 The chapter in one screen. The eating half reduces to four moves: discriminate the six presentations by weight, binge, compensation and body-image (with ARFID set apart by having no body-image disturbance); treat the refeeding syndrome as the lethal danger, marked by hypophosphataemia and prevented by correcting the electrolytes, giving thiamine and crawling the calories up; hold the two management anchors, that no drug is first-line for anorexia and that fluoxetine at sixty milligrams a day is the licensed drug for bulimia; and screen with SCOFF and the EAT-26. The sleep half reduces to the normal architecture and the two-process model as the foundation, then the disorders: cognitive behaviour therapy for insomnia first-line rather than a hypnotic, narcolepsy from orexin loss confirmed on the multiple sleep latency test, obstructive sleep apnoea graded by the apnoea-hypopnoea index and masquerading as resistant depression, REM sleep behaviour disorder as a prodrome of a synucleinopathy, and the circadian disorders reset with timed light and melatonin. Cover the recall lines and rebuild each anchor from its heading.

20.1 The master mnemonic, paid off: STARVED

Seeded at the opener, closed here. The chapter opened by seeding the master mnemonic **STARVED** at anorexia nervosa, and this is where it is paid off, because it is the single most

examined slice of the whole eating half: the physical complications of starvation, the ones that make anorexia the most lethal psychiatric disorder. **S**kin (lanugo, dry skin, carotenaemia); **T**hyroid (sick-euthyroid pattern) and low Temperature; **A**menorrhoea and the hypothalamic-pituitary-gonadal axis; **R**ate and rhythm (bradycardia, hypotension, prolonged QTc); **V**alues, the electrolytes (hypokalaemia, hyponatraemia); **E**rythron and marrow (pancytopenia); **D**igestive and Density (delayed gastric emptying, low bone mineral density). Riding alongside STARVED are the four working mnemonics the chapter leans on and you should be able to expand blind: **CORRECT, COVER, CRAWL** for refeeding prevention, the four-question **Weight? Binge? Compensation? Body-image?** for the eating differentiation, **CHESS** for the narcolepsy pentad, and **RBD warns of PDM** for the parasomnia-neurodegeneration link.

MNEMONIC

STARVED

The chapter master mnemonic, seeded at the anorexia opener and paid off here. **S**kin (lanugo, carotenaemia); **T**hyroid sick-euthyroid and low Temperature; **A**menorrhoea (hypothalamic-pituitary-gonadal axis); **R**ate and rhythm (bradycardia, hypotension, prolonged QTc, arrhythmia); **V**alues (hypokalaemia, hyponatraemia, dehydration); **E**rythron and marrow (pancytopenia); **D**igestive and Density (delayed gastric emptying, constipation, low bone mineral density). If you can expand STARVED and the four ride-along mnemonics without looking, you hold the spine of both halves of the chapter.

RULE **Learn each half by its one anchor.** The eating half hangs off two management anchors (no drug is first-line for anorexia; fluoxetine is the licensed drug for bulimia) and one danger (refeeding); the sleep half hangs off one therapy anchor (CBT-I first for chronic insomnia) and three test objects (the two-process model, the narcolepsy tetrad with the MSLT, and the AHI bands); everything else hangs off those.

20.2 Active-recall prompt list: the eating-disorder discriminators

Cover the answers and pull each one. This is a **retrieval practice** grid, not a summary. The four-question tool settles almost every eating differentiation in order (weight, then binge, then compensation, then body-image); for each row, state the discriminator before you check it against the topic that verified it. The instrument forms (the SCOFF, EAT-26, EDE-Q) are typeset centrally, so work from the accompanying scale plate rather than any pasted questionnaire.

DISORDER	THE DISCRIMINATOR TO STATE (PROMPT, THEN CHECK)
Anorexia nervosa	**Low weight from restriction plus overvaluation of shape/weight and a dread of fatness; the fear need not be spoken (the atypical, non-fat-phobic presentation still counts); severity by BMI band**
Bulimia nervosa	Recurrent binges with recurrent *compensation* (vomiting, laxatives, fasting, exercise) at a *normal or above-normal* weight; DSM-5-TR floor once weekly over three months

DISORDER	THE DISCRIMINATOR TO STATE (PROMPT, THEN CHECK)
Binge eating disorder	**Loss-of-control binges *without* regular compensation; three or more of the five features (rapid, alone, guilt, until uncomfortably full, not hungry); weight loss is not a therapy target**
ARFID	**Avoidant or restrictive intake driven by low interest, sensory aversion or fear of aversive consequence, *with no* body-image disturbance; that missing overvaluation is what separates it from anorexia**
Atypical anorexia / OSFED	Full anorexia cognition and behaviour but weight in or above the normal range (atypical anorexia), or subthreshold pictures (purging disorder, night-eating syndrome); a real disorder, not a mild one

The eating-disorder discriminator grid: the block is carved by weight, then binge, then compensation, then body-image, with ARFID marked by the absent overvaluation (verified against the anorexia, bulimia, binge-eating, ARFID and atypical/OSFED topics).

GOOD TO REMEMBER

- **Anorexia nervosa:** the defining criterion is low weight maintained by restriction *plus* overvaluation of shape and weight; the discriminator you must hold is that the dread of fatness can be unspoken and the weight can even be normal in atypical anorexia, so a non-fat-phobic presentation is still anorexia.
- **Bulimia versus binge eating disorder:** the one question that separates them is *compensation*, present in bulimia and absent in binge eating disorder; and the one question that separates both from ARFID is *body-image overvaluation*, present in the eating disorders proper and absent in ARFID.

20.3 Active-recall prompt list: refeeding thresholds and the two drug anchors

These are the values examiners want verbatim. The eating half turns on one danger and two prescribing rules, and each carries a number to pull cold. Retrieve the refeeding hallmark and rate, then the anorexia rule, then the bulimia dose, before checking against the refeeding, anorexia-management and bulimia topics.

- **The refeeding hallmark.** Prompt: the signature electrolyte, and its two companions? (Hypophosphataemia is the hallmark of refeeding syndrome, with falls in potassium and magnesium as insulin drives them intracellularly; a near-normal admission panel does *not* exclude risk.)
- **The refeeding prevention and rate.** Prompt: the three moves and the starting numbers? (CORRECT the electrolytes, COVER with thiamine before or with the first feed, CRAWL the calories up, and know that the two numeric sources disagree: NICE CG32 1.4.8 caps the high-risk start at **10 kcal per kg per day** and uses only **5 kcal per kg per day** when the BMI is under 14, reaching full needs within **4 to 7 days**, whereas RCPsych MEED CR233 2022 starts at **20 kcal per kg per day** and warns against underfeeding; NICE NG69 2017 gives no

figure and refers to MEED, so quote the source the question names. Monitor electrolytes daily through the first week.)

- **The anorexia drug rule.** Prompt: what is first-line, and what medication is *not*? (No drug is first-line: nutritional restoration plus a psychological therapy is primary, CBT-ED, MANTRA or SSCM for adults and family therapy FT-AN for young people; medication is never the sole treatment and olanzapine is not for routine use; NICE NG69 2017.)
- **The bulimia drug anchor.** Prompt: the one licensed drug and its dose? (Fluoxetine (Prodep, Fludac, Flunil) at **60 mg per day**, the anti-binge dose above the 20 to 40 mg antidepressant range, given *alongside* a psychological therapy such as guided self-help then CBT-ED, never instead of it; WFSBP 2023.)

10	20	60	2
NICE CG32 MAXIMUM REFEEDING START AT HIGH RISK (KCAL PER KG PER DAY)	RCPSYCH MEED CR233 2022 REFEEDING START (KCAL PER KG PER DAY)	FLUOXETINE, THE LICENSED DRUG FOR BULIMIA (MG PER DAY)	SCOFF POSITIVE SCREEN (YES ANSWERS)

TRAP **Refeeding a starved patient too fast, or reading a normal phosphate as safety.** The exam-fatal error is to correct the calorie deficit briskly or to be reassured by a near-normal admission electrolyte panel; the phosphate falls only once feeding starts, so the danger is missed until the patient arrests. Start low, replace phosphate *while* feeding continues, and monitor daily through the opening days.

GOOD TO REMEMBER

- **Refeeding syndrome:** the one value is that hypophosphataemia is the hallmark; the one principle is correct-electrolytes, give-thiamine, start-slow (NICE CG32 caps the high-risk start at 10 kcal per kg per day and uses only 5 when the BMI is under 14, full needs within 4 to 7 days, while RCPsych MEED CR233 2022 starts at 20 and warns against underfeeding, so quote the source the question names), and the single strongest lever against the syndrome is the feeding rate, the one variable fully under your control.
- **The two eating drug anchors:** no drug is first-line for anorexia (nutrition plus psychological therapy is primary), and fluoxetine 60 mg per day is the one licensed drug for bulimia, always adjunctive to therapy, never the sole treatment for either disorder.

INDIA

Eating disorders are widely **under-recognised in India**, partly because the classic Western fat-phobic script is often absent: the presentation is frequently the **atypical, non-fat-phobic anorexia** in which restriction is rationalised as loss of appetite, gastric discomfort or religious fasting rather than a stated fear of fatness, so the low weight is investigated medically for months before the eating disorder is named. Holding the rule that the dread of fatness can be unspoken, and that atypical anorexia at a normal weight is still a disorder, is what turns a missed case into a diagnosed one.

20.4 Active-recall prompt list: sleep architecture and the two-process model

The physiology is pure structure, so drill the structure. The sleep half opens on normal architecture, and the two most-asked objects are the proportions of a night and the model that

governs when it happens. Retrieve each before checking against the normal sleep physiology topic.

- **The stages.** Prompt: the NREM ladder and its markers? (NREM runs N1, light transition with alpha dropout; N2, defined by sleep spindles and K-complexes; N3, slow-wave delta sleep, the deepest and most restorative; then REM with its atonia and dreaming.)
- **The proportions.** Prompt: the REM share and the cycle length? (REM is about **20 to 25%** of total sleep time in a young adult; the NREM-REM cycle and the first REM latency are around **90 minutes**; N3 dominates the first half of the night and REM lengthens across the second half.)
- **The two-process model.** Prompt: the two processes and what opens the sleep gate? (Borbely's **two-process model**: Process S is the homeostatic sleep pressure that builds with time awake; Process C is the circadian alerting signal; sleep is triggered in the evening when Process C falls away and the accumulated Process S is suddenly unopposed.)

20 to 25	90	≤8	>30
REM SHARE OF THE NIGHT (% OF TOTAL SLEEP TIME)	FIRST REM LATENCY AND NREM-REM CYCLE (MINUTES)	MSLT POSITIVE MEAN SLEEP LATENCY (MINUTES)	SEVERE OBSTRUCTIVE SLEEP APNOEA (AHI, EVENTS PER HOUR)

GOOD TO REMEMBER

- **Sleep architecture:** the number to hold is REM at 20 to 25% of total sleep time on a roughly 90-minute cycle; the principle is that N3 slow-wave sleep loads the first half of the night and REM loads the second, and the two-process model explains the timing (homeostatic Process S against circadian Process C), the frame the deep sleep-neurotransmitter systems build on in the Functional Neuroanatomy and Neurophysiology notes.

20.5 Active-recall prompt list: the insomnia and CBT-I rule

State the first-line before any drug. Chronic insomnia has the cleanest management rule in the sleep half, and it should be the first sentence of any answer: the therapy comes before the tablet. Retrieve the rule and the scale bands before checking against the insomnia and CBT-I topics.

- **The first-line.** Prompt: what is offered before any drug, and its two engines? (CBT-I, the multicomponent package, is first-line for chronic insomnia and is offered before any hypnotic; its two behavioural engines are *sleep restriction* and *stimulus control*, steadied by sleep hygiene, cognitive therapy and relaxation; BAP 2019, NICE 2023.)
- **The drug place.** Prompt: where does a hypnotic sit, and which is a maintenance-insomnia option? (Not first-line; a short-term, second-line measure for when CBT-I fails, is unavailable or cannot be engaged with, matching the agent's half-life to the pattern; low-dose doxepin at **1 to 6 mg per day** suits late-night awakenings, and daridorexant is the licensed long-term option after CBT-I.)
- **The scale.** Prompt: the insomnia scale and its cut-off? (The Insomnia Severity Index; a score of **10 or higher** screens positive, with the moderate clinical band at 15 to 21; chronic insomnia needs symptoms three or more nights a week for three months.)

RULE **CBT-I is first-line for chronic insomnia; a hypnotic is not.** The therapy is offered before any drug and is the only intervention that durably resets the sleep, matching the twist across the whole management block: the non-pharmacological move leads, and the drug, when used, is time-limited and second.

GOOD TO REMEMBER

- **CBT-I (the first-line management step):** the one value is that CBT-I, not a hypnotic, is first-line for chronic insomnia and is offered before any drug; its two engines are sleep restriction and stimulus control, and the signature caution is that a hypnotic is a short-term second-line measure to be tapered slowly with concurrent CBT-I, never the long-term answer.

INDIA

Two Indian reflexes work against this rule. First, structured CBT-I is scarce, so practice defaults to a **benzodiazepine or z-drug plus a sleep-hygiene leaflet**, precisely the two moves the evidence flags as insufficient on their own (sleep hygiene is not a stand-alone treatment). Second, the resulting **long-term hypnotic over-use for insomnia** is entrenched and dependence-forming; the corrective, and the exam answer, is CBT-I first with the hypnotic reserved, time-limited and tapered, the wider taper being developed in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes.

20.6 Active-recall prompt list: the narcolepsy tetrad, the AHI bands and RBD

Three sleep-disorder objects, three sets of numbers. The remaining high-yield sleep retrievals are the narcolepsy picture and its investigation, the sleep-apnoea severity bands, and the one parasomnia that carries a neurodegenerative warning. Retrieve each before checking against the narcolepsy, obstructive sleep apnoea and parasomnias topics.

OBJECT	THE DISCRIMINATOR AND NUMBER TO STATE (PROMPT, THEN CHECK)
Narcolepsy tetrad	**Excessive daytime sleepiness with sleep attacks, cataplexy, sleep paralysis, hypnagogic hallucinations (CHESS pentad adds disturbed nocturnal sleep); sleepiness is the constant, cataplexy the specific one**
Narcolepsy mechanism and confirmation	Loss of hypothalamic orexin (hypocretin) neurons; CSF orexin under 110 pg per mL defines type 1; the MSLT confirms at a mean sleep latency of 8 minutes or less with two or more sleep-onset REM periods
Narcolepsy treatment	**Modafinil (Modalert, Provake) 200 to 400 mg per day first-line for the sleepiness (does not touch cataplexy); sodium oxybate for cataplexy but not marketed in India, so an SSRI/SNRI or clomipramine is used there**

OBJECT	THE DISCRIMINATOR AND NUMBER TO STATE (PROMPT, THEN CHECK)
Obstructive sleep apnoea (AHI)	Mild 5 to 15, moderate 15 to 30, severe over 30 events per hour (DSM-5-TR writes the mild band as under 15 with the diagnostic floor at five); STOP-BANG three or more screens positive, five or more is high risk; CPAP is first-line, not sole, therapy
REM sleep behaviour disorder	**Dream enactment with lost REM atonia; a *prodrome of a synucleinopathy* (Parkinson's disease, dementia with Lewy bodies, multiple system atrophy), not a nightmare disorder**

The three high-yield sleep-disorder objects and their verified numbers: the narcolepsy tetrad with the MSLT and orexin cut-off, the AHI severity bands, and RBD as a synucleinopathy prodrome (verified against the narcolepsy, obstructive sleep apnoea and parasomnias topics).

TRAP **Missing narcolepsy behind "treatment-resistant depression", or reading RBD as a nightmare.** Sleepiness and amotivation get labelled depression and the cataplexy is never asked about; and dream-enactment violence in an older man gets called a nightmare disorder, missing that REM sleep behaviour disorder heralds a synucleinopathy, the neurodegenerative link developed in the Dementias and neurocognitive disorders notes and the Neurology foundations for psychiatrists notes.

GOOD TO REMEMBER

- **Narcolepsy:** the defining criterion is excessive daytime sleepiness plus cataplexy from orexin loss; the confirming values are an MSLT mean sleep latency of 8 minutes or less with two or more sleep-onset REM periods, and a CSF orexin under 110 pg per mL for type 1.
- **Narcolepsy management (the value anchor):** modafinil 200 to 400 mg per day is first-line for the sleepiness but does nothing for cataplexy, and because sodium oxybate is not marketed in India the cataplexy is treated there with an SSRI, SNRI or clomipramine.
- **Obstructive sleep apnoea:** the AHI bands are mild 5 to 15, moderate 15 to 30 and severe over 30 events per hour, and CPAP is first-line but adjunct, never sole, therapy.

20.7 The whole-chapter synthesis map, framed cover-the-branches

Build the tree, then redraw it blind. The strongest single revision act for this block is to **redraw from memory** a **synthesis map** that hangs every disorder off its trunk. The map has two trunks. The *eating disorders* are carved by the four questions (weight, binge, compensation, body-image) and governed by two management anchors and one danger (no drug first for anorexia, fluoxetine for bulimia, refeeding to fear). The *sleep-wake disorders* are carved by the presenting complaint (cannot sleep, too sleepy, moves in sleep, sleeps at the wrong time) and governed by one therapy rule (CBT-I first) and three test objects (the two-process model, the narcolepsy tetrad with the MSLT, and the AHI bands). From each trunk hang the disorders, and from each disorder hang its one discriminator, its scale or investigation, and its first-line move. The accompanying figure draws this map; use it as a retrieval test by covering all the branches and regenerating them, then uncovering to score yourself, exactly the cover-the-branches method that makes **retrieval practice** work.

How to use it. First pass: cover everything but the two trunks and name the disorders under each. Second pass: for each disorder, cover the discriminator and pull it. Third pass: cover the treatment column and recite the first-line move and the one number. A branch you cannot regenerate is a branch to re-read in its own topic; a branch you can is one you can leave. Repeated over spaced sittings, the map converts the chapter from something you recognise into something you can produce.

PEARL

The chapter collapses to two trunks, four anchors and one danger. Trunk one, the *eating disorders*, are carved by weight, binge, compensation and body-image, and answer to psychological therapy first, with no drug first-line for anorexia and fluoxetine 60 mg per day for bulimia; the danger threaded through it is refeeding syndrome, whose hallmark is hypophosphataemia and whose antidote is correct-electrolytes, give-thiamine, start-slow. Trunk two, the *sleep-wake disorders*, are carved by the complaint, and turn on CBT-I first for chronic insomnia, the narcolepsy tetrad confirmed by the MSLT, the AHI bands for apnoea, and RBD as the synucleinopathy prodrome. Cover the branches, redraw the tree, and you own the block.

HOLD THIS

Redraw the two-trunk synthesis map from memory: the eating disorders (carved by weight, binge, compensation and body-image, psychological therapy first, no drug first-line for anorexia, fluoxetine 60 mg per day for bulimia, and refeeding syndrome as the hypophosphataemic danger you crawl the calories to avoid) and the sleep-wake disorders (carved by the complaint, CBT-I first for chronic insomnia, the narcolepsy tetrad confirmed on the MSLT at 8 minutes or less with two or more sleep-onset REM periods, the AHI bands of mild 5 to 15 / moderate 15 to 30 / severe over 30, and RBD heralding a synucleinopathy).

Previously asked

This territory is examined at two levels at once: the syndrome (its clinical features, its differential diagnosis and its course) and the treatment (which first-line agent, how to refeed safely, which psychological therapy). The reliable pattern is that bulimia nervosa carries the most weight in the eating section and is asked at both essay and short-note length, that binge eating disorder recurs as a standalone note, and that insomnia is the dominant sleep essay while the circadian rhythm disorders recur as a note. Every long essay ends in a management plan, so the guideline-anchored first-line recommendation and the reason for it must be exam-ready: no drug is first-line for anorexia, fluoxetine is the licensed drug for bulimia, and cognitive behaviour therapy for insomnia is first-line for chronic insomnia. The genuine questions on record are grouped by band below. The deep hypnotic and antidepressant pharmacology these disorders are treated with is developed in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes and the Mood disorders: pharmacotherapy notes; the sleep neurochemistry and the ascending-arousal anatomy in the Neurochemistry, neuroendocrinology, neuroimaging and basic psychopharmacology notes and the Functional neuroanatomy and neurophysiology notes; while cognitive behaviour therapy for insomnia, the eating-disorder cognitive behaviour therapy and

family-based treatment, and the sleep architecture, the hypnogram and polysomnography are owned here.

? HOW THIS TERRITORY IS ACTUALLY TESTED

Q **Bulimia nervosa, the dominant eating essay.** "Etiopathogenesis, clinical features and management of bulimia nervosa" has come as a full 25-mark essay, and "Bulimia nervosa" recurs as a standalone 10-mark note. Prepare the binge-purge cycle and the compensatory behaviours, the medical complications (the hypokalaemia and metabolic alkalosis, Russell's sign, dental erosion), and the guideline-anchored management (cognitive behaviour therapy for eating disorders and guided self-help first-line, fluoxetine as the licensed drug at the high dose). MUHS 2014, 2016

Q **Binge eating disorder as a standalone note.** "Binge eating disorder" has come as a 10-mark note. Prepare the recurrent binge eating with loss of control but without the regular compensatory behaviour that defines bulimia, the association with obesity, and the cognitive-behaviour-therapy-first management. MUHS 2014

Q **Anorexia nervosa and safe refeeding.** Anorexia and its refeeding are high-yield across the exams even where the exact wording varies: prepare the diagnostic criteria (the significantly-low-weight criterion and the dropping of amenorrhoea in DSM-5), the medical complications by body system, the refeeding syndrome (hypophosphataemia as the hallmark, correct the electrolytes, give thiamine and start slow), and the management (no drug first-line, the psychological therapies and family-based treatment). Refeeding and its electrolyte monitoring are exactly the kind of dose-and-value detail an examiner probes. high-yield across sittings

Q **Insomnia, the dominant sleep essay.** "Classify insomnia and discuss its evaluation, management and prognosis" has come as a 10-mark question. Prepare the classification and the sleep-history assessment, and above all the management: cognitive behaviour therapy for insomnia is first-line for chronic insomnia, a hypnotic is not first-line and is short-term, and the pharmacology and its taper are cross-referenced. MUHS 2013

Q **The circadian rhythm sleep-wake disorders as a note.** "Circadian sleep-wake rhythm" has recurred as a short answer within the sleep and organic material. Prepare the phase types (delayed and advanced sleep-wake phase, non-24-hour, shift-work and jet lag) and the management with timed light and melatonin according to the phase-response curve. MUHS 2012, 2015

Q **Normal sleep, narcolepsy and the parasomnias, prepared for the spot and the note.** Normal sleep architecture and the hypnogram, the narcolepsy tetrad and the multiple sleep latency test, obstructive sleep apnoea and its psychiatric masquerade, and REM sleep behaviour disorder as a prodrome of a synucleinopathy are all examinable as spotters and short notes. Prepare each to be recognised and named, with the values (the sleep-architecture percentages, the AHI severity bands) exam-ready. spot and short note

Prepare this material to be diagnosed and treated, not just recited: the eating-disorder differentiation grid, the refeeding electrolyte thresholds and rate, the scale cut-offs (SCOFF, the ISI bands, the ESS and STOP-BANG cut-offs) and the AHI severity bands, and the value-anchored good-to-remember boxes in these notes are built to the way the block is examined. The deep hypnotic pharmacology lives in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes; the deep antidepressant pharmacology in the Mood disorders: pharmacotherapy notes; the sleep neurochemistry and the ascending-arousal anatomy in the Neurochemistry notes and the Functional neuroanatomy notes; and REM sleep behaviour disorder as a neurodegenerative prodrome is followed up in the Dementias and neurocognitive disorders notes and the Neurology foundations for psychiatrists notes.

Quick review

THE EATING DISORDERS: DISCRIMINATE, REFEED SAFELY, FIRST-LINE	
THE DISCRIMINATOR	Separate the six by **weight** (low in anorexia, normal or above in bulimia, often raised in binge eating disorder), the presence of a **binge**, the **compensatory behaviour**, and the **weight-shape overvaluation**. ARFID is the trap: food restriction with weight loss but **no body-image concern**, so it is not anorexia.
ANOREXIA NERVOSA	Significantly low weight, fear of weight gain, body-image disturbance (amenorrhoea dropped in DSM-5). Complications by system; the cardiac (bradycardia, long QT, arrhythmia) and electrolyte (hypokalaemia) ones kill. **No drug is first-line**: medical stabilisation, nutritional rehabilitation, and the psychological therapies (CBT-ED, MANTRA, SSCM in adults; family-based treatment in the young).
REFEEDING SYNDROME	The lethal danger of recovery. Starvation depletes intracellular phosphate, potassium and magnesium; carbohydrate refeeding drives an insulin surge that crashes the serum, with **hypophosphataemia the hallmark**. Prevent it: correct electrolytes (magnesium before potassium), give **thiamine before feeding**, and start slow, remembering that the two numeric sources differ: NICE CG32 caps the high-risk start at **10 kcal per kg per day** (only **5 if BMI is under 14**) with full needs within **4 to 7 days**, while RCPsych MEED CR233 2022 starts at **20 kcal per kg per day** and warns against underfeeding. NG69 gives no figure.
BULIMIA AND BINGE EATING DISORDER	Bulimia: normal weight, binge-purge cycle, hypokalaemia, Russell's sign, dental erosion; **CBT-ED first-line** plus **fluoxetine 60 mg per day**, the licensed drug. Binge eating disorder: recurrent binge **without** regular compensation, associated with obesity; CBT-ED and guided self-help first-line.
ARFID, OSFED, THE FEEDING DISORDERS	ARFID: restriction from sensory aversion, low interest or fear of aversive consequences, no weight-shape overvaluation. OSFED and atypical anorexia meet some but not all criteria; the non-fat-phobic presentation is common in India. Pica and rumination are the feeding disorders.
THE SCREENS	**SCOFF**: five items, **two or more** positive is a positive screen. **EAT-26**: total **20 or more** prompts assessment. Both are screens, not diagnoses.

NORMAL SLEEP AND THE DISORDERS OF TOO LITTLE OR TOO MUCH	
NORMAL ARCHITECTURE	NREM stages N1, N2 (spindles and K-complexes) and N3 (slow-wave), plus REM, cycling every **about 90 minutes** across four to five cycles. First REM at a latency of **about 90 minutes**; N3 dominates the first third of the night and REM lengthens toward morning. Regulated by process S (homeostatic drive) and process C (circadian rhythm), with a wake-promoting ascending arousal system and a sleep-promoting VLPO in a flip-flop switch stabilised by orexin.
INSOMNIA AND CBT-I	Difficulty initiating or maintaining sleep with daytime consequences despite adequate opportunity. **CBT-I is first-line for chronic insomnia**, not a hypnotic: stimulus control, sleep restriction (the engine), sleep hygiene, cognitive therapy and relaxation. Hypnotics (z-drugs, melatonin in the older adult) are short-term; the **ISI** bands run 0 to 7, 8 to 14, 15 to 21 and 22 to 28.
NARCOLEPSY	Loss of the orexin neurons destabilises the sleep-wake switch, so REM intrudes into wake: the **tetrad** of excessive daytime sleepiness, cataplexy (defines type 1), sleep paralysis and hypnagogic hallucinations. Type 1 has cataplexy, low CSF orexin and HLA-DQB1*06:02. Diagnosed on the **MSLT: mean sleep latency 8 minutes or less with 2 or more sleep-onset REM periods**. Treat with modafinil, solriamfetol or pitolisant, and sodium oxybate for cataplexy.
SLEEP APNOEA, THE PARASOMNIAS, AND THE CIRCADIAN DISORDERS	
OBSTRUCTIVE SLEEP APNOEA	Repetitive upper-airway collapse with apnoea or hypopnoea, desaturation and arousal. Graded by the apnoea-hypopnoea index: **mild 5 to 15, moderate 15 to 30, severe over 30** events per hour. It masquerades as treatment-resistant depression and cognitive impairment, so exclude it; **CPAP** is the mainstay. The **STOP-BANG** screen stratifies risk 0 to 2, 3 to 4 and 5 to 8.
PARASOMNIAS	NREM parasomnias (confusional arousals, sleepwalking, sleep terrors) arise from deep slow-wave sleep in the **first third of the night**, with amnesia and a childhood peak. REM parasomnias include **REM sleep behaviour disorder**, the loss of REM atonia with dream enactment, which is a **prodrome of a synucleinopathy** (Parkinson's disease, dementia with Lewy bodies, multiple system atrophy). Do not mistake it for a nightmare disorder.
CIRCADIAN AND MOVEMENT DISORDERS	Circadian disorders are a clock-schedule mismatch (delayed phase in teens, advanced phase in the elderly, non-24 in the blind, shift-work, jet lag); reset with **timed light and melatonin** along the phase-response curve (morning light and evening melatonin advance; evening light delays). Restless legs syndrome: the urge to move worse at rest and in the evening, relieved by movement; check **ferritin**, use dopaminergic or alpha-2-delta agents, and watch for dopaminergic augmentation.

THE NUMBERS TO HOLD	
REFEEDING START RATE	The two sources disagree. NICE CG32 1.4.8: maximum **10** kcal per kg per day at high risk, only **5** if BMI is under 14, full needs within **4 to 7 days**. RCPsych MEED CR233 2022: start at **20**, never below the pre-admission intake, avoid underfeeding. NG69 gives no figure. Quote whichever the question names.
BULIMIA DRUG	**Fluoxetine 60 mg per day**, the licensed drug (higher than the antidepressant dose)
EATING SCREENS	SCOFF **two or more** positive; EAT-26 total **20 or more**
ISI SEVERITY	0 to 7 none, 8 to 14 subthreshold, 15 to 21 moderate, 22 to 28 severe
ESS AND PSQI	Epworth **over 10** is excessive daytime sleepiness; PSQI global **over 5** is poor sleep quality
NARCOLEPSY MSLT	Mean sleep latency **8 minutes or less** with **2 or more** sleep-onset REM periods
SLEEP APNOEA AHI	Mild **5 to 15**, moderate **15 to 30**, severe **over 30** events per hour; STOP-BANG high risk **5 to 8**
SLEEP ARCHITECTURE	Cycle and REM latency **about 90 minutes**; N3 early, REM late; four to five cycles a night

Prepare this material to be diagnosed and treated, not just recited: the eating-disorder differentiation, the refeeding electrolyte thresholds and rate, the scale cut-offs and the AHI severity bands are the value-anchored points an examiner probes, and the first-line rules (no drug for anorexia, fluoxetine for bulimia, CBT-I for chronic insomnia) are the ones a wrong answer is marked down for. The deep hypnotic and antidepressant pharmacology lives in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes and the Mood disorders: pharmacotherapy notes; the sleep neurochemistry in the Neurochemistry, neuroendocrinology, neuroimaging and basic psychopharmacology notes; and REM sleep behaviour disorder as a neurodegenerative prodrome in the Dementias and neurocognitive disorders notes.

References

The eating-disorder and sleep-wake content is grounded in the standard psychiatry and sleep-medicine sources (the source hierarchy below), with Kaplan and Sadock and the New Oxford Textbook as the depth bar for the phenomenology, the neurobiology and the sleep architecture, Kaufman's Clinical Neurology for Psychiatrists for the polysomnography and the sleep-stage detail. The management is guideline-first: the eating half is led by the NICE eating-disorders guideline (NG69) with the MARSIPAN guidance for the medical management and refeeding of the severely ill patient, and the sleep half by the British Association for Psychopharmacology consensus on insomnia, parasomnias and circadian-rhythm disorders, with NICE, the Indian Psychiatric Society, the American Academy of Sleep Medicine and the United States VA/DoD. Every refeeding value, drug dose, scale cut-off, AHI band and first-line recommendation was checked against these sources and the adversarial content pass; anything that could not be confirmed, including the exact serum electrolyte thresholds and the lower edge of the mild-apnoea band, was flagged rather than guessed. Each journal PMID below was verified against PubMed this build and matched on title, first author and year; identifiers that resolved to the

wrong paper were corrected or dropped. Books and guideline documents are cited by author, title and year without a PMID.

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PART XI

XI

Somatic-Symptom, Sexual and Impulse-Control Disorders and Suicide

Body, desire, impulse and self-harm: the somatic-symptom, sexual and impulse-control disorders, and suicide.

01 Somatic symptom and related disorders

02 Sexual dysfunctions, paraphilias and gender

03 Psychosomatic medicine and consultation-liaison

04 Impulse-control disorders

05 Suicide and self-harm

06 Apply and consolidate

PAPER II

Somatic-symptom, sexual, impulse-control disorders and suicide

Five sections . one complete notes document

This material gathers the somatic-symptom, sexual, impulse-control and suicide-related disorders into one document, by syndrome and by management. The first band is **the somatic symptom and related disorders**: somatic symptom disorder and the somatoform-to-SSD nosology shift with its positive psychological criterion, illness anxiety disorder, conversion or functional neurological symptom disorder placed on the spectrum, factitious disorder and malingering, and the management of medically unexplained symptoms. The second band is **the sexual dysfunctions, paraphilias and gender**: the normal sexual response cycle, the male and female sexual dysfunctions and their management, the paraphilic disorders, gender incongruence and the affirmative-care pathway, Dhat and the culture-bound presentations, and medication-induced sexual dysfunction. The third band is **psychosomatic medicine and consultation-liaison**, taught here as the psychosomatic concept with the service model and disease-specific aspects cross-referenced. The fourth band is **the impulse-control disorders**. The fifth band is **suicide and self-harm**, the high-stakes clinical core, written throughout with strict safe-messaging: the structured risk assessment and the balance of risk and protective factors, the management of the suicidal patient and collaborative safety planning, deliberate self-harm, prevention through means restriction and gatekeeper training, and the anti-suicidal pharmacology. The examinable skill is the safe, guideline-anchored assessment and management of each: the positive criterion behind a somatic presentation, factitious versus malingering, the first-line for erectile dysfunction, the affirming frame for gender incongruence, and the structured, compassionate assessment and safety planning of a person at risk.

HOW TO USE THESE NOTES

Read the five bands as one continuous account of how these disorders are assessed and managed. The **somatic symptom and related** band builds the nosology: the shift from the somatoform disorders to somatic symptom disorder with its positive psychological criterion, illness anxiety disorder, and the discrimination of the somatic disorders from factitious disorder and malingering by voluntariness and external incentive. The **sexual, paraphilias and gender** band teaches the sexual response cycle, the male and female dysfunctions and their guideline-anchored management, the paraphilic disorders, gender incongruence taught in the affirming ICD-11 frame with the Indian legal position, and Dhat as a culture-bound presentation. The **psychosomatic and consultation-liaison** band teaches the psychosomatic concept compactly. The **impulse-control** band teaches the disorders of urge and control. The **suicide and self-harm** band is the core: the structured risk assessment and the balance of risk and protective factors, the limits of individual-risk prediction, the compassionate non-judgemental assessment of self-harm, collaborative safety planning, and prevention through means restriction, all written with strict safe-messaging, stating the burden without method specifics and framing means restriction, help-seeking and safety planning positively. Every management recommendation is guideline-anchored, led by NICE for the self-harm and suicide pathway with the WHO LIVE LIFE frame, ISSM and BSSM for the sexual dysfunctions and WPATH SOC-8 for gender, on the where-to-treat, target-by-phase, modes-of-treatment spine; every named syndrome ends with a **Good to remember** box giving the criterion, the discriminator and the first step, and every named management step ends with one giving the principle and the first move. Figures declare one axis and code it in colour: **petrol** marks structure and the neutral case, **coral** marks the trap or the danger, and **marigold** highlights the number to hold; every suicide figure is conceptual and non-sensational, with no method depiction. The rating scales are reproduced as the actual instruments where the licence permits, the Columbia scale the key plate, credited to their sources, or typeset from their structure where it does not. Several boundaries are stated up front: conversion or functional neurological symptom disorder is taught in full in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes and cross-referenced here; the consultation-liaison service model and the disease-specific psychiatric aspects in the Consultation-liaison, geriatric and transcultural psychiatry notes; body dysmorphic disorder in the Anxiety, OCD and trauma-related disorders notes; and the deep antidepressant, antipsychotic and the lithium and clozapine pharmacology in the Mood disorders: pharmacotherapy notes and the Schizophrenia: management, antipsychotics and adverse effects notes. The somatic nosology, the factitious and malingering discrimination, the sexual and gender syndromes, Dhat, the impulse-control disorders and the whole suicide and self-harm band are owned and fully taught here. This is doctor-facing revision, so the full technical vocabulary is used, brand names lead with the Indian brand, and every dose, scale cut-off, criterion and legal provision is verified against a source or omitted and flagged.

Somatic symptom and related disorders

1 · Somatic symptom disorder and the somatoform nosology shift

This is the opening topic of a chapter that runs from the body that *complains* to the body that *desires*, then to the urge that *acts* and finally to the life that must be *protected*; the whole arc is

stitched together by one master mnemonic seeded here and paid off at consolidation. It opens with **somatic symptom disorder** because that entity is the product of the single largest reclassification in this part of the syllabus: the DSM-IV and ICD-10 **somatoform disorders**, a scattered family diagnosed by what could *not* be found on investigation, have collapsed forward into one positively defined diagnosis. Examiners test this **nosology shift** two ways, and you must be fluent in both: a straight "what replaced what" crosswalk, and a discrimination task where a vignette must be placed in the right modern category and defended against its neighbour.

How to use this page. Fix the three DSM-5-TR criteria first, then unpack Criterion B (the **positive psychological criterion**) because that clause carries most of the marks, then internalise the one conceptual break, that being **medically unexplained** is no longer a requirement, so a symptom may be fully medically explained and still qualify. After that, learn the ICD-10 family that was folded in, the DSM-5 specifiers, and the parallel ICD-11 move to **bodily distress disorder**; finish with the assessment scales and the guideline-anchored first moves in management. The cardinal error the chapter is built to prevent is calling this diagnosis "medically unexplained".

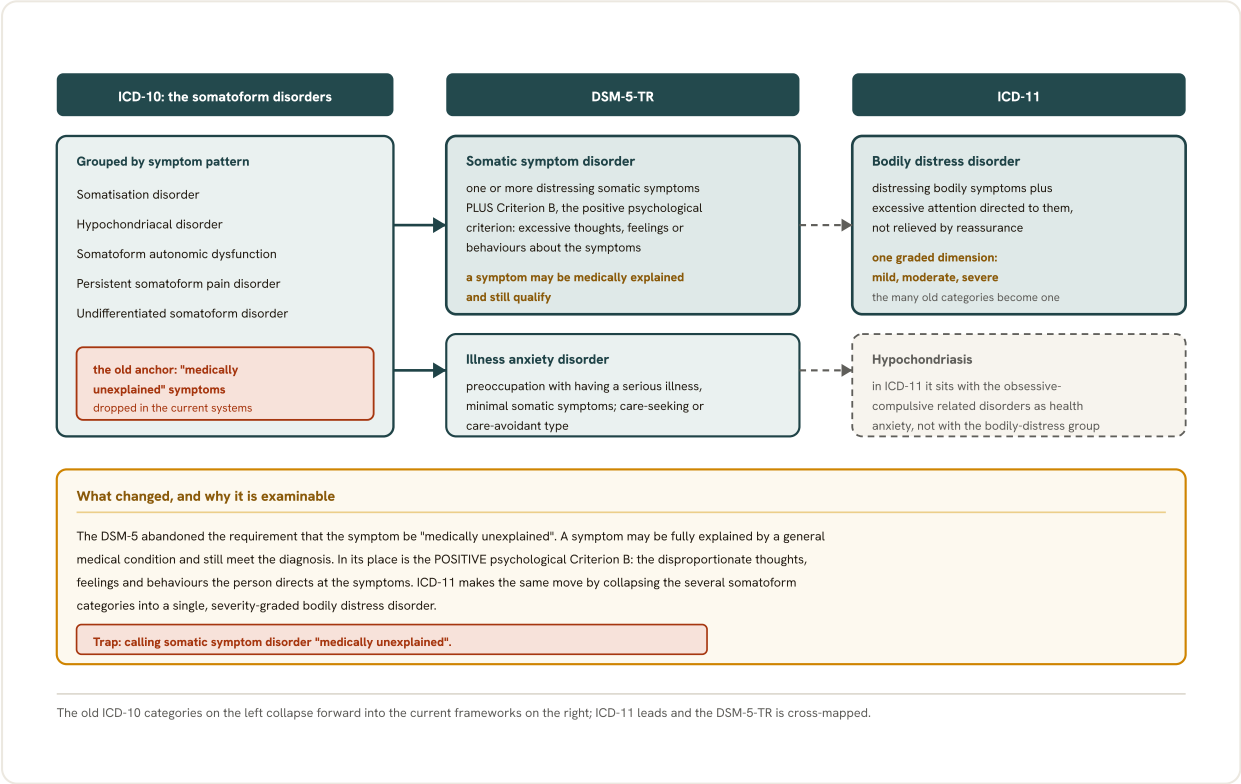


Fig 18.1 The somatic-symptom nosology shift. The ICD-10 somatoform disorders, grouped by the pattern of symptoms, collapse forward into a much simpler current picture. The DSM-5-TR replaces the whole group with somatic symptom disorder, which turns on a POSITIVE psychological criterion (excessive thoughts, feelings and behaviours about the symptoms) rather than on the symptom being medically unexplained, so a medically explained symptom may still qualify; hypochondriasis becomes illness anxiety disorder. ICD-11 goes further and folds the categories into a single, severity-graded bodily distress disorder, while placing hypochondriasis with the obsessive-compulsive related disorders as health anxiety. The examinable move, and the classic trap, is the retirement of "medically unexplained" in favour of the positive criterion.

Patient Health Questionnaire-15: Physical Symptoms

During the last 4 weeks, how much have you have been bothered by any of the following problems? Please place a check mark in the box to indicate your answer.

		Not bothered	Bothered a little	Bothered a lot
		0	1	2
1.	Stomach pain	☐	☐	☐
2.	Back pain	☐	☐	☐
3.	Pain in your arms, legs, or joints (knees, hips, etc)	☐	☐	☐
4.	Menstrual cramps or other problems with your periods [women only]	☐	☐	☐
5.	Headaches	☐	☐	☐
6.	Chest pain	☐	☐	☐
7.	Dizziness	☐	☐	☐
8.	Fainting spells	☐	☐	☐
9.	Feeling your heart pound or race	☐	☐	☐
10.	Shortness of breath	☐	☐	☐
11.	Pain or problems during sexual intercourse	☐	☐	☐
12.	Constipation, loose bowels, or diarrhea	☐	☐	☐
13.	Nausea, gas, or indigestion	☐	☐	☐
14.	Feeling tired or having low energy	☐	☐	☐
15.	Trouble sleeping	☐	☐	☐
TOTAL SCORE =				

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Source instrument available at http://www.phqscreeners.com/
Consortium version 12May2013. Available at http://www.rdc-tmdinternational.org/

The PHQ-15: 15 common somatic symptoms, each scored 0 to 2 over the last four weeks (total out of a possible 30); the bands are 0 to 4 minimal, 5 to 9 low, 10 to 14 medium and 15 to 30 high somatic-symptom burden.

PHQ-15 (Kroenke, Spitzer and Williams, 2002); PHQ family, no permission required to reproduce; free non-commercial educational use.

SSD-12 (SOMATIC SYMPTOM DISORDER - B CRITERIA SCALE)	STRUCTURE AND THE VERIFIED CUT-OFF
What it measures	the DSM-5 Criterion B psychological burden (the thoughts, feelings and behaviours directed at the symptoms), not the somatic symptoms themselves
Structure	12 items across three subscales (cognitive, affective, behavioural), each item scored 0 to 4
Total and cut-off	**out of a possible 48; the validated cut-off is 23 and above (Toussaint 2016); a lower primary-care threshold of 13 and above has been proposed (Cao 2020)**

SSD-12 (Toussaint et al, 2016); copyright the authors and Mapi Research Trust, permission required, so typeset here in summary with the verified cut-off rather than reproduced.

Fig 18.2 The somatic-symptom assessment scales. The PHQ-15 grades the burden of the somatic symptoms themselves: fifteen common complaints, each scored 0 to 2 over four weeks for a total out of a possible 30, banded 0 to 4 minimal, 5 to 9 low, 10 to 14 medium and 15 to 30 high. The SSD-12 measures the other half of the modern diagnosis, the positive Criterion B, rating the excessive thoughts, feelings and behaviours the person directs at the symptoms across twelve items for a total out of a possible 48, with a validated cut-off of 23 and above. The PHQ-15 is shown as its actual freely reproducible form; the SSD-12 is permission-required and is summarised from its verified structure.

1.1 Somatic symptom disorder: the three DSM-5-TR criteria

One entity, defined by symptoms plus a psychological response. Somatic symptom disorder (DSM-5-TR) is built on three criteria (DSM-5-TR 2022). **Criterion A** requires one or more somatic symptoms that are distressing or result in significant disruption of daily life; the symptom may be specific, such as localised pain, or non-specific, such as fatigue, and it may or may not accompany a diagnosable medical condition. **Criterion B** is the heart of the diagnosis: excessive thoughts, feelings or behaviours related to the somatic symptoms or the associated health concerns. **Criterion C** requires that, although any single symptom need not be continuously present, the *state of being symptomatic* is persistent, typically for more than six months. The suffering is authentic whether or not it is medically explained; the diagnosis rests on the person's disproportionate response to bodily symptoms, not on the symptoms being unfounded.

GOOD TO REMEMBER

- **Somatic symptom disorder (the diagnosis):** Criterion A, one or more distressing or disruptive somatic symptoms; Criterion B, excessive thoughts, feelings or behaviours about the symptoms (the positive psychological criterion); Criterion C, persistent symptomatic state, typically more than six months. The single discriminator from every predecessor diagnosis is that Criterion B, not the absence of a medical explanation, defines it.

1.2 Criterion B: the positive psychological criterion

Three ways the excessive response can show, any one of which suffices. The **positive psychological criterion** is met by at least one of three manifestations (DSM-5-TR 2022): first, *disproportionate and persistent thoughts* about the seriousness of one's symptoms; second, a *persistently high level of anxiety* about health or symptoms; third, *excessive time and energy* devoted to the symptoms or health concerns, such as repeated bodily checking, help-seeking and reassurance-seeking. Only one of the three is required for the diagnosis, though the count of them then drives the severity specifier. This is the criterion that shifts the diagnostic gaze from the investigation report to the patient's cognitive, affective and behavioural relationship with the body, which is exactly why it can be measured directly by a Criterion-B scale rather than by cataloguing negative test results.

PEARL

Hold Criterion B as **T-A-B**: excessive **T**houghts (disproportionate and persistent), high **A**nxiety about health, and excessive **B**ehaviour and time devoted to symptoms. Any one of the three, running alongside a distressing somatic symptom, is enough; the number present grades the severity.

RULE **Diagnose on the positive criterion, not on a normal work-up.** Somatic symptom disorder is established by the excessive thoughts, feelings and behaviours of Criterion B, present alongside a distressing somatic symptom; whether the symptom is medically explained is irrelevant to whether the criteria are met.

1.3 The cardinal break: "medically unexplained" is gone

A medically explained symptom can still qualify. The defining conceptual move of the shift is the deletion of the old **medically unexplained** symptoms requirement (DSM-5-TR 2022; Kaplan and Sadock CTP 2024). Under DSM-IV and ICD-10, a somatoform diagnosis demanded that the symptoms lack an adequate physical explanation, which forced clinicians into an unreliable and often adversarial hunt to *exclude* disease before they could name distress. DSM-5 abolished that. The diagnosis now turns on the presence of the positive psychological features, so a patient whose symptom is entirely accounted for by a genuine medical condition, an uncomplicated myocardial infarction, say, still meets criteria if their thoughts, anxiety and behaviour about that symptom are clearly excessive and disabling. Somatic symptoms without a medical explanation are, on their own, *not* sufficient for the diagnosis; the psychological response is what is required. This single change also dissolves the old mind-body dualism the somatoform label carried, letting the diagnosis sit comfortably alongside, rather than in place of, medical disease.

WORKED EXAMPLE

A man is fully rehabilitated after an uncomplicated myocardial infarction with a normal ejection fraction, yet several months on he remains housebound, checks his pulse dozens of times a day, has abandoned work and exercise, and cannot be reassured by repeated normal reviews. His chest symptoms are medically explained, but his response is grossly disproportionate; he meets Criterion A (distressing symptom), Criterion B (all three manifestations) and Criterion C (persistent), so he has somatic symptom disorder *with* established cardiac disease. Under the old rules he would have been un-diagnosable because nothing was "unexplained".

TRAP **Calling somatic symptom disorder "medically unexplained".** That is the abolished DSM-IV and ICD-10 criterion. The modern diagnosis is defined by the positive psychological criterion; a medically explained symptom with an excessive response qualifies, and an unexplained symptom without that response does not.

1.4 The forward collapse: what DSM-5 moved where

Many old boxes, one new home, with a few relocations. DSM-5 replaced the DSM-IV "somatoform disorders" chapter with "somatic symptom and related disorders", and folded most of the old members forward into somatic symptom disorder (Kaplan and Sadock CTP 2024). DSM-IV somatisation disorder, undifferentiated somatoform disorder and pain disorder are all now captured by somatic symptom disorder, the last of them by its predominant-pain specifier. Hypochondriasis was *split*: roughly three-quarters of former cases, those with prominent somatic symptoms, become somatic symptom disorder, and the remainder, with high health anxiety but few or no somatic symptoms, become the new illness anxiety disorder. Two members left the

chapter's core in different directions: conversion disorder was retained but renamed functional neurological symptom disorder, and body dysmorphic disorder migrated to the obsessive-compulsive and related disorders. Factitious disorder was, conversely, brought *into* this chapter. The positive signs and management of the conversion presentation are developed in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes, and body dysmorphic disorder on the obsessive-compulsive spectrum in the Anxiety, OCD and trauma-related disorders notes.

DSM-IV SOMATOFORM MEMBER	DSM-5-TR DESTINATION	THE ONE-LINE REASON
Somatisation disorder	Somatic symptom disorder	**Positive Criterion B replaces the multi-system symptom count**
Undifferentiated somatoform disorder	Somatic symptom disorder	**Same positive-criterion home, no symptom threshold to meet**
Pain disorder	Somatic symptom disorder, with predominant pain	**Becomes a specifier, not a separate diagnosis**
Hypochondriasis	Split: somatic symptom disorder / illness anxiety disorder	**Somatic symptoms present goes to the former; health anxiety with few symptoms to the latter**
Conversion disorder	Functional neurological symptom disorder (retained, renamed)	**Kept, because it still needs incompatibility with disease, not a psychological criterion**
Body dysmorphic disorder	Obsessive-compulsive and related disorders	**Repetitive checking and preoccupation place it on the OCD spectrum**

The forward collapse of the DSM-IV somatoform disorders into DSM-5-TR, with the two relocations shown in the nosology-shift diagram alongside (Kaplan and Sadock CTP 2024, DSM-5-TR 2022).

ICD-10 TO DSM-5: WHAT CHANGED

ICD-10 (F45) **kept a family of separate somatoform diagnoses**, each requiring symptoms not fully explained by physical disorder: somatisation disorder (F45.0), undifferentiated somatoform disorder (F45.1), hypochondriacal disorder (F45.2), somatoform autonomic dysfunction (F45.3) and persistent somatoform pain disorder (F45.4), with neurasthenia sitting nearby at F48.0. DSM-5 **discarded both the family structure and the medically-unexplained rule**, replacing the lot with one positively defined somatic symptom disorder (plus a separate illness anxiety disorder for the health-anxiety remnant). The old names still get tested because clinicians and ICD-10-using services still speak them, so you must read fluently in both the old family and the new single diagnosis.

1.5 The ICD-10 somatoform family that was folded in

Five members, each with its own discriminator. The ICD-10 F45 group is worth holding intact, both because ICD-10 is still in service and because the members are the classic viva names (ICD-10). Somatisation disorder (F45.0), historically Briquet syndrome, needs multiple, recurrent and

frequently changing physical symptoms across several body systems for at least two years, with refusal to accept reassurance and resulting social impairment. Undifferentiated somatoform disorder (F45.1) is the sub-threshold version, the same picture without the full symptom load or duration. Hypochondriacal disorder (F45.2) is a persistent preoccupation with the possibility of having one or more serious progressive physical disorders, the focus being on the feared *diagnosis* rather than the symptoms themselves. Somatoform autonomic dysfunction (F45.3) presents symptoms as though arising from an autonomically innervated organ, with objective autonomic arousal (palpitations, sweating, tremor, flushing) plus subjective organ-referred complaints; its cardiovascular subtype is the eponymous Da Costa syndrome or cardiac neurosis. Persistent somatoform pain disorder (F45.4) is severe, distressing pain not fully explained physiologically, arising with emotional or psychosocial conflict.

ICD-10 SOMATOFORM MEMBER	CORE REQUIREMENT	THE DISCRIMINATOR TO HOLD
Somatisation disorder (F45.0)	Multiple, changing, multi-system symptoms for at least two years	**Symptom multiplicity plus the two-year duration; Briquet syndrome**
Undifferentiated somatoform (F45.1)	Same picture below the full threshold	**Fewer symptoms or shorter than two years**
Hypochondriacal disorder (F45.2)	Preoccupation with having a serious disease	**Focus is the feared diagnosis, not the symptom itself**
Somatoform autonomic dysfunction (F45.3)	Organ-referred symptoms with objective autonomic arousal	**Autonomic signs plus a named organ system; Da Costa for the heart**
Persistent somatoform pain (F45.4)	Persistent severe pain with emotional or psychosocial conflict	**Pain is the whole presentation, tied to psychosocial context**

The ICD-10 F45 somatoform family, all now subsumed forward into somatic symptom disorder (or, for the health-anxiety type, into illness anxiety disorder) under DSM-5-TR (ICD-10).

GOOD TO REMEMBER

- **Somatisation disorder / Briquet syndrome (the ICD-10 diagnosis):** multiple, recurrent, frequently changing physical symptoms across several systems for at least two years, with refusal to accept reassurance; the discriminator from hypochondriacal disorder is that the focus is the symptoms, not the fear of a specific disease.
- **Somatoform autonomic dysfunction / Da Costa syndrome (the ICD-10 diagnosis):** objective autonomic arousal plus subjective symptoms referred to a single autonomically innervated organ system; the discriminator is the presence of true autonomic signs attached to a named organ.

1.6 The specifiers of somatic symptom disorder

Two descriptive specifiers and a severity grade counted from Criterion B. DSM-5-TR lets the diagnosis be qualified in three ways (DSM-5-TR 2022). The *with predominant pain* specifier (formerly the separate pain disorder) is used when the somatic symptoms predominantly involve pain. The *persistent* specifier marks a course characterised by severe symptoms, marked impairment and long duration, running beyond six months. Severity is then graded directly by how many of the Criterion-B manifestations are fulfilled: *mild* when only one is present, *moderate*

when two or more are present, and *severe* when two or more are present together with multiple somatic complaints or one very severe somatic symptom. This is a neat, examinable structure because severity is read off the positive psychological criterion itself rather than off symptom counts, which keeps the whole diagnosis anchored to Criterion B.

SEVERITY GRADE	CRITERION-B MANIFESTATIONS FULFILLED	ADDITIONAL REQUIREMENT
Mild	Only one	**None**
Moderate	Two or more	**None**
Severe	Two or more	**Plus multiple somatic complaints, or one very severe somatic symptom**

DSM-5-TR severity is graded from the count of Criterion-B manifestations, not from the number of somatic symptoms (DSM-5-TR 2022).

GOOD TO REMEMBER

- **Specifiers (the diagnostic qualifiers):** *with predominant pain* replaces the old pain disorder; *persistent* marks severe, impairing symptoms beyond six months; severity is mild (one Criterion-B feature), moderate (two or more), or severe (two or more plus multiple or one very severe somatic symptom). The rule to hold is that severity counts Criterion B, not symptoms.

1.7 The ICD-11 parallel: bodily distress disorder

ICD-11 made the same positive-criterion move under a different name. ICD-11 discarded the ICD-10 somatoform family and created the grouping "disorders of bodily distress and bodily experience", whose principal member is bodily distress disorder (6C20), sitting beside the newly introduced body integrity dysphoria (6C21) (ICD-11 CDDR; Kaplan and Sadock CTP 2024). The **icd-11 bodily distress** disorder is characterised by bodily symptoms that are distressing to the individual together with *excessive attention* directed toward them, shown as persistent preoccupation with the symptoms' severity or as repeated health-care contacts substantially in excess of what is medically necessary, and this attention persists despite appropriate examination, investigation and reassurance. Symptoms must be present on most days for at least several months, roughly three months or more. Like DSM-5, ICD-11 defines the disorder by these positive psychological features and *not* by the absence of a medical explanation, and it grades severity as mild, moderate or severe by impact on functioning. The two systems therefore converge on mechanism while differing on detail.

Where they still diverge. Two differences are examinable. First, the duration floor: DSM-5 speaks of a symptomatic state typically beyond six months, whereas ICD-11 sets its threshold at several months, giving the example of three months or more. Second, and more important, the health-anxiety patient is placed differently: DSM-5 keeps illness anxiety disorder *within* this chapter, whereas ICD-11 moves hypochondriasis *out*, into the obsessive-compulsive and related disorders, on the logic that its repetitive checking and reassurance-seeking are compulsion-like. In ICD-11 the bodily distress patient is preoccupied with the symptoms themselves and their

impact on life; the hypochondriasis patient is driven instead by the fear that the symptoms signify a serious progressive illness.

FEATURE	ICD-11	DSM-5-TR
Umbrella diagnosis	Bodily distress disorder (6C20)	**Somatic symptom disorder**
Defining basis	Distressing symptoms plus excessive attention	**Distressing symptoms plus excessive thoughts, feelings, behaviours (Criterion B)**
Medically-unexplained rule	Dropped	**Dropped**
Duration floor	Most days for at least several months (about three)	**Persistent state, typically beyond six months**
Health-anxiety type	Hypochondriasis, moved to obsessive-compulsive and related disorders	**Illness anxiety disorder, kept within this chapter**
Severity grading	Mild / moderate / severe by functional impact	**Mild / moderate / severe by Criterion-B count**

The ICD-11 to DSM-5-TR cross-map: convergent on the positive-criterion logic, divergent on duration and on where the health-anxiety patient sits (ICD-11 CDDR, DSM-5-TR 2022).

GOOD TO REMEMBER

- **Bodily distress disorder (the ICD-11 diagnosis):** distressing bodily symptoms with excessive attention (preoccupation with severity, or repeated medically unnecessary health-care contacts), persisting despite appropriate examination and reassurance, present on most days for at least several months (about three); graded mild, moderate or severe by functioning. The two discriminators to hold are that it is positively defined, not unexplained-based, and that ICD-11 hypochondriasis sits with the obsessive-compulsive and related disorders, not here.

1.8 Epidemiology and course

Common, female-predominant, and heavily concentrated in general medical settings. Population-based studies using DSM-5 criteria place the general adult prevalence of somatic symptom disorder at roughly 4 to 6 percent, well above the under-1-percent rate of the old, more restrictive DSM-IV somatisation disorder (DSM-5-TR 2022). The disorder is markedly commoner in general medical than in psychiatric settings: a twelve-month prevalence around 10 to 20 percent is plausible among primary-care attenders, rising to between 40 and 60 percent in services that specialise in psychosomatic or functional disorders. Women report more somatic symptoms than men, so the prevalence is higher in women. Onset is typically early, often in adolescence or before the age of thirty, and the course is characteristically chronic and fluctuating, its trajectory shaped by symptom number, age, degree of impairment and comorbidity; lower harm-avoidance and greater cooperativeness predict a shorter time to remission. Because these patients present to physicians rather than to mental-health services and may meet the suggestion of psychiatric referral with surprise or refusal, the disorder is easily missed and heavily over-investigated.

1.9 Assessment: the somatic-symptom scales

Two scales measure the symptom burden, one measures the positive criterion. Structured instruments grade severity and track change alongside the clinical interview; the reproduced forms sit in the accompanying scale plate, and only the verified bands matter here. The PHQ-15, the Patient Health Questionnaire-15, rates fifteen common somatic symptoms, each scored 0 to 2, summing to a total out of a possible 30, with cut-points at 5, 10 and 15 marking low, medium and high somatic-symptom severity (Kroenke and Spitzer). The SSS-8, the Somatic Symptom Scale-8, is its brief eight-item derivative, each item scored 0 to 4 over the past seven days, summing to a total out of a possible 32, banded as none-to-minimal (0 to 3), low (4 to 7), medium (8 to 11), high (12 to 15) and very high (16 to 32) (Gierk). Both of these read Criterion A, the somatic burden. The SSD-12, the twelve-item Somatic Symptom Disorder-B Criteria Scale, is different in kind: its twelve items, each 0 to 4 for a total out of a possible 48, measure the cognitive, affective and behavioural aspects of Criterion B itself, so it is the instrument that captures the positive psychological criterion rather than the symptoms. The clean pairing to remember is a symptom-burden scale (PHQ-15 or SSS-8) plus a Criterion-B scale (SSD-12).

15	16	4-6%
PHQ-15 HIGH-SEVERITY CUT-OFF (0 TO 30 SCALE)	SSS-8 VERY-HIGH BAND, LOWER BOUND (0 TO 32 SCALE)	SOMATIC SYMPTOM DISORDER, GENERAL-ADULT PREVALENCE

GOOD TO REMEMBER

- **PHQ-15 (the scale):** fifteen somatic symptoms, each 0 to 2, total out of a possible 30; cut-points at 5, 10 and 15 for low, medium and high somatic-symptom severity; it measures Criterion A, the symptom burden.
- **SSD-12 (the scale):** twelve items, each 0 to 4, total out of a possible 48; it measures Criterion B, the excessive thoughts, feelings and behaviours, and so is the direct read-out of the positive psychological criterion.

1.10 The guideline-anchored first moves in management

Physician-centred care first, psychological therapy next, drugs only for a comorbidity. Management is led by non-pharmacological, physician-centred care (IPS_CPG 2020, psychotherapies for somatoform disorders): build a therapeutic alliance, validate that the symptoms and the distress are real, restrict unnecessary investigations and referrals, treat any concurrent depression or anxiety early, and shift the focus from symptoms toward functioning, seeing stable patients about once every one to two months. Cognitive behaviour therapy is the first-line psychotherapy, targeting the catastrophic misinterpretation of bodily sensations and rebuilding activity, with a brief package of psychoeducation, relaxation and reattribution as an alternative first-line approach. The pharmacological rule is restrictive and heavily tested: do *not* prescribe anti-anxiety or antidepressant medicines for medically unexplained somatic complaints unless a specialist advises it (WHO mhGAP 2016); antidepressants are reserved for a genuinely comorbid depressive or anxiety disorder, or for a dominant chronic-pain component, where an SNRI such as duloxetine or a low-dose tricyclic such as amitriptyline is preferred for its analgesic action. Drugs supplement, and never replace, physician-centred and psychological care.

GOOD TO REMEMBER

- **Physician-centred care (the management step):** the guideline first-line (IPS_CPG 2020), being therapeutic alliance, validation of real symptoms, restriction of unnecessary tests and referrals, early treatment of comorbid mood or anxiety, and a shift toward functioning; the first move is the alliance, not a prescription.
- **Antidepressants in somatic symptom disorder (the drug principle):** the guideline rule (WHO mhGAP 2016) is not to prescribe anti-anxiety or antidepressant drugs for medically unexplained somatic symptoms unless a specialist advises; reserve them for comorbid depression or anxiety, or for a dominant chronic-pain component, where an SNRI (duloxetine) or low-dose amitriptyline is preferred.

MNEMONIC

SEED

The master mnemonic for the whole chapter, seeded here and reaped at consolidation. **S** is the *Somatic* room, somatic symptom disorder and bodily distress, where the body complains. **E** is *Eros*, the sexual dysfunctions and gender incongruence, where the body desires and identity is affirmed. **E** is the *Explosive urges*, the impulse-control disorders, where the urge acts. **D** is the *Defence of life*, suicide risk assessment, prevention and the protective, compassionate stance the chapter closes on. Four rooms, one house: S-E-E-D.

INDIA

Somatic presentation is the Indian norm rather than the exception: psychological distress is very commonly expressed and first brought to the clinician as bodily symptoms, so a large share of primary-care and general-hospital attenders sit in this diagnostic space, and the Indian evidence base is anchored by the IPS_CPG 2020 guideline on psychotherapies for somatoform disorders and by indigenous tools such as the Scale for Assessment of Somatic Symptoms (SASS). The most examinable India-specific presentation is the culture-bound Dhat syndrome, a somatic and anxious preoccupation attributed to perceived loss of vital fluid, which must be read through a cultural formulation rather than pathologised on its surface content; its wider transcultural frame and the consultation-liaison service model that most often meets these patients are developed in the Consultation-liaison, geriatric and transcultural psychiatry notes.

HOLD THIS

Somatic symptom disorder is diagnosed by the POSITIVE psychological criterion (Criterion B, excessive thoughts, feelings or behaviours about the somatic symptoms), not by the symptoms being medically unexplained, so a medically explained symptom can still qualify; DSM-5 collapsed the DSM-IV somatoform disorders into it, splitting hypochondriasis into somatic symptom disorder and illness anxiety disorder and renaming conversion as functional neurological symptom disorder, while ICD-11 made the parallel move to bodily distress disorder (6C20, positively defined, present on most days for at least several months) but sent its hypochondriasis to the obsessive-compulsive and related disorders.

2 · Illness anxiety disorder

Hypochondriasis, renamed and re-sorted. **Illness anxiety disorder** is the modern label for the health-anxious patient whose problem is the *fear of illness* rather than the *burden of symptoms*: a preoccupation with having or acquiring a serious illness, held with **minimal or no somatic symptoms** and a high level of **health anxiety**. It is what DSM-5 carved out of the old **hypochondriasis** once the term was retired for its stigma, and the examiner's favourite hook is the split it created: the same clinical tradition now flows into two boxes, illness anxiety disorder where the body is quiet and the mind is frightened, and somatic symptom disorder where distressing bodily symptoms dominate.

This note owns the diagnosis and the discrimination: the reconceptualisation of hypochondriasis, the DSM-5-TR criteria with the **care-seeking type** and **care-avoidant type** specifiers and the six-month duration, the ICD-11 position that kept the name and moved it onto the obsessive-compulsive spectrum, the sharp line against somatic symptom disorder, and the management, where the discipline of limited reassurance, first-line CBT, and treating comorbid anxiety and depression carries the whole load. The somatic symptom disorder that sits on the other side of the split is developed in the somatic symptom disorder topic in these notes; body dysmorphic disorder, its close obsessive-compulsive relative, is in the Anxiety, OCD and trauma-related disorders notes; and the wider consultation-liaison and transcultural frame is in the Consultation-liaison, geriatric and transcultural psychiatry notes.

2.1 The reconceptualisation of hypochondriasis

One old diagnosis, split in two. Because of the pejorative weight the word carried, DSM-5 removed the classical term hypochondriasis and redistributed its patients (Kaplan and Sadock 2024). The majority, roughly three-quarters, carry prominent bodily symptoms and are now diagnosed as somatic symptom disorder. The minority, about one in five (roughly 20%), have relatively minor somatic symptoms and are instead preoccupied with the fear that they will get sick or already harbour an undiagnosed disease; these become illness anxiety disorder. The line between the two boxes is simply the *severity of the somatic symptoms*.

ICD-11 kept the word but changed its home. ICD-11 retained the label hypochondriasis, added *health anxiety disorder* as an official alternative name, and, crucially, placed it not among the somatic disorders but within the obsessive-compulsive and related disorders grouping, on the strength of the shared phenomenology (intrusive health-related preoccupations plus repetitive checking or reassurance behaviours) and a similar treatment response (ICD-11 CDDR). In ICD-11 the presence of somatic symptoms is explicitly *not* an essential feature. The classic triad to name is **disease conviction**, **disease fear**, and **bodily preoccupation**.

RULE **Symptom load decides the box.** Prominent, distressing somatic symptoms mean somatic symptom disorder; a fear-of-illness preoccupation with minimal or no somatic symptoms and high health anxiety means illness anxiety disorder.

2.2 DSM-5-TR criteria and the two specifiers

The criteria to state. DSM-5-TR defines illness anxiety disorder as a preoccupation with having or acquiring a serious illness, in which somatic symptoms are *absent or only mild*; if a real medical condition or genuine risk is present, the preoccupation is clearly excessive or disproportionate (DSM-5-TR 2022). There is a high level of anxiety about health and the person is easily alarmed about their health status. They either perform excessive health-related behaviours (repeatedly checking the body) or show maladaptive avoidance (staying away from appointments and hospitals). The preoccupation has lasted at least six months, although the specific feared illness may change over that time, and it is not better explained by another mental disorder.

Then choose the specifier. DSM-5-TR asks the clinician to specify one of two behavioural phenotypes. In the care-seeking type, medical care (physician visits, tests and procedures) is frequently used. In the care-avoidant type, medical care is rarely used because contact with doctors and health information is itself frightening. The two look opposite at the surface yet spring from the same engine of health anxiety, which is the point examiners test.

DSM-5-TR CRITERION (ILLNESS ANXIETY DISORDER)	WHAT IT REQUIRES
A. Preoccupation	**Preoccupation with having or acquiring a serious illness**
B. Somatic symptoms	**Somatic symptoms absent or only mild; if a condition or risk exists, the worry is disproportionate**
C. Health anxiety	High anxiety about health; easily alarmed about personal health status
D. Behaviour	Excessive health-related behaviours (checking, reassurance-seeking) or maladaptive avoidance
E. Duration	**Illness preoccupation present at least six months (the specific feared illness may change)**
F. Exclusion	Not better explained by another mental disorder

The DSM-5-TR criteria for illness anxiety disorder; the discriminating pair is Criterion B (somatic symptoms absent or mild) and the six-month duration, then specify care-seeking type or care-avoidant type (DSM-5-TR 2022).

GOOD TO REMEMBER

- **Illness anxiety disorder (the syndrome):** preoccupation with having or acquiring a serious illness, with somatic symptoms absent or only mild, a high level of health anxiety, and either excessive health behaviours or maladaptive avoidance, present at least six months; the defining criterion is the fear-of-illness preoccupation on a body that is largely symptom-free, and the mandatory specifier is care-seeking type versus care-avoidant type.

2.3 ICD-11 hypochondriasis and its insight specifiers

The ICD-11 essential features. ICD-11 requires a persistent preoccupation or fear about the possibility of having one or more serious, progressive or life-threatening illnesses, accompanied by *either* repetitive and excessive health-related behaviours (repeated body-checking, exhaustive searching for information, repeated reassurance-seeking and multiple consultations) *or*

maladaptive avoidance related to health (avoiding medical appointments), with resulting significant distress or impairment (ICD-11 CDDR). The catastrophic misinterpretation of ordinary bodily sensations, for example reading a tension headache as a brain tumour, is the additional clinical hallmark.

Insight is coded, not assumed. ICD-11 attaches an insight specifier: *hypochondriasis with fair to good insight* (6B23.0), where the person can much of the time entertain that their belief may be untrue, and *hypochondriasis with poor to absent insight* (6B23.1), where they are convinced most or all of the time and, in a small minority, hold the belief with near-delusional conviction. Because insight can swing with the level of anxiety, it is judged over a period long enough to allow for fluctuation, a few days or a week. Onset is typically in early to mid-adulthood, and the course is chronic and relapsing.

FEATURE	ILLNESS ANXIETY DISORDER (DSM-5-TR)	HYPOCHONDRIASIS / HEALTH ANXIETY DISORDER (ICD-11)
Term retained	Renamed from hypochondriasis	**Term hypochondriasis kept; health anxiety disorder is the alternative name**
Classification home	Somatic symptom and related disorders	**Obsessive-compulsive and related disorders**
Somatic symptoms	Must be absent or only mild (Criterion B)	Not an essential feature; may be present or absent
Behavioural specifier	Care-seeking type / care-avoidant type	Excessive health behaviours or maladaptive avoidance built into the criteria
Insight specifier	Poor-insight / with-delusional-beliefs qualifiers	**Fair-to-good (6B23.0) vs poor-to-absent (6B23.1)**

The same construct across the two systems; the crunchy contrast is where it is filed, somatic-symptom-and-related in DSM-5-TR versus obsessive-compulsive-and-related in ICD-11, and whether somatic symptoms are required at all (DSM-5-TR 2022; ICD-11 CDDR).

GOOD TO REMEMBER

- **Hypochondriasis (ICD-11, health anxiety disorder):** persistent preoccupation or fear of having a serious, progressive or life-threatening illness plus *either* excessive health-related behaviours *or* maladaptive avoidance, causing distress or impairment; filed under obsessive-compulsive and related disorders, somatic symptoms are not required, and insight is coded as fair-to-good (6B23.0) or poor-to-absent (6B23.1).

2.4 Illness anxiety disorder versus somatic symptom disorder

The examiner's discriminator. Both patients are anxious about their health, so the split turns on the *weight of somatic symptoms*. In illness anxiety disorder the body is largely quiet: symptoms are absent or mild and the suffering is the fear itself, the conviction or dread of a disease not yet found. In somatic symptom disorder the patient carries one or more genuinely distressing somatic symptoms with disproportionate thoughts, feelings and behaviours about them; the symptoms drive the picture. DSM-5 also made somatic symptom disorder a *positive* psychological

diagnosis, resting on the excessive health-related thoughts, feelings and behaviours, rather than the old requirement that symptoms be medically unexplained.

DISCRIMINATOR	ILLNESS ANXIETY DISORDER	SOMATIC SYMPTOM DISORDER
Somatic symptoms	**Absent or only mild**	**One or more, prominent and distressing**
Core suffering	Fear of having or acquiring a disease	Burden of the symptoms and their meaning
Basis of the diagnosis	Health preoccupation despite reassurance	Positive psychological criterion (excessive thoughts, feelings, behaviours)
Behavioural axis	Care-seeking type or care-avoidant type	High health-related anxiety and effort directed at symptoms
Share of old hypochondriasis	About one in five (roughly 20%)	About three-quarters

Illness anxiety disorder against somatic symptom disorder; the one line to hold is that illness anxiety disorder is fear on a quiet body while somatic symptom disorder is a loud body (Kaplan and Sadock 2024; DSM-5-TR 2022).

TRAP **Do not diagnose on "medically unexplained".** Somatic symptom disorder now rests on a *positive* psychological criterion, not on symptoms being unexplained; a symptom can have a full medical explanation and the diagnosis still stand, and illness anxiety disorder is missed if you demand unexplained symptoms it does not require.

2.5 Epidemiology, comorbidity and course

Common and easily missed. Health anxiety is frequent: it may affect about **4% to 6%** of all patients, with primary-care rates around 3% to 7% (Kaplan and Sadock 2024), and DSM-5-TR puts the 6-month to one-year prevalence in ambulatory medical populations at roughly 2.2% to 8% (weighted mean about 3%), rising to nearly one-fifth in specialty clinics; it is about equally common in men and women (DSM-5-TR 2022). Onset is usually early to mid-adulthood, and identification is often delayed because these patients present to physicians rather than to mental-health services.

The company it keeps. Psychiatric comorbidity is the rule: depression in about **40%**, panic disorder in 10% to 20%, and generalised anxiety disorder in 5% to 10%, alongside obsessive-compulsive disorder (Kaplan and Sadock 2024). The course tends to be chronic and relapsing, with more than 60% still symptomatic after several years of follow-up. That chronicity, plus the fact that comorbid mood and anxiety often carry the distress, is exactly why the management targets the comorbidity as hard as the health anxiety.

PEARL

Two facts reframe the whole encounter. First, most of these patients sit in medical clinics, not psychiatric ones, so the diagnosis is made by whoever is willing to look past the presenting organ. Second, depression rides along in about four in ten, and it is frequently the treatable driver of the health anxiety, so screening for and treating a comorbid depressive or anxiety disorder is often the single most useful move.

2.6 Management: reassurance limits, CBT, treat the comorbidity

Reassurance is a trap if it is unlimited. The paradox of health anxiety is that reassurance relieves the fear for minutes and then feeds it, so that endless testing and "one more scan" become part of the disorder. The workable stance mirrors physician-centred care for somatic symptom disorder: a single trusted clinician, regular scheduled appointments that are not triggered by each new symptom, a genuine but *bounded* acknowledgement that the symptoms and fear are real, and a deliberate restraint on repeat investigations and referrals once an adequate work-up is done. Reassurance is offered once, clearly, and then the focus shifts from the question "am I ill" to living well despite the uncertainty.

CBT is first-line, and it is what works. Cognitive-behavioural therapy is the prototype, evidence-based first-line treatment, targeting the catastrophic misinterpretation of bodily sensations and the reassurance-seeking and checking that maintain the cycle (Kaplan and Sadock 2024; Barsky and Ahern 2004). India's own guidance is aligned: the IPS Clinical Practice Guidelines recommend, for hypochondriacal or illness-anxiety presentations, CBT with cognitive restructuring and exposure and response prevention as first line, with mindfulness-based cognitive therapy or acceptance and commitment therapy as second line (IPS_CPG 2020).

Medication treats the comorbidity, chiefly. Where a comorbid depressive or anxiety disorder is present, an SSRI is reasonable and the health anxiety often improves in parallel. The best single-drug evidence is for fluoxetine (Prozac), where a double-blind placebo-controlled trial at **20 to 80 mg per day** showed a moderate, well-tolerated benefit (Fallon and colleagues). The guideline caution to keep in view is that drugs are not started reflexively for medically unexplained somatic complaints without a clear comorbid indication or specialist advice (WHO mhGAP 2016); psychological care leads, and medication supplements it.

GOOD TO REMEMBER

- **First-line treatment (guideline):** CBT is the prototype first-line therapy; IPS_CPG 2020 specifies CBT with cognitive restructuring and exposure and response prevention first line for illness-anxiety presentations, with MBCT or ACT second line.
- **Reassurance principle:** unlimited reassurance and repeat testing maintain the disorder; offer a single trusted clinician, regular scheduled visits, a bounded validation of the distress, and restraint on further investigations once an adequate work-up is complete.
- **Pharmacotherapy (guideline):** an SSRI is used mainly for comorbid depression or anxiety; fluoxetine 20 to 80 (mg per day) has the best trial evidence; do not prescribe reflexively for medically unexplained symptoms without a clear indication (WHO mhGAP 2016).

COMMON TRAP

Chasing the fear with tests. Each new investigation buys a few minutes of calm and then raises the next question, deepening the care-seeking cycle and risking iatrogenic harm and doctor-shopping. The corrective is not to withhold care but to move from symptom-driven testing to scheduled, relationship-based follow-up, and to treat the health anxiety and any comorbid depression directly rather than through the radiology department.

6	~20%	20 to 80	3 to 8%
MINIMUM MONTHS OF PREOCCUPATION (DSM-5-TR)	OF OLD HYPOCHONDRIASIS NOW ILLNESS ANXIETY DISORDER	FLUOXETINE DOSE (MG PER DAY)	HEALTH ANXIETY IN AMBULATORY CARE

INDIA

Health anxiety fits the Indian care landscape closely. Most patients present to physicians and specialists rather than to psychiatry, and a fragmented, largely out-of-pocket fee-for-service system makes doctor-shopping and repeated investigation easy, so the **care-seeking type** is readily and iatrogenically reinforced by the very system meant to reassure. National guidance is clear and usable: the IPS Clinical Practice Guidelines anchor CBT with cognitive restructuring and exposure and response prevention as first line for illness-anxiety and hypochondriacal presentations (IPS_CPG 2020). The related culture-bound presentation of Dhat, and the wider transcultural handling of health anxiety, are developed in the Consultation-liaison, geriatric and transcultural psychiatry notes.

WORKED EXAMPLE

A 34-year-old man attends his fourth physician in six months, each time with a new fear, a heart attack, then a brain tumour, then bowel cancer, prompted by a normal sensation such as a skipped beat or a headache. Examinations and an extensive work-up are repeatedly normal, yet reassurance calms him only briefly before the next worry arrives, and he arranges further scans himself. He has no substantial ongoing bodily symptoms; the suffering is the dread. This is illness anxiety disorder, care-seeking type: preoccupation with acquiring a serious illness, somatic symptoms minimal, high **health anxiety**, over six months. Management is a single named clinician with scheduled visits, bounded reassurance, no further tests without a fresh indication, first-line CBT with exposure and response prevention, and screening for the comorbid depression that so often sits underneath.

HOLD THIS

Illness anxiety disorder is DSM-5's carve-out of hypochondriasis for the fear-of-illness patient whose body is quiet, preoccupation with having or acquiring a serious illness, somatic symptoms absent or mild, high health anxiety, at least six months, specify care-seeking type or care-avoidant type; somatic symptom disorder is the loud-body sibling with prominent symptoms and a positive psychological criterion; ICD-11 keeps the name hypochondriasis and files it under obsessive-compulsive and related disorders; and management is bounded reassurance plus first-line CBT with exposure and response prevention (IPS_CPG 2020), with an SSRI such as fluoxetine reserved for comorbid depression or anxiety.

3 · Conversion and functional neurological symptom disorder

The neurology-facing member of the family. **Conversion disorder**, renamed **functional neurological symptom disorder** in DSM-5, is the diagnosis given when a patient has a genuine neurological symptom, a motor, sensory or seizure-like disturbance, that is demonstrably *incompatible* with any recognised neurological disease. It sits on the **somatic spectrum** as the one condition defined not by how much the patient worries about a symptom but by an examination

finding, which is why examiners like it: the whole diagnosis turns on a sign you can elicit at the bedside. Across these notes the disorder is abbreviated fnd.

This note does one job, and does it precisely: it *places* functional neurological symptom disorder in the somatic nosology map, states the two shifts DSM-5 made (dropping the requirement for a preceding psychological stressor, and moving from a diagnosis of exclusion to a **positive signs** rule-in), and names the cardinal trap of the whole topic, missing an organic disease behind a presentation labelled "conversion". The actual bedside **positive signs** (Hoover's sign, the tremor entrainment test, the give-way weakness pattern) and the full management are taught in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes and are cross-referenced there rather than re-taught here. What follows is how to recognise the disorder and where it belongs. The term "conversion" is Charcot-era and psychoanalytic, the idea that unconscious conflict is "converted" into a bodily deficit; the modern label keeps the phenomenon and drops the theory.

3.1 Where it sits on the somatic spectrum, and the DSM versus ICD split

One disorder, two homes. The **somatic spectrum** groups conditions in which bodily symptoms dominate the presentation and are first met in medical rather than psychiatric settings. Within it, conversion / functional neurological symptom disorder is the pole defined by *loss or alteration of a function* (weakness, abnormal movement, sensory loss, non-epileptic attacks) rather than by distressing symptoms plus excessive health thoughts. Its neighbours on the somatic spectrum are these: somatic symptom disorder (positive distressing symptoms with disproportionate cognition), illness anxiety disorder (health anxiety with few or no symptoms), factitious disorder (deliberately produced signs, no external incentive) and, outside this chapter, body dysmorphic disorder, which belongs on the obsessive-compulsive spectrum and is developed in the Anxiety, OCD and trauma-related disorders notes.

The two classifications disagree on the address. This is a favourite discriminator. DSM-5-TR files the disorder inside *Somatic Symptom and Related Disorders* as functional neurological symptom disorder. ICD-11 instead places it among the *dissociative disorders*, as dissociative neurological symptom disorder (code 6B60), sitting beside dissociative amnesia and trance and possession disorders (ICD-11 CDDR). Both describe the same clinical picture, motor, sensory, seizure-like or speech symptoms not consistent with a recognised nervous-system disease; they simply differ on whether the mechanism is best framed as somatic or dissociative.

FRAMEWORK	NAME AND CODE	CHAPTER IT LIVES IN
DSM-5-TR	Functional neurological symptom disorder (conversion disorder)	**Somatic Symptom and Related Disorders**
ICD-11	Dissociative neurological symptom disorder (6B60)	**Dissociative Disorders**
ICD-10 (historical)	Dissociative (conversion) disorders (F44)	Neurotic, stress-related and somatoform disorders

The same disorder, two homes: DSM-5-TR keeps it on the somatic spectrum, ICD-11 files it under the dissociative disorders as 6B60, and the coexisting motor / sensory / seizure specifiers run in parallel across both.

3.2 The DSM-5-TR criteria and the two shifts

Four criteria, A to D. DSM-5-TR requires (A) one or more symptoms of altered voluntary motor or sensory function; (B) clinical findings that provide evidence of *incompatibility* between the symptom and recognised neurological or medical conditions; (C) the symptom is not better explained by another medical or mental disorder; and (D) it causes clinically significant distress or impairment, or warrants medical evaluation (DSM-5-TR 2022). Symptom-type specifiers name the presentation (with weakness or paralysis, abnormal movement, non-epileptic attacks or seizures, anaesthesia or sensory loss, speech or special-sensory symptoms), and course is specified as acute episode or persistent.

The two things DSM-5 changed, and both are examinable. First, it became a *rule-in* diagnosis: Criterion B demands positive evidence of incompatibility, so the disorder is no longer diagnosed by exclusion, no longer requires normal investigations, and can be made even in a patient who also has a recognised neurological disease. Second, DSM-5 *dropped the requirement for a preceding psychological stressor*. A stressor may be specified when present, but it is not necessary, precisely because an identifiable stressor is absent in up to **50%** of patients, and the diagnosis is not withheld for want of one.

RULE **Positive incompatibility, not normal scans.** The diagnosis rests on a positive examination finding of internal inconsistency (a sign present one way and gone another), never on "all the tests came back normal" or on the symptom looking bizarre; it is a rule-in diagnosis that can coexist with genuine neurological disease.

GOOD TO REMEMBER

- **Functional neurological symptom disorder (the syndrome):** altered voluntary motor or sensory function whose *defining* criterion is positive clinical evidence of incompatibility with recognised neurological disease (DSM-5-TR Criterion B); it is a rule-in, not an exclusion, diagnosis, needs no preceding stressor, and may be diagnosed alongside a real neurological disorder.

3.3 The positive signs, named here and taught elsewhere

What "incompatibility" looks like at the bedside. The demonstration is *internal inconsistency*: a deficit that changes when attention is redirected or when the same movement is tested a different way. The three the examiner wants named are Hoover's sign (functional hip-extension weakness that returns to normal power when the opposite hip is flexed against resistance), the tremor entrainment test (a functional tremor that entrains to, is suppressed by, or cannot copy a rhythm tapped by the other hand), and the give-way, or collapsing, weakness pattern (power that gives way suddenly rather than yielding smoothly). These, and the dissociative (non-epileptic) attack features, plus the full management, are worked through in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes; the point for this note is only that such **positive signs** exist and carry the diagnosis.

Two old signs that do not carry it. La belle indifférence (a bland lack of concern about a disabling deficit) and the presence of "secondary gain" were once treated as diagnostic; both are non-specific, occur in organic disease too, and must *not* be used to make the diagnosis (DSM-5-TR 2022). The diagnosis is built on the overall clinical picture and the positive signs, not on a single feature and not on the patient's affect.

GOOD TO REMEMBER

- **Positive signs (the discriminator):** Hoover's sign, the tremor entrainment test and give-way weakness demonstrate internal inconsistency and rule the diagnosis in; la belle indifférence and "secondary gain" are non-specific and do not diagnose it. Full teaching sits in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes.

WORKED EXAMPLE

A 26-year-old woman develops sudden left-leg weakness after a family crisis and cannot lift the leg on the couch. On examination the strength of left hip extension is absent when tested directly but returns to full power the moment she flexes the opposite hip against your hand: a positive **Hoover's sign**. She is oddly untroubled by the disability. The positive sign rules the diagnosis in as functional neurological symptom disorder; the flat affect (la belle indifférence) is a footnote, not the evidence, and you still document a neurological screen because fnd can sit on top of real disease.

3.4 The cardinal trap: missing organic disease

The reassuring modern number, and why it does not license complacency. Eliot Slater's influential but methodologically flawed 1965 study suggested that up to two-thirds of patients labelled "hysteria" in fact had misdiagnosed neurological disease, and it wrongly persuaded a generation that the diagnosis was unsafe. The evidence since is very different: a systematic review pooling 27 outcome studies found a misdiagnosis rate of under **5%** from 1970 onward, in the era before MRI and video-telemetry (New Oxford Textbook of Psychiatry). Functional neurological symptoms are, in fact, the second commonest reason to see a neurologist, so a confident positive diagnosis is both possible and expected.

But the traps are specific and worth memorising. Comorbid neurological disease is common: around **one in five** patients with dissociative (non-epileptic) seizures *also* have epilepsy (DSM-5-TR 2022), so finding a functional attack never excludes a real one. Misreading true disease as fnd is most likely with an isolated gait disorder that examines normally on the couch, with frontal-lobe epilepsy (which can look odd and show a normal surface EEG), and with autoimmune encephalitis or the prodrome of a degenerative disease such as Parkinson's (New Oxford Textbook of Psychiatry). The discipline is to base the diagnosis on positive signs, and to re-examine if the picture becomes progressive.

TRAP **"Tests are normal, so it is conversion."** Missing organic disease behind a "conversion" label is the cardinal error; diagnose on positive incompatibility, remember functional and organic disease coexist (one in five non-epileptic-seizure patients also have epilepsy), and re-examine a progressive course.

4	5-15%	<5%	1 in 5
DSM-5-TR CRITERIA (A TO D)	OF NEUROLOGY-CLINIC PATIENTS HAVE FND	MISDIAGNOSIS RATE ON FOLLOW-UP SINCE 1970	NON-EPILEPTIC-SEIZURE PATIENTS ALSO HAVE EPILEPSY

INDIA

Conversion and dissociative presentations, pseudoseizures (dissociative attacks), functional weakness and possession or trance states, are among the commonest reasons a young or rural patient reaches Indian psychiatric services, often through a physician or neurologist first. ICD-11's placement of the disorder among the dissociative disorders, beside trance and possession disorder, fits this clinical reality well. The wider transcultural framing of possession and trance is developed in the Consultation-liaison, geriatric and transcultural psychiatry notes; the applied lesson here is to demonstrate the positive sign and rule out organic disease before attributing an attack to "hysteria" or a spiritual cause.

HOLD THIS

Conversion / functional neurological symptom disorder is a genuine neurological symptom shown by positive signs (Hoover's sign, tremor entrainment, give-way weakness) to be internally inconsistent and incompatible with recognised disease; DSM-5 made it a rule-in diagnosis and dropped the required stressor, ICD-11 files it as dissociative neurological symptom disorder (6B60) rather than on the somatic spectrum, and the cardinal trap is missing organic disease, so diagnose on the positive sign, not on normal scans, remembering that fnd and real neurological disease coexist.

4 · Factitious disorder and Munchausen syndrome

The one diagnosis defined by a deception. **Factitious disorder** is the intentional falsification or induction of physical or psychological signs and symptoms, driven not by any outside reward but by the internal need to occupy the **sick role**, to be seen and cared for as a patient. That single motive is what makes it examinable: it sits at the tip of a three-way spectrum of illness deception, distinguished from the unconscious somatic disorders on one side (where the symptom is not deliberately produced) and from malingering on the other (where the production is deliberate but the incentive is external). DSM-5 moved it into the somatic symptom and related disorders chapter precisely because these patients present with somatic complaints, most often first to the general physician.

How to use this page. Fix the DSM-5-TR criteria and the internal-versus-external incentive rule first, because that rule carries most of the marks. DSM-5-TR names two forms, factitious disorder imposed on self (historically **Munchausen syndrome**) and factitious disorder imposed on another (Munchausen by proxy); this note abbreviates them factitious imposed on self and factitious imposed on another. Then learn Munchausen syndrome as the severe chronic phenotype, factitious imposed on another as a form of child abuse whose first duty is safeguarding, and Ganser syndrome as a brief borderland name. The chapter closes on the therapeutic, non-punitive stance that management demands.

4.1 The core: intentional falsification, the sick role, no external incentive

Four criteria, A to D, for factitious imposed on self. DSM-5-TR defines factitious disorder imposed on self (F68.10) by four criteria (DSM-5-TR 2022): (A) falsification of physical or psychological signs or symptoms, or induction of injury or disease, associated with identified deception; (B) the individual presents to others as ill, impaired or injured; (C) the deceptive behaviour is evident even in the absence of obvious external rewards; and (D) it is not better explained by another mental disorder such as a delusional or psychotic disorder. The course is specified as a single episode or as recurrent episodes, the latter meaning two or more events of falsifying illness or inducing injury. The patient may feign symptoms (report chest pain that is not felt), simulate signs (manipulate a thermometer), or genuinely induce disease (self-inject a contaminant), and often carries a detailed, superficial medical vocabulary and a history of multiple procedures.

The whole diagnosis turns on Criterion C. The behaviour is conscious and goal-directed, but the goal is *internal*, the psychological gratification of being a patient, not money, drugs, disability or escape from duty. This is what separates it from malingering, and it is why the ICD codes it as a genuine mental disorder (6D50 imposed on self, 6D51 imposed on another) whereas malingering is not a disorder at all. Note the nuance that examiners like: the presence of some external reward does not automatically exclude factitious disorder, because the two can coexist, but the deception must be evident even when no external reward is on offer.

Symptom production

Conscious and deliberate in factitious disorder and malingering; unconscious in somatic symptom and conversion disorders.

Motivation

Internal, to assume the sick role, in factitious disorder; external and tangible in malingering; absent or unconscious in the somatic disorders.

Deception

Identified deception is required for factitious disorder (Criterion A); the somatic disorders involve no deception at all.

GOOD TO REMEMBER

- **Factitious disorder imposed on self (the syndrome):** intentional falsification or induction of signs or symptoms with identified deception (Criterion A), self-presented as ill (B), evident *even in the absence of obvious external rewards* (C, the defining criterion), and not better explained by another mental disorder (D); the internal motive is to occupy the sick role, coded 6D50 in ICD-11.

4.2 Factitious disorder versus malingering, and versus the unconscious somatic disorders

Two axes settle every vignette. Place the presentation on two questions: is the symptom produced *deliberately*, and is the motive *internal or external*. Somatic symptom disorder and conversion (functional neurological symptom disorder) answer "no" to deliberate production, the suffering is authentic and unwilled. Factitious disorder answers "yes, deliberate" and "internal motive" (the sick role). Malingering answers "yes, deliberate" and "external motive" (compensation,

narcotics, avoiding work or legal jeopardy). Only the middle column is defined by a lie told for its own psychological sake.

PRESENTATION	SYMPTOM PRODUCTION	MOTIVATION	STATUS
Somatic symptom / conversion disorder	Unconscious, not deliberate	None conscious; symptom is unwilled	**A mental disorder; genuine distress**
Factitious disorder	Intentional, with deception	Internal: to assume the sick role	**A mental disorder (ICD-11 6D50 / 6D51)**
Malingering	Intentional, with deception	External: money, drugs, escape from duty	**Not a disorder; a focus of clinical attention (ICD-11 QC30)**

The illness-deception spectrum: deliberate production plus internal motive is factitious disorder; deliberate production plus external reward is malingering; neither is present in the unconscious somatic disorders (DSM-5-TR 2022; Kaplan and Sadock CTP 2024).

RULE **Internal motive is factitious; external reward is malingering.** Both produce symptoms deliberately and deceptively; the discriminator is the pay-off, the psychological sick role versus a tangible external gain, and only factitious disorder is a mental disorder.

TRAP **Calling a factitious presentation "malingering."** Naming the deception is not enough; you must locate the motive. If there is no external incentive, the label is factitious disorder, not malingering, and the patient needs psychiatric care rather than discharge.

4.3 Munchausen syndrome: the severe, chronic, wandering form

The severe end of factitious imposed on self. Munchausen syndrome is the term Asher applied in his 1951 Lancet paper to the most chronic and dramatic patients, the "hospital addicts," "hospital hoboes" and "professional patients" who repeatedly simulate or induce disease for the sole purpose of obtaining medical attention. Two features beyond simple simulation define it: pseudologia fantastica, fluent, plausible, self-aggrandising lying in which the tale often contains a kernel of truth, and peregrination, the tendency to travel widely from hospital to hospital, discharging against advice and beginning the performance anew elsewhere. Antisocial traits are common, evidence of earlier surgery accumulates as multiple scars (the classic "gridiron abdomen"), and the mortality of severe induced disease is real.

But the commoner phenotype does not wander. A second, more prevalent form, sometimes called common or non-peregrinating factitious disorder, confines the behaviour to one locality and a narrow set of complaints. Its prototypical patient is younger, more often female, and frequently has a health-care background. The teaching point is that Munchausen syndrome is the memorable extreme, not the whole of factitious disorder, and the eponym is often wrongly stretched to cover every case.

4 DSM-5-TR CRITERIA (A TO D), IMPOSED ON SELF	**2+** FALSIFICATION EVENTS DEFINE RECURRENT EPISODES	**1951** ASHER NAMES MUNCHAUSEN SYNDROME (LANCET)	**1977** MEADOW DESCRIBES IT BY PROXY (CHILD ABUSE)

WORKED EXAMPLE

A woman in her thirties presents to a fourth hospital in a year with dramatic haematemesis and a spellbinding account of nursing in a war zone; the notes are thin, the story shifts, and a laparotomy scar suggests earlier surgery elsewhere. No compensation claim, no controlled-drug request and no legal case are in play. Recurrent presentations, **pseudologia fantastica** and **peregrination**, with deception and no external reward, point to Munchausen syndrome (severe factitious imposed on self), not malingering, and she needs a psychiatric alliance rather than another endoscopy.

PEARL

The eponym is a double misnomer worth knowing. It honours Baron von Munchausen, the fictional teller of tall tales, so it captures the *storytelling* but not the *self-harm*; and because the label was so widely misapplied to milder cases, DSM-5-TR retired it in favour of the plain descriptor factitious disorder imposed on self. Reserve "Munchausen" for the chronic, peregrinating, pseudologia-rich extreme.

GOOD TO REMEMBER

- **Munchausen syndrome (the syndrome):** the severe chronic form of factitious imposed on self, its two discriminators being pseudologia fantastica (fluent self-aggrandising lies with a kernel of truth) and peregrination (wandering hospital to hospital); Asher, 1951; the commoner non-peregrinating phenotype is younger, more often female and health-care linked.

4.4 Factitious disorder imposed on another (Munchausen by proxy): abuse, not curiosity

The illness is fabricated in someone else. Factitious disorder imposed on another (F68.A; ICD-11 6D51), the entity Meadow named Munchausen by proxy in 1977, applies its four criteria to a perpetrator who falsifies or induces illness in a victim, most often a preverbal child, sometimes a dependent elder or disabled adult, and presents that victim to others as ill (DSM-5-TR 2022). The reward the perpetrator seeks is still internal, the vicarious sick role and the attention of clinicians, with no obvious external incentive. The single most tested fact is the direction of the diagnosis: **the perpetrator, not the victim, receives the diagnosis**, and the perpetrator is most commonly the mother. It is formally recognised as a form of abuse, and, like any physical abuse, the diagnosis does not depend on proving the caregiver's motive.

Safeguarding is the first and overriding step. The moment factitious imposed on another is suspected, protection of the victim outranks every diagnostic nicety: the induced illness itself can be lethal, and the child cannot self-report. Contemporaneous, factual documentation, separation of the fabricated history from verified findings, senior and multidisciplinary involvement and referral into the statutory child-protection pathway are the priorities. Confronting the caregiver alone, without safeguards in place, can escalate risk to the victim and is not the first move.

INDIA

Two India-specific realities matter. First, a fragmented, largely out-of-pocket, multi-provider health system with no unified medical record makes peregrination and repeated fresh presentations easy and hard to detect, so a suspicious index and a request for old records across facilities do real work. Second, when factitious imposed on another is suspected, safeguarding runs through India's child-protection framework: the child is a "child in need of care and protection" under the Juvenile Justice (Care and Protection of Children) Act 2015, with reporting to the Child Welfare Committee, alongside the consultation-liaison team that most often first meets these patients. The wider consultation-liaison service model is developed in the Consultation-liaison, geriatric and transcultural psychiatry notes.

GOOD TO REMEMBER

- **Factitious imposed on another / Munchausen by proxy (the syndrome):** falsification or induction of illness in another (usually a preverbal child), with deception and no obvious external reward; the perpetrator (commonly the mother), not the victim, receives the diagnosis; it is a recognised form of abuse, so safeguarding the victim is the first and overriding step (DSM-5-TR; Meadow, 1977).

4.5 Ganser syndrome: the factitious and dissociative borderland

The syndrome of approximate answers. Ganser syndrome, described by Ganser in the 1890s and historically labelled "prison psychosis," is defined by vorbeireden, the giving of approximate answers, responses that are wrong but wrong in a near-miss way that betrays that the question was fully understood (asked how many legs a horse has, the patient answers "three"). It classically runs with a clouded or twilight state, may carry conversion-like somatic features and pseudohallucinations, and is often followed by amnesia for the episode. It has never had a settled home, sitting at the borderland of dissociation, factitious behaviour and malingering; ICD-11 files it among the dissociative disorders, and it earns a place here because the approximate answer looks feigned yet, unlike malingering, seeks no external reward. It is grouped under the dissociative disorders as hysterical pseudodementia.

GOOD TO REMEMBER

- **Ganser syndrome (the syndrome):** the syndrome of approximate answers, vorbeireden, where replies are wrong but near-miss in a way that proves the question was understood, classically with a clouded/twilight state and historically seen in prison inmates ("prison psychosis"); it sits at the dissociative/factitious/malingering borderland and is classed by ICD-11 among the dissociative disorders.

4.6 Management: a therapeutic, non-punitive stance

No specific drug; treat the person, not the deception. There is no standard pharmacological treatment for factitious disorder itself; medication is directed only at a comorbid psychiatric disorder, such as a depressive, anxiety or personality disorder, or at the emotional distress that precipitated the illness behaviour (Kaplan and Sadock CTP 2024). The core of management is a stance: build a therapeutic alliance, adopt a supportive, face-saving and explicitly non-confrontational approach that addresses the patient's genuine emotional needs rather than the

fabricated ones, and steer toward psychiatric care without aggressive direct exposure. Because these patients split teams and generate intense negative feeling, care is coordinated through a multidisciplinary team with regular meetings to contain countertransference and reduce staff conflict, and iatrogenic harm is minimised by restricting unnecessary investigations and procedures.

Confrontation cautions. Blunt accusatory confrontation typically ruptures the alliance and drives the patient to abscond and re-present elsewhere, so it is avoided; when the deception is addressed it is done gently and truthfully. There is no role for the clinician's own deception either, no disguised placebos and no misrepresented tests; the double-bind manoeuvre (framing a treatment such that improvement is expected if the complaint is genuine, giving a face-saving exit) is a described technique to be used sparingly and honestly, never as a trap. Where the presentation is factitious imposed on another, this therapeutic stance is subordinate to safeguarding: protecting the victim comes first, always.

GOOD TO REMEMBER

- **Management of factitious disorder (the principle):** no specific drug treatment, treat only the comorbidity; the first line is a supportive, face-saving, non-confrontational therapeutic alliance, not exposure; coordinate through a multidisciplinary team, manage countertransference and splitting, minimise iatrogenic investigation, and for factitious imposed on another let safeguarding override everything (Kaplan and Sadock CTP 2024).

HOLD THIS

Factitious disorder is the deliberate, deceptive falsification or induction of signs or symptoms with an *internal* motive (the sick role) and *no* external incentive, which is exactly what separates it from malingering (external reward) and from the unconscious somatic disorders (no deliberate production); Munchausen syndrome is its severe wandering form (pseudologia fantastica plus peregrination), factitious imposed on another / Munchausen by proxy is a form of abuse in which the perpetrator, not the victim, is diagnosed and safeguarding comes first, and management is a non-confrontational therapeutic stance with no specific drug, treating only the comorbidity.

5 · Malingering and its differentiation from factitious disorder

This is the discrimination step of the somatic chapter, the point where every disorder met so far is separated by asking two questions rather than one: is the symptom *produced*, and if so, *why*. The genuine **somatic disorders** answer the first question with no, the symptom is real and not deliberately made; malingering and factitious disorder both answer yes, the symptom is feigned, and then part company on the second question, the motive. Examiners love this space precisely because it is a two-axis grid and a vignette can be walked through it cleanly, so the whole topic reduces to holding one figure in the head.

How to use this page. Fix malingering first, its definition, its status as a condition rather than a disorder, and the clinical pointers that raise suspicion. Then recall factitious disorder in a single frame so the contrast is sharp. Then learn the two discriminators the paper actually tests: the **voluntariness**-by-incentive grid that separates the two feigned conditions from each other and

from the genuine disorders, and the fuller five-way map that places somatic symptom disorder, illness anxiety disorder, conversion and these two side by side. The single error the whole topic is built to prevent is confusing factitious disorder, where no external incentive is present, with malingering, where one is.

Disorder	Core feature	Symptom production	External incentive	The discriminator
Somatic symptom d.	distressing somatic symptom(s) plus excessive thoughts, feelings or behaviours (Criterion B)	genuine, not feigned	**No**	the positive psychological criterion; the symptom may be medically explained
Illness anxiety d.	preoccupation with having a serious illness; minimal actual somatic symptoms	genuine, not feigned	**No**	the fear is of the illness, not the somatic burden
Conversion / FND	a neurological symptom incompatible with disease; positive signs on examination	not consciously feigned	**No**	positive functional signs (Hoover, entrainment); taught in the Dissociative notes
Factitious disorder	signs or symptoms deliberately produced or falsified	consciously feigned	**No** (internal sick role)	feigned but NO external gain; the motive is the sick role
Malingering	symptoms feigned or exaggerated	consciously feigned	**Yes** (external gain)	feigned WITH an external incentive; not a disorder

Read down the external-incentive column: it is the single line that separates factitious disorder (feigned, no external gain) from malingering (feigned, external gain).

Fig 18.3 The somatic and related disorders discriminated. Somatic symptom disorder and illness anxiety disorder are genuine, not feigned, and carry no external incentive; they are told apart by whether the problem is the symptom burden with a positive psychological criterion or a preoccupation with having an illness. Conversion or functional neurological symptom disorder is also not consciously feigned and is recognised by its positive signs on examination, taught in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes. The two feigned conditions are separated by one thing only: factitious disorder is feigned for the internal reward of the sick role with no external gain, whereas malingering is feigned for an external incentive and is not a mental disorder at all.

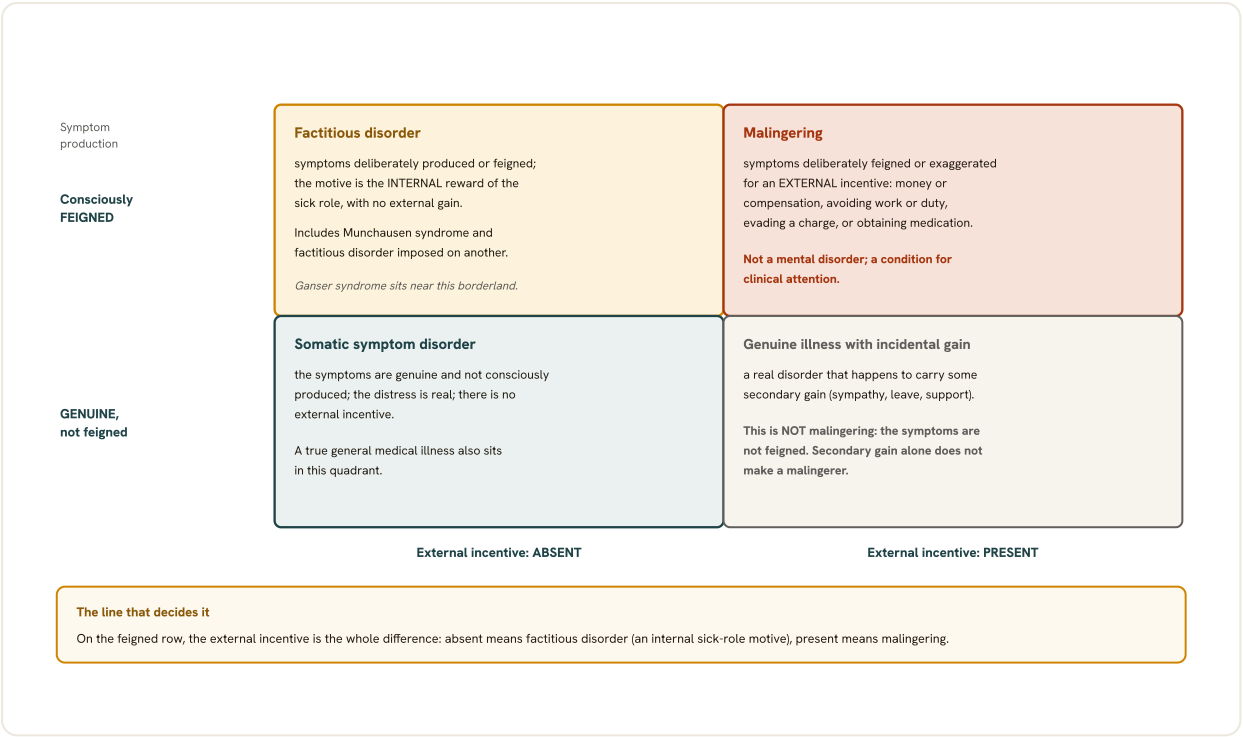


Fig 18.4 Feigning by incentive. Two questions place any of these presentations. First, are the symptoms consciously feigned or genuine? Somatic symptom disorder and a true medical illness are genuine and sit on the lower row; factitious disorder and malingering are feigned and sit on the upper row. Second, is there an external incentive? On the feigned row this is the entire distinction: factitious disorder is feigned for the internal reward of occupying the sick role, with no external gain, while malingering is feigned for an external incentive such as money, avoiding duty or evading a charge, and is not a mental disorder. The lower-right quadrant is the common trap: a genuine illness that carries some incidental secondary gain is not malingering, because nothing is being feigned.

5.1 Malingering: feigning driven by an external incentive

Not a disorder, a condition, defined by the motive behind the feigning. The essential feature of malingering is the intentional production of false or grossly exaggerated physical or psychological symptoms, motivated by an **external incentive** such as avoiding military duty, avoiding work, obtaining financial compensation, evading criminal prosecution, or obtaining drugs (DSM-5-TR 2022; Kaplan and Sadock CTP 2024). Two features anchor it. First, the symptoms are under voluntary control and the **feigning** is conscious and deliberate; the person is aware of the presentation as a strategy. Second, and decisively, the motive is external: some tangible reward is sought, or some obligation avoided. Because of that motive it is coded in DSM-5-TR as Z76.5, a condition that may be a focus of clinical attention and expressly *not* a mental disorder. It may even be adaptive in the right context, the classic example being a captive who feigns illness while held by an enemy in wartime, which is why it is described neutrally as illness behaviour rather than psychopathology.

GOOD TO REMEMBER

- **Malingering (the condition):** intentional production of false or grossly exaggerated physical or psychological symptoms motivated by an **external incentive** (avoiding work or service, financial compensation, evading prosecution, obtaining drugs); coded Z76.5 as a condition for clinical attention, *not* a mental disorder. The single defining criterion is the external incentive; remove it and the label cannot stand.

5.2 The pointers that raise suspicion

Suspect, do not diagnose, on a combination of pointers. DSM-5-TR states that malingering should be *strongly suspected* when any combination of four features is present (DSM-5-TR 2022). These are a medicolegal context (the person is referred by an attorney, or self-refers while litigation or criminal charges are pending); a marked discrepancy between the claimed distress or disability and the objective findings; a lack of cooperation with the evaluation and with the prescribed treatment; and the presence of antisocial personality disorder. The word to hold is *suspected*: no single pointer confirms anything, and the diagnosis requires firm, documented evidence gathered across time, examiners and settings, with collateral information weighed carefully. The clinician's role here is medical, to assess the presentation and document inconsistency in a non-pejorative way, not to pronounce on honesty or fraud.

DSM-5-TR POINTER	WHAT IT LOOKS LIKE
Medicolegal context	**Attorney referral, or self-referral while litigation or criminal charges are pending**
Discrepancy	**Claimed stress or disability far exceeds the objective findings and observed behaviour**
Non-cooperation	**Poor engagement with the evaluation and with the prescribed treatment regimen**
Antisocial personality disorder	**Present as an associated feature (a pointer, not proof, and not a prerequisite)**

The four DSM-5-TR features that should raise suspicion of malingering; any combination warrants suspicion, none alone confirms it (DSM-5-TR 2022).

PEARL

Certainty in malingering is *graded, not binary*. The literature codes it along a ladder, indeterminate, then strongly suspected, then provisional, then probable, then deemed likely present, according to how far the pointers, associated features and collateral corroboration line up (Kaplan and Sadock CTP 2024). Genuine illness, by contrast, is consistent across examiners, contexts and even when the person is distracted; feigned illness tends to be inconsistent and shifting.

COMMON TRAP

Treating antisocial personality disorder as proof of malingering. It is only one associated pointer. Studies do *not* show that people with antisocial personality disorder malinger more often, or more successfully, than the general population, and mild symptom exaggeration or ordinary impression management is not malingering. A firm attribution needs converging, documented evidence, not a personality label.

SUBTYPES AND DETECTION INSTRUMENTS

Resnick's classical trichotomy (Resnick) names three forms: *pure malingering*, complete fabrication of a non-existent disorder; *partial malingering*, exaggeration of genuinely present symptoms; and *false imputation*, consciously attributing real symptoms to a false, unrelated cause. Structured aids to detection, used mainly in forensic assessment, include the SIRS (Structured Interview of Reported Symptoms), the M-FAST (Miller Forensic Assessment of Symptoms Test), the SIMS (Structured Inventory of Malingered Symptomatology) and the TOMM (Test of Memory Malingering); they support, but never replace, the clinical judgement built on collateral data.

5.3 Factitious disorder in one frame: feigned, but no external incentive

Deliberate deception with an internal motive, to be a patient. Factitious disorder imposed on self (F68.10) is defined by the falsification of physical or psychological signs or symptoms, or the induction of injury or disease, associated with identified deception; the person presents themselves to others as ill, impaired or injured; and, the decisive clause, the deceptive behaviour is evident *even in the absence of obvious external rewards*, and is not better explained by another mental disorder such as a psychotic illness (DSM-5-TR 2022). The symptoms are produced intentionally and consciously, exactly as in malingering, but the aim is internal: to occupy the sick role and receive care, attention and medical procedures. This is the classical **primary gain** of the sick role, not the tangible **secondary gain** of the malingerer. The diagnosis rests on objectively identifying the falsification, not on proving the inner motive. Its severe, chronic, wandering form is Munchausen syndrome, named for the Baron of tall tales, estimated at roughly five to ten percent of factitious cases; when the illness is fabricated or induced in another person, usually a dependent, it is factitious disorder imposed on another, and the perpetrator, not the victim, receives the diagnosis.

4	5	5-10%
DSM-5-TR MALINGERING POINTERS	CODED DEGREES OF CERTAINTY	MUNCHAUSEN SHARE OF FACTITIOUS CASES

GOOD TO REMEMBER

- **Factitious disorder imposed on self (the diagnosis, F68.10):** falsification of signs or symptoms, or induction of injury or disease, with identified deception; presents self as ill; the deception is present *even without obvious external rewards*; not better explained by another disorder. The one discriminator to hold is Criterion C, the absence of an external reward, which is exactly the axis that separates it from malingering.

5.4 Voluntariness by incentive: the factitious versus malingering grid

Two feigned conditions, told apart on one axis. Both malingering and factitious disorder are, by definition, deliberately produced, so **voluntariness** of symptom production is *shared* and cannot separate them; what separates them is the incentive. This is the whole of the **factitious versus malingering** discrimination: an external incentive present points to malingering (secondary gain, a reward or an avoided obligation), an external incentive absent points to factitious disorder (primary gain, the sick role itself). The genuine somatic disorders sit off this axis entirely, because their symptoms are not intentionally produced at all. The accompanying figure lays this out as a

two-by-two of intentional-or-not production against external-or-internal incentive; the same content is tabulated below (New Oxford Textbook of Psychiatry; DSM-5-TR 2022).

CONDITION	SYMPTOM INTENTIONALLY PRODUCED?	INCENTIVE PRESENT
Genuine somatic disorder (somatic symptom disorder, conversion)	No, involuntary and unintentional	**Neither; symptoms are not made to a purpose (secondary gain may coexist but is not the cause)**
Factitious disorder	Yes, intentional and conscious	**Internal only, the sick role (primary gain); external reward absent**
Malingering	Yes, intentional and conscious	**External incentive present, a tangible reward or avoided obligation (secondary gain)**

The voluntariness-by-incentive grid; production separates the genuine disorders from the two feigned conditions, and the external incentive separates malingering from factitious disorder (New Oxford Textbook of Psychiatry).

RULE **Same production, different incentive.** Malingering and factitious disorder are both consciously feigned; the discriminator is the external incentive, present in malingering (secondary gain), absent in factitious disorder (the internal sick role, primary gain).

5.5 The fuller somatic-disorders discriminator

Five neighbours placed on production and motivation. The examiner's synthesis extends the grid across the whole chapter, so that **somatic versus factitious** versus malingering can be read off two columns at a glance. Somatic symptom disorder carries genuine, not feigned, distressing symptoms with an excessive psychological response and no external incentive; illness anxiety disorder is genuine health fear on a largely quiet body; conversion, or functional neurological symptom disorder, is a genuine deficit whose *internal inconsistency* is demonstrated by positive signs rather than being deliberately produced. Factitious disorder is feigned with no external incentive, and malingering is feigned with an external incentive. The full bedside recognition of conversion, its positive signs and its management, is developed in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes, and body dysmorphic disorder, which belongs on the obsessive-compulsive spectrum, in the Anxiety, OCD and trauma-related disorders notes. The figure alongside renders this as the five-row discriminator map.

CONDITION	SYMPTOMS GENUINE OR FEIGNED	EXTERNAL INCENTIVE	THE ONE-LINE DISCRIMINATOR
Somatic symptom disorder	Genuine, not feigned	Absent	**Real distressing symptom plus excessive thoughts, feelings and behaviours (positive psychological criterion)**
Illness anxiety disorder	Genuine, not feigned	Absent	**Fear of having or acquiring illness on a quiet body; symptoms absent or mild**
Conversion / functional neurological symptom disorder	Genuine, not intentionally produced	Absent	**Positive signs of internal inconsistency (for example Hoover's sign) rule it in**
Factitious disorder	Feigned, intentionally produced	Absent	**Deception to occupy the sick role; primary gain, no external reward**
Malingering	Feigned, intentionally produced	Present	**External incentive drives the feigning; secondary gain**

The five-way somatic-disorders discriminator, keyed on symptom production and on motivation; the two feigned conditions split only on the external incentive (Kaplan and Sadock CTP 2024; New Oxford Textbook of Psychiatry; DSM-5-TR 2022).

GOOD TO REMEMBER

- **The discriminator (the synthesis):** ask production first, then motivation. Genuine somatic disorders are not intentionally produced. Of the two feigned conditions, factitious disorder has no external incentive (sick role, primary gain) and malingering has an external incentive (secondary gain). That single external-incentive axis carries the **differentiation**.

TRAP **Confusing factitious disorder with malingering.** Both are consciously feigned, so they feel alike; the difference is the external incentive. Factitious disorder has none (the motive is the sick role); malingering has one. Reading a compensation or medicolegal claimant as factitious, or a sick-role patient as a malingerer, inverts the whole grid.

INDIA

Malingering surfaces most in Indian medicolegal work, where it is examined rather than treated: disability and compensation certification, fitness assessments, and above all the malingered insanity defence, where a defendant may feign mental illness to influence criminal responsibility (Jiloha, Forensic Psychiatry, An Indian Perspective). Assessment leans on structured aids such as the SIRS, M-FAST, SIMS and TOMM alongside collateral history, and Indian professional guidance recognises malingering as one of the grounds on which a doctor may decline to continue a therapeutic relationship. The register throughout is medical and non-accusatory: the task is to document inconsistency and weigh evidence, not to brand a person dishonest, which also guards against the opposite error of dismissing a genuinely ill or culturally distressed patient, such as one presenting somatically, as a fraud.

HOLD THIS

Malingering and factitious disorder are both consciously feigned, so voluntariness of production does not separate them; the discriminator is the external incentive, present in malingering (secondary gain, coded Z76.5 as a condition and not a mental disorder, strongly suspected on the four DSM-5-TR pointers) and absent in factitious disorder (Criterion C, the deception persists without obvious external reward, the motive being the sick role and primary gain), while the genuine somatic disorders, somatic symptom disorder, illness anxiety disorder and conversion, are not intentionally produced at all, so the whole map reduces to two questions asked in order, is the symptom produced, and if so, for an external incentive or for the sick role.

6 · Body dysmorphic disorder and bodily distress

Two disorders, one abbreviation, opposite chapters. This short topic sits at the somatic/BDD boundary and its whole job is to keep two look-alikes apart. **Body dysmorphic disorder** is a preoccupation with a perceived defect in appearance and lives on the **obsessive-compulsive and related disorders** spectrum; **bodily distress disorder** is the ICD-11 label for the symptom-led somatic presentation that replaced somatoform disorder. Both get shortened to "BDD" in the wards and both were once filed as somatoform, which is exactly why examiners like the trap. Name each, place each, and know the one mapping the examiner wants: how ICD-11 bodily distress disorder lines up against DSM-5 somatic symptom disorder.

This is a naming and cross-reference note, not the full teaching. The complete work-up of body dysmorphic disorder, its phenomenology, comorbidity, suicidality and management, belongs with its obsessive-compulsive kin and is developed in the Anxiety, OCD and trauma-related disorders notes. The two somatic siblings that bracket it, somatic symptom disorder and illness anxiety disorder, are their own topics in these notes, and the wider transcultural frame, including Dhat as a culturally patterned bodily-distress presentation, is in the Consultation-liaison, geriatric and transcultural psychiatry notes.

6.1 Body dysmorphic disorder on the OCRD spectrum

A perceived flaw, not a real one. Body dysmorphic disorder is a preoccupation with one or more perceived defects or flaws in physical appearance that are *not observable or appear only slight to others* (DSM-5-TR 2022, Criterion A). The person performs repetitive behaviours (mirror

checking, excessive grooming, skin picking, reassurance seeking) or mental acts (comparing their appearance with others) in response to the concern (Criterion B), which causes clinically significant distress or impairment (Criterion C) and is not better explained by an eating disorder's concern with fat or weight (Criterion D). There is no duration threshold. Two riders matter: the muscle dysmorphia specifier (preoccupation that the build is too small or insufficiently muscular, seen mostly in men), and an insight specifier graded good-or-fair, poor, or absent insight with delusional beliefs, the last absorbing what older systems called delusional dysmorphophobia.

It migrated out of the somatic chapter. Historically dysmorphophobia was treated as a variant of hypochondriasis and filed with the somatoform disorders (Companion to Psychiatric Studies), which is the root of the confusion. DSM-5 and ICD-11 both moved it firmly onto the obsessive-compulsive and related disorders grouping (ICD-11 code 6B21), alongside hypochondriasis, olfactory reference disorder and hoarding, on the strength of the shared engine of intrusive preoccupation plus repetitive checking and reassurance. That placement on the OCRD spectrum is the single fact this note exists to fix. The full teaching, the bdd cross-reference for phenomenology, comorbidity and treatment, is carried in the Anxiety, OCD and trauma-related disorders notes.

RULE **Appearance, not illness, and OCRD, not somatic.** A preoccupation with a perceived *appearance* defect that others cannot see, driven by checking and comparing, is body dysmorphic disorder and it belongs on the obsessive-compulsive and related disorders spectrum, not among the somatic disorders.

GOOD TO REMEMBER

- **Body dysmorphic disorder (the syndrome):** preoccupation with one or more perceived defects or flaws in appearance that are unobservable or slight to others, plus repetitive behaviours (mirror checking, grooming, reassurance seeking) or mental acts (comparing with others), causing distress or impairment and not explained by an eating disorder; the defining criterion is the unobservable-defect preoccupation, the classic specifier is muscle dysmorphia, and its home is the OCRD spectrum (6B21), not the somatic chapter (DSM-5-TR 2022; ICD-11 CDDR).

6.2 Bodily distress disorder and its map to somatic symptom disorder

The ICD-11 replacement for somatoform. Bodily distress disorder (ICD-11 code 6C20) is the major ICD-11 change that swept away ICD-10's somatoform disorders. It is characterised by the presence of bodily symptoms that are distressing to the person and by an *excessive* level of attention directed toward those symptoms, which typically leads to repeated contact with health services (ICD-11 CDDR; Kaplan and Sadock 2024). Like DSM-5's construct, it is defined by *positive* psychological features, the distress and the excessive thoughts and behaviours, rather than by the old requirement that symptoms be medically unexplained. It is graded on a continuum as mild, moderate or severe by the impact on functioning, and it sits in the ICD-11 grouping "disorders of bodily distress and bodily experience" alongside the rare body integrity dysphoria.

The mapping the examiner wants. ICD-11 bodily distress disorder maps onto DSM-5 somatic symptom disorder: both are symptom-led, both rest on the positive psychological criterion, and

both replaced the medically-unexplained model. The two are easily held side by side. They are close cousins rather than identical twins, ICD-11 foregrounds the excessive attention and repeated healthcare contact, DSM-5 foregrounds disproportionate thoughts, feelings and behaviours, but for a one-line answer they are the same idea in two manuals.

AXIS	ICD-11 BODILY DISTRESS DISORDER (6C20)	DSM-5 SOMATIC SYMPTOM DISORDER
Replaces	**ICD-10 somatoform disorders**	**DSM-IV somatoform disorders**
Core feature	Distressing bodily symptoms plus excessive attention to them	Distressing somatic symptoms plus disproportionate thoughts, feelings, behaviours
Basis of diagnosis	**Positive psychological features, not absence of medical explanation**	**Positive psychological criterion, not medically unexplained**
Severity grading	Mild, moderate, severe by functional impact	Mild, moderate, severe; specify persistent, predominant pain
Grouping	Disorders of bodily distress and bodily experience	Somatic symptom and related disorders

ICD-11 bodily distress disorder against DSM-5 somatic symptom disorder; the one line to hold is that both are the symptom-led, positive-criterion successors to somatoform disorder (ICD-11 CDDR; DSM-5-TR 2022; Kaplan and Sadock 2024).

TRAP **"BDD" is not one thing.** Body dysmorphic disorder is an appearance-preoccupation on the OCRD spectrum; bodily distress disorder is the ICD-11 somatic-symptom successor to somatoform disorder. Same abbreviation, different chapters, do not let the letters merge them.

GOOD TO REMEMBER

- **Bodily distress disorder (the syndrome):** ICD-11 6C20, distressing bodily symptoms with an excessive level of attention directed to them and repeated healthcare contact, defined by positive psychological features rather than absence of a medical explanation and graded mild to severe; it is the ICD-11 replacement for somatoform disorder and maps onto DSM-5 somatic symptom disorder (ICD-11 CDDR; Kaplan and Sadock 2024).

6.3 Where each is taught, and the one management anchor

Route the reader, then give the anchor. Keep the full detail where it belongs: body dysmorphic disorder with its obsessive-compulsive relatives in the Anxiety, OCD and trauma-related disorders notes, and the symptom-led somatic disorders in the somatic symptom disorder and illness anxiety disorder topics here. For the one management fact worth carrying: body dysmorphic disorder is treated first-line with CBT that centres on exposure and response prevention, and where symptoms are moderate to severe an SSRI is added, used at the higher doses and the longer trial familiar from obsessive-compulsive disorder rather than the lower antidepressant doses of depression (NICE CG31; Maudsley Prescribing Guidelines). Bodily distress disorder is managed as its somatic siblings are, physician-centred care and psychological therapy first, with drugs reserved for a genuine comorbid depression or anxiety, developed in the somatic symptom disorder topic.

GOOD TO REMEMBER

- **Management anchor (guideline):** body dysmorphic disorder is first-line CBT with exposure and response prevention, adding an SSRI for moderate-to-severe illness at OCD-range higher doses and a longer trial (NICE CG31, obsessive-compulsive disorder and body dysmorphic disorder); bodily distress disorder follows the somatic pathway, physician-centred care and psychological therapy first, medication only for a comorbid mood or anxiety disorder.

INDIA

Bodily distress disorder fits the Indian clinic closely: symptom-led somatic presentations dominate general practice, and the ICD-11 positive-criterion frame is a better match than the old "medically unexplained" label for patients who present the body first. The culturally patterned bodily-distress presentation of Dhat, and its transcultural handling, are developed in the Consultation-liaison, geriatric and transcultural psychiatry notes. Body dysmorphic disorder is easy to miss here because it hides behind repeated requests for cosmetic and dermatological procedures rather than a psychiatric complaint, so the referral often arrives from the skin or surgery clinic, not from the patient naming a fear.

2.4%	13 to 15%	16 to 17
BODY DYSMORPHIC DISORDER POINT PREVALENCE, ADULTS (DSM-5-TR)	AMONG GENERAL COSMETIC SURGERY PATIENTS (DSM-5-TR)	MEAN AGE AT ONSET, BODY DYSMORPHIC DISORDER (YEARS)

HOLD THIS

Body dysmorphic disorder is an appearance-defect preoccupation on the OCRD spectrum (ICD-11 6B21, DSM-5 obsessive-compulsive and related disorders), unobservable or slight defect plus checking and comparing, muscle dysmorphia and insight specifiers, full teaching in the Anxiety, OCD and trauma-related disorders notes; bodily distress disorder is the different beast, ICD-11 6C20, the positive-criterion successor to somatoform disorder that maps onto DSM-5 somatic symptom disorder; same three letters, opposite chapters.

7 · Management of medically unexplained symptoms

This topic takes the somatic patient from diagnosis to a plan. **Medically unexplained symptoms** (MUS) are bodily complaints that persist without a physical disease that fully accounts for them; over decades the label has drifted from "somatization" through "medically unexplained symptoms" to "functional somatic symptoms" (Kaplan and Sadock CTP 2024). The examinable point is that the **management of medically unexplained symptoms** is *not* a hunt for the missing disease and *not* a prescription. It is a physician-led, relationship-based, psychological-first package in which drugs are held back deliberately. Get the order of moves right and you have the marks: physician-centred care first, structured psychological work next, and medication only for a genuine comorbidity.

How to use this page. Fix the guideline spine first, that being the Indian Psychiatric Society somatoform CPG (IPS_CPG 2020) and the WHO mhGAP OTH module (WHO mhGAP 2016), because both put non-pharmacological, physician-centred strategies as the first line and both restrict medication for the somatic symptoms themselves. Then learn the **reattribution** model as

the signature technique, the psychological evidence, the one restrictive drug rule, and the follow-up posture. Close with the functional somatic syndromes, which are managed on exactly these principles. The one cross-chapter link to keep is that the positive signs and specific management of a conversion presentation belong to the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes.

Medically unexplained symptoms (MUS)
Distressing bodily symptoms not fully explained by a detectable physical disease; a description, not a single diagnosis.

Physician-centred care
A management stance in which one coordinating clinician builds an alliance, validates the distress, restrains testing, and shifts focus to functioning.

Reattribution
A brief structured technique that helps the patient re-link bodily symptoms to psychosocial stress, moving from cause to functioning.

7.1 Physician-centred care: the foundation of management

One coordinating clinician, one continuing relationship, and restraint. The guideline foundation is physician-centred care (IPS_CPG 2020; WHO mhGAP 2016): emphasise non-pharmacological strategies as the first line of treatment, and build management on a small number of durable moves. A single named clinician holds the case, so care stops fragmenting across specialists. That clinician establishes a **therapeutic relationship**, the alliance that carries every other step and is undermined by prescription-drug dependence, benzodiazepine dependence in particular, which the IPS CPG flags explicitly. The clinician validates that the symptoms and the distress they cause are real and not imaginary, restricts unnecessary diagnostic testing and specialist referrals to those with a clear medical indication such as abnormal vital signs, identifies and treats any concurrent anxiety or depression early, and shifts the clinical focus away from symptoms and toward functioning. WHO mhGAP adds two explicit "do not" moves that sit inside this foundation, that being not ordering further investigations without a clear indication and not giving vitamin injections or other ineffective treatments.

ELEMENT OF PHYSICIAN-CENTRED CARE	WHAT IT MEANS IN THE ROOM	WHY IT IS THE ACTIVE INGREDIENT
Single coordinating clinician	One named doctor holds and continues the case	**Stops fragmented care and repeated doctor-shopping**
Therapeutic relationship	A trusting, continuing alliance with the patient	**The vehicle every other step travels on**
Validate symptoms and distress	State plainly that the symptoms are real, not imagined	**Removes the felt need to keep proving illness**
Restrict testing and referrals	Investigate only on a clear medical indication	**Breaks the iatrogenic loop of chasing disease**
Treat comorbidity early	Screen and treat concurrent depression or anxiety	**Relieves a driver of the somatic burden itself**
Shift toward functioning	Target coping and function, not symptom eradication	**A realistic, sustainable goal that reduces distress**

The six elements of physician-centred care, the guideline-anchored first line for medically unexplained symptoms (IPS_CPG 2020, WHO mhGAP 2016), set out step by step here.

MNEMONIC

CARVES

The physician-centred foundation, the way it carves the plan out of the chaos. **C**oordinating clinician, one named doctor; **A**lliance, the therapeutic relationship; **R**estrict tests and referrals; **V**alidate the real symptoms and distress; treat **E**motional comorbidity early; **S**hift from symptoms to functioning. Six moves, no prescription among them.

RULE **Physician-centred care is the treatment, not the waiting room.** In MUS the coordinating clinician, the therapeutic alliance, validation and restraint on testing *are* the active first-line intervention (IPS_CPG 2020); the alliance is the first move, not the prescription.

GOOD TO REMEMBER

- **Physician-centred care (the management step):** the guideline first line (IPS_CPG 2020, WHO mhGAP 2016), being a single coordinating clinician, a therapeutic relationship, validation that the symptoms and distress are real, restriction of unnecessary tests and referrals, early treatment of comorbid mood or anxiety, and a shift toward functioning. The first move is the alliance, and non-pharmacological strategies lead.

7.2 The reattribution model

A brief four-stage technique that re-links body to mind. Reattribution is the classic structured method for MUS in primary and general-hospital care, originally taught by Goldberg and Gask, and it runs in four stages (AIIMS Consultation Liaison handbook 2020). The first stage is *feeling understood*: focused history, focused physical examination and supportive listening to build the alliance. The second stage *broadens the agenda*: give feedback, acknowledge the concerns, and pick up cues of underlying distress. The third stage is the *normalising link*: connect the bodily symptoms to psychosocial problems, negotiate that unnecessary tests and doctor-shopping will

be curtailed with the assurance that tests will be arranged if genuinely needed, and target improved functioning and reduced distress rather than complete symptom removal; scheduling regular follow-up here both strengthens the alliance and prevents the patient from generating a new symptom as a ticket to a new physician. The fourth stage *makes the change*: agree a management plan and negotiate the goals of treatment. The model is effective, feasible and acceptable in routine primary care.

REATTRIBUTION STAGE	TASK IN THE ROOM	THE MOVE TO HOLD
Feeling understood	Focused history and examination, supportive listening	**Build the alliance before anything else**
Broadening the agenda	Give feedback, acknowledge concerns, read distress cues	**Open the emotional agenda without confrontation**
Making the link	Normalise, connect symptoms to psychosocial stress	**Aim at functioning, curb needless testing**
Negotiating the plan	Agree a management plan and shared goals	**Convert insight into an actionable plan**

The four stages of the reattribution model, from feeling understood to negotiating a plan (AIIMS Consultation Liaison handbook 2020, after Goldberg and Gask), run in order here.

GOOD TO REMEMBER

- **Reattribution (the management step):** a brief four-stage technique, that being feeling understood (focused history and examination), broadening the agenda (feedback and distress cues), making the link (normalise symptoms to psychosocial stress, aim at functioning, curb needless testing), and negotiating the plan. The guiding principle is to move from proving or disproving disease to restoring function.

7.3 The psychological therapies: CBT, psychoeducation, relaxation, mindfulness

Cognitive behaviour therapy leads, with a brief package close behind. The structured psychological evidence is the substance of the plan once the alliance is set. Cognitive behaviour therapy for somatic presentations, the **cbt somatic** evidence base, is the first-line psychotherapy (IPS_CPG 2020): it targets the catastrophic misinterpretation of bodily sensations, adds relaxation and pleasurable, meaningful activities, and rebuilds functioning through behavioural activation and cognitive restructuring; sessions typically range from four to sixteen over roughly three months. Running alongside it as an alternative first-line approach is a brief intervention that bundles psychoeducation, relaxation therapy and reattribution training. Psychoeducation emphasises the *mechanism* of symptoms over their cause, acknowledges the symptoms as real, communicates normal clinical and test findings, elicits the patient's own explanatory model, and discusses the links between emotional stress and bodily sensation, optionally paired with a consultation letter to the referring physician. Relaxation therapy means progressive muscular relaxation and slow diaphragmatic breathing. For a hypochondriacal, illness-anxiety flavoured presentation the IPS CPG puts CBT with cognitive restructuring and exposure and response prevention first line, with mindfulness-based cognitive therapy or acceptance and commitment therapy as second line; for persistent somatoform pain it puts CBT plus biofeedback first line.

WORKED EXAMPLE

A woman in her thirties has had two years of shifting aches, fatigue and gut symptoms, three normal specialist work-ups and a growing conviction that "something is being missed". Rather than order a fourth panel, her one coordinating clinician validates the symptoms as real, restricts new testing to a clear indication, and starts reattribution: focused examination to feel understood, then a gentle link between symptom flares and a difficult caregiving load, then a shared plan of scheduled monthly reviews with a functioning goal of returning to part-time work. Referral for cognitive behaviour therapy targets her catastrophic reading of each new sensation. No antidepressant is started, because there is no comorbid depression and no dominant pain syndrome.

GOOD TO REMEMBER

- **Psychological therapy in MUS (the management step):** the guideline first line (IPS_CPG 2020) is cognitive behaviour therapy targeting catastrophic misinterpretation and rebuilding function, with an alternative brief package of psychoeducation, relaxation and reattribution; psychoeducation stresses mechanism over cause. For illness-anxiety presentations, CBT with cognitive restructuring and exposure and response prevention leads, mindfulness-based approaches second line.

7.4 The pharmacological rule: restraint first, drugs for the comorbidity

Do not medicate the somatic symptoms; medicate a genuine comorbidity. The single most testable management fact here is a "do not": under the WHO mhGAP OTH module, do NOT prescribe anti-anxiety or antidepressant medicines for medically unexplained somatic complaints unless advised by a specialist (WHO mhGAP 2016). Medication is not the first-line treatment of the somatic symptoms themselves. It becomes appropriate only when there is a genuinely co-existing depressive or anxiety disorder, or a dominant chronic-pain component. Where mood or anxiety comorbidity dominates, the **ssri somatic** question is answered by treating that disorder on its own merits, so an SSRI is reasonable. Where persistent pain dominates, the analgesic antidepressants are preferred: an SNRI such as duloxetine, typically **60 mg** once daily, or a low-dose tricyclic such as amitriptyline for its analgesic action. The evidence keeps drugs firmly in a supporting role: the Cochrane review of pharmacological interventions for somatoform disorders (Kleinstauber 2014) found only low to very-low-quality evidence that new-generation antidepressants reduce somatic symptoms, so drugs supplement, and never replace, physician-centred and psychological care. Polypharmacy is avoided, and side effects matter especially here because they can amplify symptom perception.

TRAP **Reflexively prescribing an antidepressant or anxiolytic for the somatic symptoms.** WHO mhGAP (2016) says do not, unless a specialist advises; reserve drugs for a genuine comorbid depression or anxiety disorder, or a persistent-pain component, and never as a substitute for physician-centred and psychological care.

GOOD TO REMEMBER

- **Medication in MUS (the drug principle):** the guideline rule (WHO mhGAP 2016) is not to prescribe anti-anxiety or antidepressant drugs for medically unexplained somatic symptoms unless a specialist advises. Reserve them for comorbid depression or anxiety, or for a dominant chronic-pain component, where an SNRI (duloxetine, typically 60 mg once daily) or a low-dose tricyclic (amitriptyline) is preferred; deep antidepressant pharmacology sits in the Mood disorders: pharmacotherapy notes.

7.5 Follow-up: shifting from symptoms to functioning

Scheduled, time-based reviews replace symptom-driven visits. The management does not end at the first plan; the follow-up posture is itself guideline content. WHO mhGAP asks the clinician to review the person in 2 to 4 weeks if symptoms do not improve or worsen, and to reconsider the protocol or consult a specialist if there is no improvement or repeated insistence on further investigation (WHO mhGAP 2016). The IPS CPG frames maintenance around encouraging functioning and coping, keeping stable patients on roughly one visit every 1 to 2 months, and educating patient and family that minor symptom variations are common and need not be attributed to new pathology (IPS_CPG 2020). The deep principle across both is that visits are scheduled by the calendar, not triggered by each new symptom, which is precisely what stops a fresh complaint becoming the only permit to be seen.

15	4	2-4
PHQ-15 HIGH-SEVERITY CUT-OFF (0 TO 30 SCALE)	STAGES OF THE REATTRIBUTION MODEL	MHGAP SYMPTOM-REVIEW WINDOW (WEEKS)

PEARL

Grade severity with a scale to pitch the intensity of care: the PHQ-15 rates fifteen common somatic symptoms, each scored 0 to 2, for a total out of a possible 30, with cut-points at 5, 10 and 15 marking low, medium and high burden. The reproduced PHQ-15 form sits with the somatic-symptom scales; here the high-severity cut-off, at 15, is the number to carry.

GOOD TO REMEMBER

- **Follow-up in MUS (the management step):** the guideline posture (WHO mhGAP 2016, IPS_CPG 2020) is calendar-scheduled review, reassess in 2 to 4 weeks if no improvement, keep stable patients to roughly one visit every 1 to 2 months, and educate that minor symptom variation is normal and not new disease. Time-based visits replace symptom-triggered ones.

7.6 The functional somatic syndromes: chronic fatigue syndrome, fibromyalgia, phantom limb pain

Named syndromes, same management principles. Several defined conditions sit close to MUS as functional somatic syndromes and are managed on the same physician-centred, psychological-first footing, with medication reserved for a pain or comorbidity component. Chronic fatigue syndrome is defined by severe, disabling mental and physical fatigue that is not relieved by rest and is worsened by exertion, persisting for at least several months and not explained by another condition; graded activity and cognitive behaviour therapy are the mainstay psychological

approaches (Shorter Oxford; New Oxford). Fibromyalgia is defined by chronic widespread pain with tenderness, fatigue, unrefreshing sleep and cognitive complaints; here an antidepressant with an analgesic action, an SNRI such as duloxetine, has an established role alongside exercise and CBT, illustrating the "pain component" exception to the drug rule (Stahl; Kaplan and Sadock CTP 2024). Phantom limb pain is pain experienced in a limb that has been amputated, distinct from localised stump pain, and it responds in part to the analgesic antidepressants and to graded, functionally oriented rehabilitation (Kaufman's Clinical Neurology for Psychiatrists; Kaplan and Sadock CTP 2024). Across all three, the trap is to keep re-investigating a settled functional diagnosis rather than treating it.

GOOD TO REMEMBER

- **Chronic fatigue syndrome (the syndrome):** severe, disabling fatigue not relieved by rest and worsened by exertion, for at least several months, unexplained by another condition; the discriminator is post-exertional worsening, and graded activity plus CBT lead.
- **Fibromyalgia (the syndrome):** chronic widespread pain with tenderness, fatigue and unrefreshing sleep; the discriminator is the widespread pain, and an analgesic antidepressant (an SNRI such as duloxetine) plus exercise and CBT is the standard approach.
- **Phantom limb pain (the syndrome):** pain felt in an amputated limb, distinct from stump pain confined to the injury; the discriminator is the referred location in the absent limb, managed with analgesic antidepressants and functionally oriented rehabilitation.

INDIA

Somatic presentation is the Indian norm rather than the exception: emotional distress is very commonly first brought to the clinician as bodily symptoms, so a large share of primary-care and general-hospital attenders sit in exactly this management space, and the Indian evidence base is anchored by the IPS_CPG 2020 guideline on psychotherapies for somatoform disorders and by indigenous tools such as the Scale for Assessment of Somatic Symptoms. The most examinable India-specific presentation is the culture-bound Dhat syndrome, a somatic and anxious preoccupation attributed to perceived loss of vital fluid; it is managed with the same physician-centred alliance, validation and psychoeducation rather than reflexive medication, and must be read through a cultural formulation rather than pathologised on its surface content. Its wider transcultural frame and the consultation-liaison service model that most often meets these patients are developed in the Consultation-liaison, geriatric and transcultural psychiatry notes.

HOLD THIS

The management of medically unexplained symptoms is physician-centred and psychological first: one coordinating clinician builds a therapeutic relationship, validates the real symptoms and distress, restricts unnecessary testing and referrals, treats comorbid depression or anxiety early, and shifts the focus from symptoms to functioning, with reattribution and CBT as the first-line psychological work; per WHO mhGAP, anti-anxiety or antidepressant drugs are NOT prescribed for the somatic symptoms themselves unless specialist-advised, and are reserved for a comorbid mood or anxiety disorder or a persistent-pain component (an SNRI such as duloxetine, or low-dose amitriptyline), while chronic fatigue syndrome, fibromyalgia and phantom limb pain are managed on the very same principles.

Sexual dysfunctions, paraphilias and gender

8 · The normal sexual response cycle

Learn the map before the malfunctions. The **sexual response cycle** is the physiological scaffold on which every sexual dysfunction is classified, so it is the first thing to fix before any of the disorders make sense. Both DSM-5-TR and ICD-11 name their sexual dysfunctions by the *phase of response that is disrupted*, which means the examiner who asks you to define hypoactive desire, erectile dysfunction, or premature ejaculation is really asking whether you can place each complaint on this cycle. The topic is small, high-yield, and almost entirely about three named models plus one piece of neuroanatomy.

This note owns the normal frame: the **masters and johnson** four-phase model with its refractory period, Helen Singer Kaplan's triphasic reformulation that added the **desire phase** and turned the cycle into a diagnostic map, Rosemary Basson's circular model of female response, and the autonomic wiring of erection and ejaculation. The dysfunctions themselves, their criteria, and their guideline-anchored management are developed in the sexual dysfunction topics of these notes; the culture-bound frame of Dhat and semen-loss anxiety sits in the Consultation-liaison, geriatric and transcultural psychiatry notes. Keep the whole discussion clinical and schematic, and lean on the accompanying figure of the response-cycle curves.

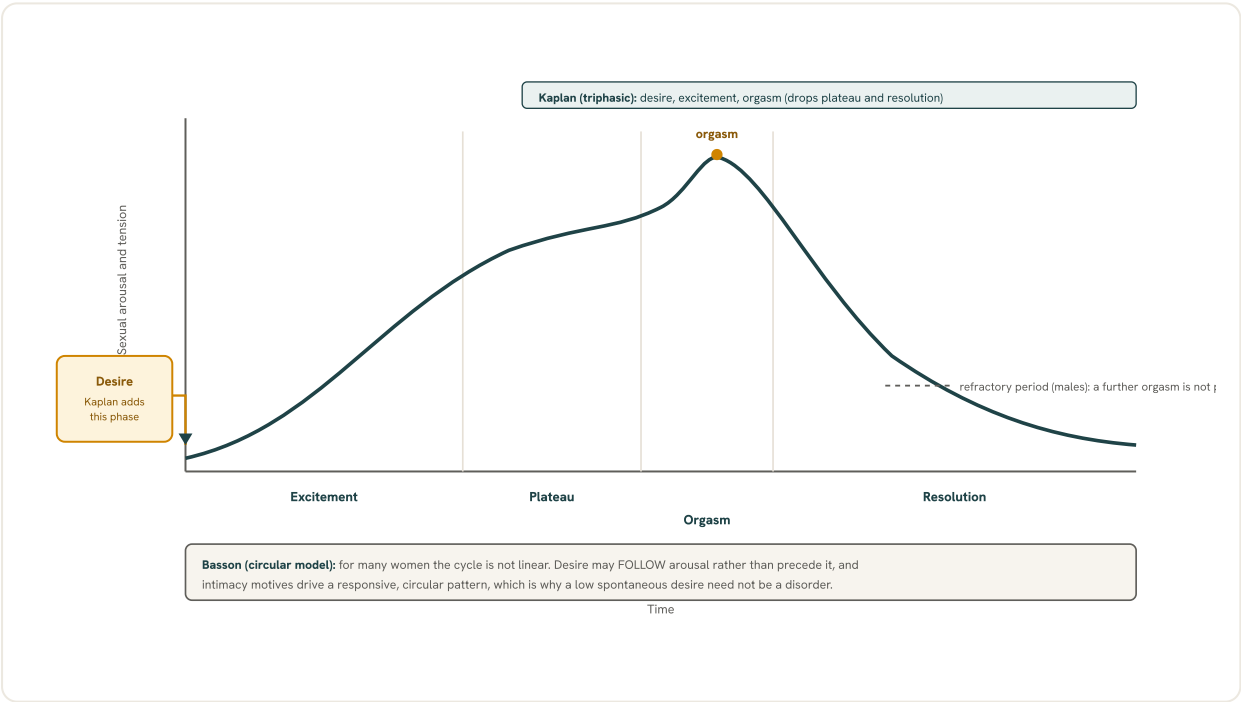


Fig 18.5 The normal sexual response cycle. Masters and Johnson described four sequential phases, drawn here as a single arousal curve: excitement, a sustained plateau, the orgasmic peak, and resolution, with a refractory period in males during which a further orgasm is not possible. Kaplan reframed the cycle as triphasic by adding an initial desire phase and collapsing plateau and resolution, which is the clinically useful version because it separates the desire, arousal and orgasm disorders. Basson's circular model captures a common female pattern in which desire is responsive, following arousal and intimacy rather than preceding them, so that a low level of spontaneous desire is not in itself a dysfunction. The figure is a neutral physiological schematic.

8.1 The Masters and Johnson four-phase model

Four sequential phases. From their laboratory observations, published as *Human Sexual Response* in 1966, Masters and Johnson described the human sexual response cycle as four sequential phases: **excitement**, **plateau**, **orgasm** and **resolution** (Kaplan and Sadock 2024). This is the **four-phase model**, and the two physiological engines running through it are vasocongestion (increased genital blood flow, giving erection in men and clitoral and vaginal engorgement with lubrication in women) and myotonia (rising skeletal and smooth-muscle tension). Excitement is the initial arousal and engorgement; plateau is the sustained high-arousal state just short of climax; orgasm is the brief peak that releases the accumulated tension; and resolution is the return to the unaroused baseline with a sense of well-being.

The refractory period is the sex difference to name. In men, resolution includes a refractory period, a recovery interval during which a further orgasm is physiologically not possible; it is short in youth and lengthens with age. Women characteristically have little or no true refractory period and can return to the orgasm phase with minimal delay, which is the physiological basis of multi-orgasmic capacity (Kaplan and Sadock 2024). That single asymmetry is the classic viva point and is exactly what the accompanying figure of the response-cycle curves is drawn to show.

PHASE (MASTERS AND JOHNSON)	CORE PHYSIOLOGICAL EVENTS
Excitement	**Onset of arousal: vasocongestion begins, penile erection, clitoral and vaginal engorgement with lubrication, breast and nipple changes, rising heart rate and blood pressure**
Plateau	Arousal sustained near its peak: testes elevate, the outer vaginal third forms the orgasmic platform, muscle tension and cardiorespiratory rate climb further
Orgasm	**Brief climax releasing sexual tension: rhythmic pelvic contractions, in men emission then ejaculation, in women rhythmic contraction of the orgasmic platform**
Resolution	**Return to baseline: detumescence and de-engorgement, well-being; men enter a refractory period, women may not**

The four-phase model of Masters and Johnson; the discriminating detail is the male refractory period in resolution, absent or minimal in women (Kaplan and Sadock 2024).

GOOD TO REMEMBER

- **Four-phase model (Masters and Johnson):** excitement, plateau, orgasm, resolution, driven by vasocongestion and myotonia; the defining sex difference is the refractory period in resolution, present in men and minimal or absent in women.

8.2 Kaplan's triphasic model and the desire phase

Kaplan added the mind before the body. Helen Singer Kaplan's 1979 reformulation, the **kaplan triphasic** model, collapsed the physiological cycle into three interdependent components and,

crucially, prefixed a psychological one: **desire**, **excitement** and **orgasm** (Kaplan and Sadock 2024). The addition of the desire phase mattered because Masters and Johnson had begun the cycle at excitement and so had no place for the many patients whose problem is an absence of sexual interest or drive before arousal is ever attempted. Desire is appetitive and centrally driven; excitement and orgasm are the peripheral, largely vascular and reflexive events that follow.

The triphasic model is a diagnostic map. Its enduring value is that each phase corresponds to a family of dysfunctions, which is why DSM-5-TR uses these phases as the basis for classifying the sexual dysfunctions (Kaplan and Sadock 2024). A desire-phase problem gives low libido (hypoactive sexual desire) or, at the other pole, hypersexuality; an excitement or arousal-phase problem gives erectile dysfunction in men and female arousal disorder; and an orgasm-phase problem gives anorgasmia or premature ejaculation. Localise the complaint to a phase and you have narrowed the differential before you have named a single criterion.

TRIPHASIC PHASE (KAPLAN)	NATURE OF THE PHASE	DYSFUNCTION WHEN DISRUPTED
Desire	**Central, appetitive drive and interest**	Hypoactive sexual desire; sexual aversion; hypersexuality
Excitement (arousal)	Peripheral vascular arousal (erection, engorgement, lubrication)	**Erectile dysfunction; female sexual arousal disorder**
Orgasm	Reflex peak and release of tension	**Anorgasmia (delayed or absent orgasm); premature ejaculation**

Kaplan's triphasic model as a map of the dysfunctions; the examiner's use of it is to place any presenting complaint on desire, excitement or orgasm (Kaplan and Sadock 2024; DSM-5-TR 2022).

RULE **The disrupted phase names the disorder.** Desire-phase failure means a desire disorder, excitement-phase failure means an arousal disorder such as erectile dysfunction, orgasm-phase failure means anorgasmia or premature ejaculation; classification follows the phase.

GOOD TO REMEMBER

- **Kaplan triphasic model:** desire, excitement, orgasm; the point of the model is that it adds the desire phase that Masters and Johnson omitted and maps each phase onto a family of dysfunctions, which is the framework DSM-5-TR adopts for classification.

8.3 Basson's circular model of female response

A circle, not a straight line. The linear models assume desire is spontaneous and always precedes arousal, an assumption that fits male experience better than female and risks over-diagnosing hypoactive desire in women (Kaplan and Sadock 2024). Rosemary Basson's circular model (2000), developed for female response, replaces the straight line with a loop that many women enter from a position of sexual neutrality, moved by a wish for emotional intimacy rather than by a spontaneous surge of drive. Willingness leads to sexual stimuli, arousal builds, and desire is then triggered by that arousal, so here desire can *follow* arousal rather than lead it. This is responsive desire, as opposed to the spontaneous desire the linear models presume.

Why it matters clinically. Basson's model reframes emotional satisfaction and relationship quality as drivers of the cycle, not incidental extras, and it normalises a pattern of desire that the linear models would misread as pathology. Although built around female response, its principles are now applied across sexes, and it is the reason a purely mechanistic, erection-and-orgasm account of a couple's difficulty so often misses the point.

PEARL

The single most testable idea from Basson is that arousal can precede desire. In her circular model a woman may begin from neutrality, choose to be receptive for intimacy, and only then, as arousal builds, experience desire. Reading that responsive pattern as a disorder of the desire phase is the commonest conceptual error at the bedside, and it is exactly what the model was written to correct.

8.4 The neurophysiology: point and shoot

Two autonomic divisions, two jobs. Erection is a parasympathetic event and ejaculation is a sympathetic one, and the whole of it is captured by the classic mnemonic point and shoot (Kaufman's Clinical Neurology for Psychiatrists). Excitatory descending impulses raise parasympathetic outflow from the sacral cord, which relaxes the smooth muscle of the genital arteries; the relaxed arteries dilate, blood flows in, and the result is penile erection in men and clitoral engorgement in women. At the tissue level the mediator is nitric oxide, released in the corpus cavernosum during arousal; it raises cyclic guanosine monophosphate, which produces the smooth-muscle relaxation and blood inflow that give the erection, and it is the enzyme that degrades that second messenger, phosphodiesterase-5, which the erectile-dysfunction drugs inhibit (Kaplan and Sadock 2024; Stahl).

Sympathetic outflow closes the sequence. With continued stimulation a predominantly sympathetic, thoracolumbar discharge produces emission (movement of seminal fluid into the posterior urethra) and then ejaculation, after which arterial tone returns and detumescence follows in resolution (Kaufman). The parasympathetic outflow for erection arises from the sacral cord at **S2 to S4** and the sympathetic outflow for emission and ejaculation from the thoracolumbar cord at **T11 to L2**; the somatic pudendal nerve (also S2 to S4) carries the erotic afferents and drives the rhythmic pelvic-floor contractions of the ejaculatory reflex. A failure of sympathetic bladder-neck closure diverts semen backwards, which is why sperm in a post-orgasm urine sample signals retrograde ejaculation.

MNEMONIC

POINT and SHOOT

Point is **P**arasympathetic and gives the erection (S2 to S4, acetylcholine, nitric oxide, arterial relaxation and inflow); **Shoot** is **S**ympathetic and gives emission and ejaculation (T11 to L2). The clinical payoff: sympathetic overdrive, as in anxiety, both softens erection and hurries ejaculation.

TRAP **Do not swap the autonomic assignments.** Erection is parasympathetic (point), not sympathetic; it is sympathetic overactivity, the physiology of anxiety, that abolishes erection and precipitates premature ejaculation, which is why performance anxiety is self-perpetuating.

GOOD TO REMEMBER

- **Autonomic control (point and shoot):** parasympathetic sacral outflow (S2 to S4) mediates erection via nitric oxide and cyclic guanosine monophosphate with smooth-muscle relaxation; sympathetic thoracolumbar outflow (T11 to L2) mediates emission and ejaculation; the pudendal nerve is the somatic afferent and ejaculatory-motor route.

8.5 Using the cycle in the clinic

The cycle is the sexual-history template. A good psychosexual history walks the phases in order and asks, for the patient and the partner, where the difficulty falls: is it a lack of interest before anything begins (desire), a failure to become or stay aroused (excitement), or a problem with climax and its timing (orgasm), with pain considered alongside (Kaplan and Sadock 2024). Because illnesses that cause pain, fatigue, vascular disease or hormonal deficiency and many medications each strike particular phases, phase-localisation immediately raises the organic differential as well as the psychological one. Erectile dysfunction, an excitement-phase vascular failure, is a recognised early marker of endothelial and cardiovascular disease, so the cycle is a screening prompt, not merely a taxonomy.

WORKED EXAMPLE

A man reports that his interest and arousal are intact and erections are firm, but climax arrives far sooner than he wishes. Walk the triphasic model: desire is normal, excitement is normal, and the problem is squarely in the orgasm phase, which localises the complaint to premature ejaculation rather than a desire or erectile disorder before a single management step is chosen. Reverse the pattern, so that interest is present but the erection will not form or hold, and you have moved one phase upstream to an excitement-phase disorder, erectile dysfunction, with its own vascular and organic differential. Localise first, name second.

INDIA

Indian teaching uses the same frame: it anchors the sexual dysfunctions to disturbance across the phases of the sexual response cycle, so the Masters and Johnson and Kaplan models are the standard Indian exam scaffold. The everyday clinical relevance is that orgasm-phase and desire-phase complaints, particularly premature ejaculation and low desire, dominate Indian psychosexual and andrology clinics, and they are frequently overlaid on the culture-bound anxiety of Dhat, in which normal physiology is misread through a fear of semen loss. Placing such a presentation on the cycle first, and reading the cultural meaning second, keeps the assessment grounded; the transcultural frame of Dhat is developed in the Consultation-liaison, geriatric and transcultural psychiatry notes.

4	3	S2 to S4	T11 to L2
MASTERS AND JOHNSON PHASES (EXCITEMENT, PLATEAU, ORGASM, RESOLUTION)	KAPLAN TRIPHASIC PHASES (DESIRE, EXCITEMENT, ORGASM)	PARASYMPATHETIC ERECTILE OUTFLOW (SACRAL)	SYMPATHETIC EMISSION AND EJACULATION OUTFLOW

HOLD THIS

Masters and Johnson gave four phases, excitement, plateau, orgasm and resolution, with a male-only refractory period; Kaplan's triphasic model added the desire phase to make desire, excitement and orgasm, and that phase map is how DSM-5-TR classifies the dysfunctions; Basson's circular model shows female desire can be responsive and follow arousal; and the wiring is point and shoot, parasympathetic sacral outflow (S2 to S4, nitric oxide) for erection and sympathetic thoracolumbar outflow (T11 to L2) for emission and ejaculation.

9 · Male sexual dysfunctions and their management

This topic sits at the *desire* and *arousal* hinge of the chapter, and it is examined as a hybrid: a short discrimination task that places a man's complaint in the right diagnostic box, then a longer, guideline-anchored management answer that most candidates under-prepare. The high-yield entity is **erectile dysfunction**, both because it is the commonest presentation the psychiatrist meets (as a side effect, a comorbidity of diabetes or vascular disease, or a primary complaint) and because its first-line drug treatment is one of the cleanest guideline positions in the syllabus. The consensus across the sexual-medicine bodies, the International Society for Sexual Medicine, the British Society for Sexual Medicine, and the operative urology guidelines, is uniform, so marks are lost only by getting a dose, a contraindication, or the testosterone principle wrong.

How to use this page. First fix the DSM-5-TR and ICD-11 map of the **male sexual dysfunctions** and the common criteria that gate every one of them; then learn erectile dysfunction properly, its definition, the organic against psychogenic split, and its meaning as a cardiovascular warning; then commit the stepwise management, first-line **PDE5 inhibitor** with its verified doses and the absolute nitrate rule, second-line injection or vacuum, third-line prosthesis, and the single testosterone principle that carries the classic trap. Finish with the **ejaculatory disorders** and hypoactive desire. The one error this page is built to prevent is starting long-term testosterone in a man whose testosterone is normal.

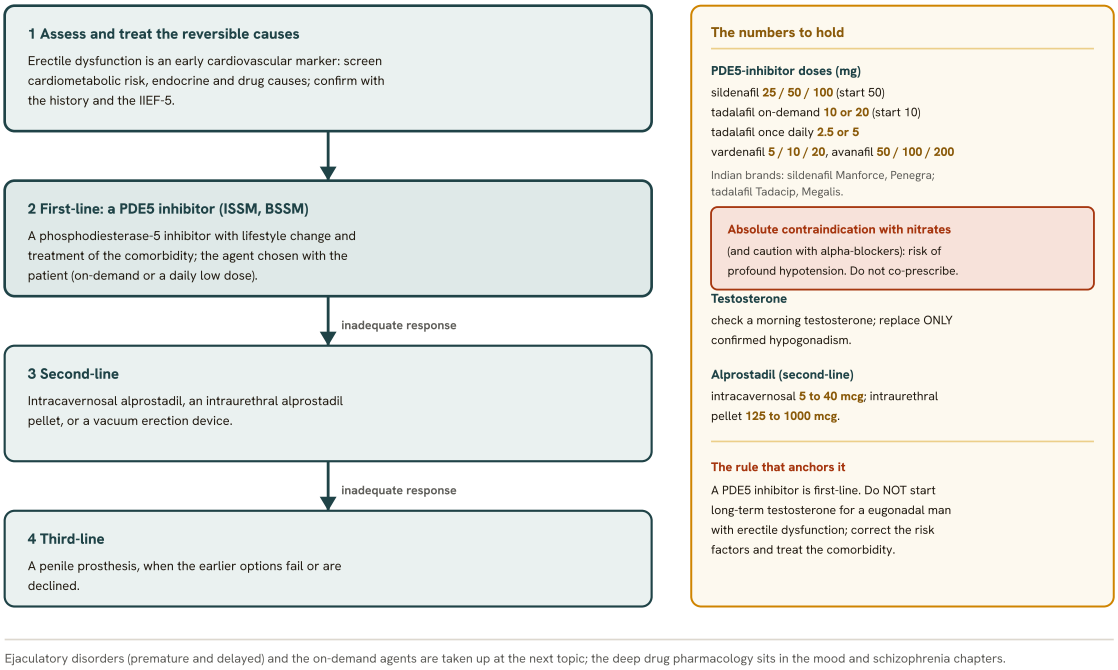


Fig 18.6 The erectile-dysfunction management algorithm. Because erectile dysfunction is often an early sign of vascular disease, the first step is to screen and treat the reversible cardiometabolic, endocrine and drug causes and to confirm the picture with the history and the IIEF-5. First-line treatment, anchored on the ISSM and BSSM guidance, is a phosphodiesterase-5 inhibitor alongside lifestyle change and treatment of the comorbidity, chosen with the patient as an on-demand agent or a daily low dose; the doses are held in the panel. A phosphodiesterase-5 inhibitor is absolutely contraindicated with nitrates. Where it fails or is unsuitable, second-line options are intracavernosal or intraurethral alprostadil or a vacuum device, and third-line is a penile prosthesis. Testosterone is checked and replaced only where hypogonadism is confirmed; empirical testosterone for a eugonadal man is a classic error.

IIEF-5 (SHIM), THE 5-ITEM SEXUAL HEALTH INVENTORY FOR MEN	SCORE BAND (OUT OF A POSSIBLE 25)
5 items on erectile function and satisfaction over the past 6 months, each scored 1 to 5; total out of a possible 25	22 to 25: no erectile dysfunction
higher total means better erectile function	17 to 21: mild
a brief screen and severity grade, not a diagnosis on its own	12 to 16: mild to moderate
tracks response to treatment over time	**8 to 11: moderate; 5 to 7: severe**

IIEF-5 / SHIM (Rosen et al, 1999); copyright the authors, permission required, so typeset here in summary with the verified severity bands rather than reproduced.

ASEX (ARIZONA SEXUAL EXPERIENCE SCALE)	INTERPRETATION
5 items: sex drive, arousal, erection or lubrication, ability to reach orgasm, and satisfaction from orgasm	each item scored 1 to 6; total out of a possible 30; higher means more sexual dysfunction
useful for tracking medication-induced sexual dysfunction across either sex	**clinically significant dysfunction if the total is 19 or more, OR any one item is 5 or more, OR any three items are 4 or more**

ASEX (McGahuey et al, 2000); University of Arizona, permission required, so typeset here in summary with the verified thresholds rather than reproduced.

Fig 18.7 The sexual-function rating scales. The IIEF-5, or Sexual Health Inventory for Men, is the brief erectile-function screen and severity grade: five items each scored 1 to 5 for a total out of a possible 25, banded from 22 to 25 (no dysfunction) down to 5 to 7 (severe). The Arizona Sexual Experience Scale is a short five-item measure usable across either sex and especially handy for tracking medication-induced sexual dysfunction, each item scored 1 to 6 for a total out of a possible 30, with clinically significant dysfunction flagged by a total of 19 or more, any single item of 5 or more, or any three items of 4 or more. Both are permission-required instruments and are summarised here from their verified structure and thresholds.

9.1 The DSM-5-TR and ICD-11 map of the male dysfunctions

Four male-relevant disorders, one shared set of gates. DSM-5-TR groups the male sexual dysfunctions into male hypoactive sexual desire disorder, erectile dysfunction (erectile disorder), premature ejaculation (premature or early ejaculation), and delayed ejaculation, alongside substance or medication-induced sexual dysfunction (Kaplan and Sadock CTP 2024; DSM-5-TR 2022). Whichever one you are diagnosing, the same qualifying criteria apply: the symptom must persist for at least six months, cause clinically significant distress, and not be better explained by a non-sexual mental disorder, relationship distress, another medical condition, or a substance. Erectile dysfunction, premature ejaculation and delayed ejaculation add a frequency gate on top of these, the symptom on roughly 75 to 100 percent of occasions; male hypoactive sexual desire disorder carries no frequency threshold in DSM-5-TR. Each is then coded as lifelong or acquired and as generalised or situational, and its severity is graded by the distress it causes. ICD-11 made the parallel move of lifting these out of the mental disorders chapter into a dedicated chapter, "Conditions related to sexual health", with gender-parallel dysfunctions (ICD-11).

DISORDER (DSM-5-TR)	CORE FEATURE	THE ONE THING TO ATTACH TO IT
Male hypoactive sexual desire disorder	Persistently deficient or absent sexual thoughts, fantasies and desire	**Measure morning testosterone; low desire correlates with low testosterone**
Erectile dysfunction (erectile disorder)	Difficulty obtaining or maintaining an erection, or reduced erectile rigidity	**Classify as organic, psychogenic or mixed; it is a cardiovascular marker**
Premature (early) ejaculation	Ejaculation within roughly one minute of penetration, sooner than wished	**On-demand dapoxetine is the only licensed first-line drug**
Delayed ejaculation	Marked delay, infrequency or absence of ejaculation	**Separate it from retrograde ejaculation, which is always organic**

The male sexual dysfunctions under DSM-5-TR, all gated by the shared six-month, distress and exclusion criteria, with the 75-to-100-percent frequency gate on every one except male hypoactive sexual desire disorder; ICD-11 places the parallel set in its sexual-health chapter (Kaplan and Sadock CTP 2024, DSM-5-TR 2022, ICD-11).

GOOD TO REMEMBER

- **The shared criteria (every male dysfunction):** at least six months, causing significant distress, not better explained by another disorder, relationship distress, a medical condition or a substance; then specify lifelong or acquired and generalised or situational. The symptom on about 75 to 100 percent of occasions is required for erectile dysfunction, premature ejaculation and delayed ejaculation, but not for male hypoactive sexual desire disorder. Missing the six-month and distress gates is the commonest under-diagnosis error.

9.2 Erectile dysfunction: definition and the organic, psychogenic, mixed split

One definition, three aetiological patterns. Erectile dysfunction is the persistent or recurrent inability to attain or maintain a penile erection sufficient for satisfactory sexual performance (Kaplan and Sadock CTP 2024). It is classified as psychogenic, organic, or mixed, and the split is drawn largely from the history. Psychogenic erectile dysfunction, driven by performance anxiety, relationship conflict or mood, tends to be situational and sudden in onset, and the man still has normal erections with masturbation, on waking, and during sleep. Organic erectile dysfunction is insidious, and erections are deficient in most contexts, nocturnal and masturbatory included. Organic causes are vascular (arterial insufficiency or venous leak), neurogenic, endocrine (hypogonadism, hyperprolactinaemia), medication-induced, or systemic; the vasculogenic type is the commonest organic aetiology, and antipsychotic and antidepressant contributions are a reversible cause the psychiatrist must actively exclude (developed in the Schizophrenia: management, antipsychotics and adverse effects notes and the Mood disorders: pharmacotherapy notes). Where doubt persists, nocturnal penile tumescence testing (erections during sleep) helps separate organic from psychogenic disease, since preserved sleep erections point away from an organic lesion.

RULE **The history sorts organic from psychogenic before any test.** Preserved morning, masturbatory and nocturnal erections with sudden, situational onset make organic disease negligible and the picture psychogenic; insidious onset with erections deficient in every context points organic and warrants a vascular and endocrine work-up.

GOOD TO REMEMBER

- **Erectile dysfunction (the diagnosis):** persistent inability to attain or maintain an erection sufficient for satisfactory performance, for at least six months, with distress; the defining discriminator is the organic, psychogenic or mixed classification, read first from preserved versus absent nocturnal and masturbatory erections.

9.3 Erectile dysfunction as a cardiovascular sentinel

The penis is a window on the arteries. Erectile dysfunction and cardiovascular disease share a pathophysiology of endothelial dysfunction, inflammation and low testosterone, and erectile dysfunction is independently associated with coronary heart disease, stroke and all-cause mortality (Kaplan and Sadock CTP 2024). The clinically load-bearing point is that vasculogenic erectile dysfunction in a younger man can be an early indicator of future cardiovascular disease, so these men should receive an appropriate cardiovascular risk assessment rather than a prescription alone. The epidemiology reinforces it: in the Massachusetts Male Aging Study the combined prevalence reached 52 percent, and after adjusting for age the strongest correlates were the classic vascular markers, hypertension, diabetes and heart disease. Among men with diabetes, roughly 50 to 75 percent develop erectile dysfunction, about three times the rate in non-diabetic men.

PEARL

Treat new-onset erectile dysfunction in a man under 50 as a reason to check blood pressure, fasting glucose or HbA1c, and lipids, not only to write for a tablet. The small penile arteries narrow before the larger coronaries, so the complaint can arrive years ahead of a cardiac event, which is exactly why the sexual-medicine guidelines fold cardiovascular risk stratification into the ED work-up.

9.4 Assessment: history, morning testosterone, the ISSM labs and the IIEF-5

Clinical diagnosis, targeted bloods, one screening scale. Diagnosis rests on the clinical presentation, not on laboratory values; the examination emphasises the nervous, vascular and genital systems, looking for signs of hypogonadism (small testes, gynaecomastia, sparse body and facial hair). The ISSM (International Society for Sexual Medicine) recommends a focused panel of fasting glucose, HbA1c, lipids and a morning total testosterone (Kaplan and Sadock CTP 2024). The morning sample matters because testosterone follows a diurnal peak; a low result must be confirmed on a repeat before it is called hypogonadism. The abridged International Index of Erectile Function, the five-item IIEF-5 or Sexual Health Inventory for Men, both screens for and grades erectile dysfunction; the reproduced instrument sits in the accompanying scale plate. A separate five-item scale, the ASEX (Arizona Sexual Experience Scale), is the tool of choice for tracking psychotropic-induced sexual dysfunction across a one-week window, scored so that a

higher total means more dysfunction (Clinical Methods in Psychiatry, AIIMS 2024; Maudsley Prescribing Guidelines).

IIEF-5 BAND (OUT OF A POSSIBLE 25)	INTERPRETATION
22 to 25	No erectile dysfunction
17 to 21	Mild
12 to 16	Mild to moderate
8 to 11	Moderate
5 to 7	Severe

The IIEF-5 (Sexual Health Inventory for Men) severity bands; the five items each score up to 5, so the total runs from 5 to 25, read against these cut-offs (see gaps). The typeset form is reproduced in the accompanying scale plate.

GOOD TO REMEMBER

- **The ED work-up (guideline-anchored, ISSM):** diagnosis is clinical; order fasting glucose, HbA1c, lipids and a morning total testosterone, confirm any low testosterone before acting on it, and use the IIEF-5 to grade severity, a total in the 22-to-25 band out of a possible 25 meaning no erectile dysfunction and 5 to 7 out of a possible 25 meaning severe.

9.5 First-line management: the PDE5 inhibitor

An oral PDE5 inhibitor plus risk-factor optimisation, for everyone without a contraindication. First-line treatment of erectile dysfunction is a phosphodiesterase-5 inhibitor combined with lifestyle and cardiovascular risk-factor management (ISSM; BSSM; EAU male sexual dysfunction; AUA 2018). All the oral agents are similarly effective, and choice turns on how the man wants to use them: sildenafil is the high-efficacy pick and tadalafil the tolerability pick with the longest window. Sildenafil is taken on-demand, roughly one hour before intercourse, with a recommended **50 mg** starting dose titrated between 25 and 100 mg; onset is 30 to 60 minutes and the window runs up to 12 hours, with absorption delayed by a high-fat meal. Tadalafil on-demand starts at **10 mg** (range 10 to 20 mg), acts from about 30 minutes, and gives the longest window of any agent, up to 36 hours, with the least food effect. Tadalafil also has a once-daily low-dose regimen, 2.5 or 5 mg with 5 mg preferred, which decouples dosing from sexual activity and is the only PDE5 inhibitor licensed for concurrent erectile dysfunction and lower-urinary-tract symptoms of benign prostatic hyperplasia at 5 mg once daily. Vardenafil (start 10 mg) and avanafil (start 100 mg, the fastest onset, taken 15 to 30 minutes before) complete the class.

AGENT	ON-DEMAND DOSE (MG)	ONSET AND WINDOW	DISTINGUISHING POINT
Sildenafil	25, 50, 100; start 50	30 to 60 min; up to 12 h	**High-efficacy pick; high-fat meal delays absorption**
Tadalafil (on-demand)	10, 20; start 10	from 30 min; up to 36 h	**Longest window; least affected by food**
Tadalafil (once-daily)	2.5 or 5 once daily; use 5	continuous, off the clock of sex	**Only PDE5 inhibitor licensed for ED with LUTS or BPH**
Vardenafil	5, 10, 20; start 10	from about 30 min	**Orally disintegrating form available**
Avanafil	50, 100, 200; start 100	fastest; take 15 to 30 min before	**Quickest onset of the class**

The oral PDE5 inhibitors, all first-line and similarly effective; the doses are the verified EAU and AUA 2018 figures (EAU male sexual dysfunction; AUA 2018).

25 IIEF-5 TOP SCORE, NO-ED BAND STARTS AT 22	**50** SILDENAFIL ON-DEMAND START (MG)	**5** TADALAFIL ONCE-DAILY DOSE (MG)	**30** DAPOXETINE ON-DEMAND START (MG)

INDIA

The generics are widely marketed in India: sildenafil (Manforce, Penegra), tadalafil (Tadacip, Megalis), and, for premature ejaculation, dapoxetine (Duralast, Sustinex, also sold in sildenafil and tadalafil fixed-dose combinations). Keep the generic primary and confirm the exact product and strength locally; the sexual-medicine advice is that dapoxetine should not routinely be combined with a PDE5 inhibitor because of syncope risk.

MNEMONIC

PILLS → POKES & PUMPS → PROSTHESIS

The ED treatment ladder in order: oral **Pills** (PDE5 inhibitor) first, then the injection and vacuum second line (**Pokes and Pumps**), then the surgical **Prosthesis** third line. You climb only when the rung below fails or is declined.

GOOD TO REMEMBER

- **First-line ED drug (guideline-anchored, ISSM, BSSM, EAU, AUA 2018):** an oral PDE5 inhibitor plus risk-factor optimisation; sildenafil starts at 50 mg on-demand about one hour before, tadalafil at 10 mg on-demand or 5 mg once daily, and tadalafil is the only agent licensed for concurrent ED and benign prostatic hyperplasia.

9.6 The absolute nitrate contraindication

One combination you never allow. The concurrent use of any organic nitrate, nitric oxide donor, nicorandil, or a recreational nitrite with any PDE5 inhibitor is an absolute contraindication (EAU male sexual dysfunction; AUA 2018). Both act on the nitric-oxide, cyclic-GMP pathway, so the combination causes cyclic-GMP to accumulate and can precipitate profound, unpredictable

hypotension. Before prescribing, ask specifically about nitrate use for angina and about recreational nitrites. Alpha-blockers are a caution rather than an absolute bar and may be co-prescribed carefully, watching for postural hypotension.

COMMON TRAP

Forgetting to ask about a nitrate. A man on a nitrate for angina, or using a recreational nitrite, must never receive a PDE5 inhibitor; screening for nitrate use is a mandatory step, not an optional one, and no dose is "safe" in this combination.

GOOD TO REMEMBER

- **PDE5 inhibitor caution (guideline-anchored, EAU and AUA 2018):** any organic nitrate, nitric oxide donor, nicorandil or recreational nitrite is an absolute contraindication with any PDE5 inhibitor because of cyclic-GMP accumulation and profound hypotension; alpha-blockers are a relative caution only.

9.7 Second-line and third-line therapy

When the tablet fails or is contraindicated, step down the ladder. Second-line options are for men in whom oral therapy fails or is contraindicated (EAU male sexual dysfunction; AUA 2018). Intracavernosal alprostadil is the most effective injectable monotherapy, dosed at 5 to 40 micrograms and producing an erection within 5 to 15 minutes, with over 70 percent efficacy but needing in-office injection training; its risks are penile pain, priapism and fibrosis. An intraurethral alprostadil pellet (MUSE, 125 to 1000 micrograms, usually initiated at 500 micrograms) and topical alprostadil cream (200 to 300 micrograms) are alternatives with more limited data. A vacuum erection device is a non-invasive, drug-free choice for well-informed men, with variable satisfaction. Third-line therapy is a surgically implanted penile prosthesis (inflatable or semi-rigid), reserved for when less-invasive options fail or the man wants a definitive solution; it has the highest satisfaction of any ED treatment, over 90 percent, its main risks being mechanical failure and infection in about 2 to 3 percent.

LINE	OPTION	DOSE OR FORM	KEY POINT
Second	Intracavernosal alprostadil	5 to 40 micrograms	**Most effective injectable; erection in 5 to 15 min; needs training**
Second	Intraurethral pellet (MUSE)	125 to 1000 micrograms, start 500	**Alternative for men declining injection; data more limited**
Second	Topical alprostadil cream	200 to 300 micrograms	**Non-injection local option**
Second	Vacuum erection device	mechanical device	**Non-invasive, drug-free; satisfaction variable**
Third	Penile prosthesis	inflatable or semi-rigid implant	**Highest satisfaction, over 90 percent; infection about 2 to 3 percent**

The second-line and third-line ED ladder, entered when oral PDE5 inhibitors fail or are contraindicated; the full stepwise route is drawn in the accompanying figure (EAU male sexual dysfunction; AUA 2018).

GOOD TO REMEMBER

- **Second and third-line ED therapy (guideline-anchored, EAU and AUA 2018):** after oral failure, intracavernosal alprostadil (5 to 40 micrograms, the most effective injectable) or a vacuum device is second line, and a penile prosthesis, with the highest satisfaction of any treatment, is third line.

9.8 Testosterone: test, then treat only confirmed hypogonadism

Measure it, but do not treat a normal level. Measure a morning total testosterone in any man with erectile dysfunction, low desire, or clinical signs of hypogonadism, and treat only biochemically confirmed hypogonadism (EAU male sexual dysfunction; AUA 2018). In a genuinely hypogonadal man who has not responded to a PDE5 inhibitor, adding testosterone can improve the response, so the two are complementary in that specific setting. What you must not do is give empirical, long-term testosterone for erectile dysfunction to a man whose testosterone is normal: it will not fix a eugonadal man's erectile dysfunction and it exposes him to the risks of unnecessary androgen therapy. This is the single commonest examined error in the topic.

TRAP **Starting long-term testosterone in a eugonadal man with erectile dysfunction.** Testosterone helps only when a low level is confirmed on a morning sample; in a man with normal testosterone it does not correct erectile dysfunction and adds needless risk. Test first, treat only proven hypogonadism.

GOOD TO REMEMBER

- **Testosterone principle (guideline-anchored, EAU and AUA 2018):** check a morning total testosterone, treat only confirmed hypogonadism, use it to rescue a hypogonadal PDE5-inhibitor non-responder, and never give empirical long-term testosterone for erectile dysfunction in a eugonadal man.

9.9 The ejaculatory disorders and hypoactive sexual desire

Three more entities, each with a clean discriminator. **Premature ejaculation** is ejaculation, before or within roughly one minute of penetration, that occurs sooner than the man wishes and causes distress; DSM-5-TR grades it as mild (about 30 seconds to 1 minute), moderate (about 15 to 30 seconds), or severe (at the start of, or within about 15 seconds of, penetration). Its pharmacological management, on-demand dapoxetine as the only licensed first-line agent (started at 30 mg, maximum 60 mg, not more than once every 24 hours), off-label daily SSRIs, topical anaesthetics, and behavioural methods, is developed in full in the dedicated premature ejaculation and dapoxetine topic. **Delayed ejaculation** is a marked delay in, infrequency of, or absence of ejaculation despite adequate stimulation; the crucial separation is from retrograde ejaculation, in which semen passes backward into the bladder, which always has an organic cause (genitourinary surgery, autonomic neuropathy, alpha-blocker or anticholinergic drugs). Male hypoactive sexual desire disorder is persistently deficient or absent sexual thoughts and desire for at least six months with distress, and it prompts a check of testosterone, mood, relationship factors and medication.

GOOD TO REMEMBER

- **Premature ejaculation (the diagnosis):** ejaculation within about one minute of penetration, sooner than wished, with distress and control lost; graded mild, moderate or severe by latency, with on-demand dapoxetine the only licensed first-line drug.
- **Delayed and retrograde ejaculation (the discriminator):** delayed ejaculation is a marked delay or absence of ejaculation; retrograde ejaculation, semen passing into the bladder, is a separate, always-organic entity tied to genitourinary surgery, autonomic neuropathy, or alpha-blocker and anticholinergic drugs.
- **Male hypoactive sexual desire disorder (the diagnosis):** persistently deficient or absent sexual thoughts and desire for at least six months with distress; the first step is to measure a morning testosterone and screen mood, medication and relationship factors.

HOLD THIS

Erectile dysfunction is first-line an oral PDE5 inhibitor (sildenafil start 50 mg on-demand, tadalafil start 10 mg on-demand or 5 mg once daily); a nitrate in any form is an absolute contraindication, and you never start long-term testosterone in a man whose testosterone is normal.

10 · Female sexual dysfunctions and their management

This topic mirrors the male-dysfunction page but flips the emphasis: the diagnostic map is a little denser (a merger and a subsuming category the examiner loves), and the management answer is deliberately un-showy, because the pharmacology is thin and the marks live in the **biopsychosocial** and couple-based first line. The high-yield facts are the DSM-5-TR trio and their shared gates, the single biggest reclassification (desire and arousal merged into one female disorder), and the one management principle that the whole chapter turns on: in women, psychological, relational and physiotherapeutic approaches lead, and drugs are a narrow, licence-limited adjunct.

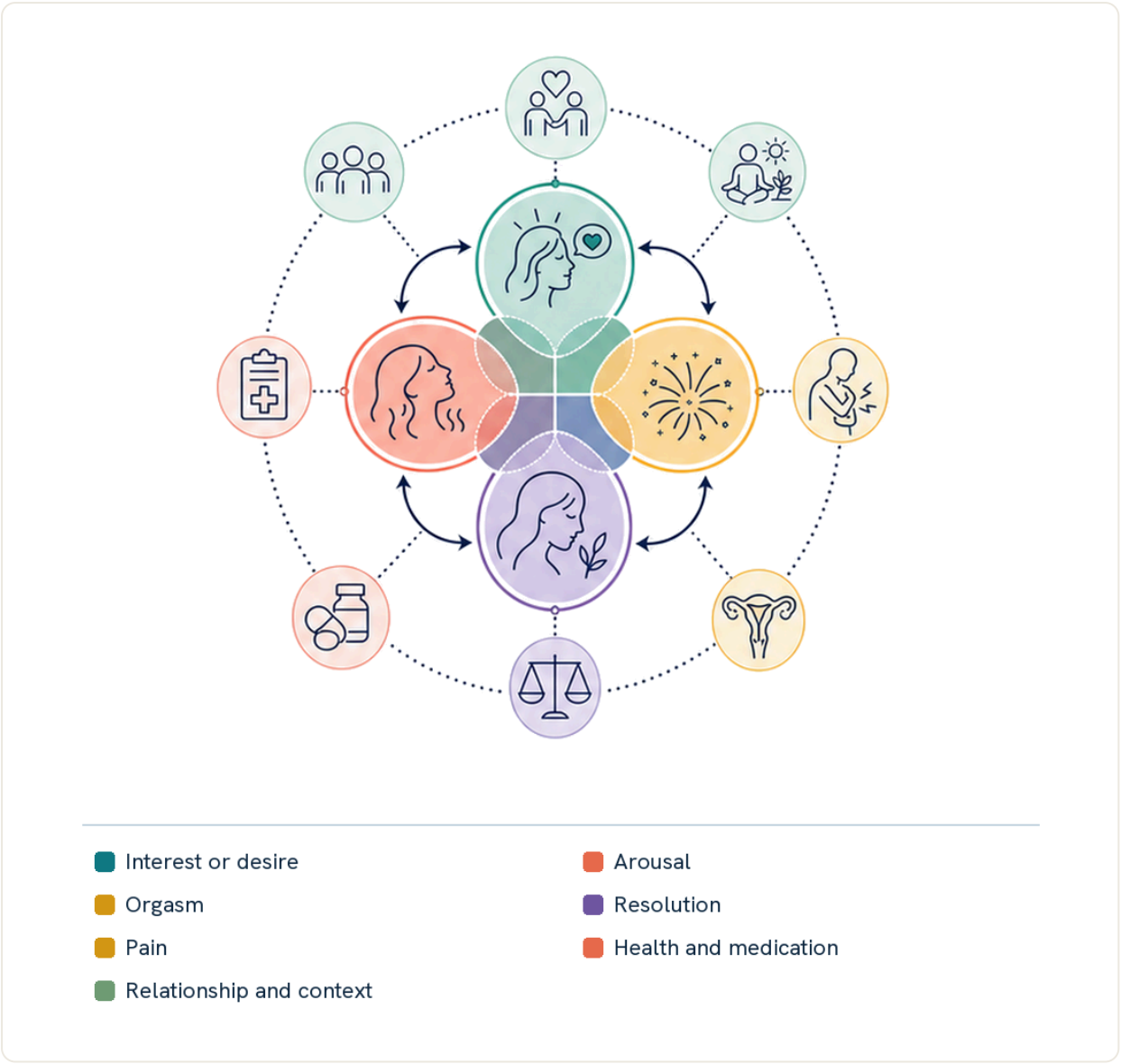


Fig 18.8 Female sexual response is non-linear and context-sensitive. Difficulties in interest, arousal, orgasm or pain may be shaped by physical health, medication, hormonal state and relational context.

How to use this page. First fix the DSM-5-TR and ICD-11 map of the female sexual dysfunctions; then take each of the three disorders in turn, learning the defining criterion and the one discriminator that keeps you out of trouble; then commit the multimodal management, biopsychosocial assessment, psychoeducation and sex therapy, the pelvic-floor and graded-dilator work that is specific to the pain-penetration disorder, local oestrogen for the menopausal cause of painful sex, and the two licensed drugs, which are covered fully in the dedicated flibanserin topic. The error this page is built to prevent is labelling painful sex psychogenic before an organic cause has been excluded.

10.1 The DSM-5-TR trio and the ICD-11 framing

Three female disorders, one shared set of gates, one big merger. DSM-5-TR recognises three **female sexual dysfunctions**: female sexual interest/arousal disorder, female orgasmic disorder, and genito-pelvic pain/penetration disorder (alongside substance or medication-induced sexual dysfunction, which is gender-neutral) (Kaplan and Sadock CTP 2024; DSM-5-TR 2022). The defining structural change from DSM-IV is that the old hypoactive sexual desire disorder and

female sexual arousal disorder were combined into a single interest-and-arousal category, on the evidence that low desire and low arousal co-occur so heavily in women that separating them is artificial. Whichever of the three you are diagnosing, the same qualifying gates apply: the symptom must persist for at least approximately six months, cause clinically significant distress in the woman herself, and not be better explained by a non-sexual mental disorder, severe relationship distress or partner violence, another medical condition, or a substance. Each is then specified as lifelong or acquired and graded mild, moderate or severe by distress. ICD-11 lifts the equivalent conditions out of the mental disorders chapter into a new chapter, "Conditions related to sexual health"; notably, and unlike DSM-5, ICD-11 does *not* merge desire and arousal, keeping hypoactive sexual desire dysfunction and female sexual arousal dysfunction as separate categories, with anorgasmia and a sexual pain-penetration disorder completing the female set (ICD-11).

DISORDER (DSM-5-TR)	CORE FEATURE	THE DISCRIMINATOR TO ATTACH
Female sexual interest/arousal disorder	Merged low desire and low arousal; at least three of six indicators	**A mere "desire discrepancy" with a partner is not the disorder**
Female orgasmic disorder	Marked delay, infrequency, absence, or reduced intensity of orgasm	**Clitoral-not-coital orgasm, and inadequate stimulation, are excluded**
Genito-pelvic pain/penetration disorder	Penetration difficulty, pain, fear of pain, or pelvic-floor tensing (any one of four)	**Subsumes vaginismus and dyspareunia; the only one with no generalized/situational specifier**

The three DSM-5-TR female sexual dysfunctions, each gated by the shared roughly-six-month, distress and exclusion criteria and specified lifelong or acquired; ICD-11 places the parallel set in its "Conditions related to sexual health" chapter but keeps desire and arousal apart (Kaplan and Sadock CTP 2024, DSM-5-TR 2022, ICD-11).

GOOD TO REMEMBER

- **The shared gates (every female dysfunction):** the symptom for at least approximately six months, causing clinically significant distress in the woman, not better explained by another mental disorder, severe relationship distress, a medical condition or a substance; then specify lifelong or acquired and grade by distress. The single biggest DSM-5 change is the merger of desire and arousal into one female disorder.

10.2 Female sexual interest arousal disorder, the merged desire and arousal disorder

At least three of six indicators, for at least approximately six months, with distress. Female sexual interest/arousal disorder requires a lack of, or significantly reduced, sexual interest or arousal shown by at least three of six indicators: reduced interest in sexual activity; reduced erotic thoughts or fantasies; no or reduced initiation and typical unreceptiveness to a partner's initiation; reduced excitement or pleasure during almost all (roughly 75 to 100 percent) encounters; reduced arousal to any internal or external erotic cues; and reduced genital or non-genital sensations during almost all encounters (DSM-5-TR 2022). Two diagnostic subtleties carry marks. First, a *desire discrepancy*, where a woman simply wants sex less often than her partner, is explicitly not sufficient for the diagnosis. Second, a lifelong lack of desire that is better

understood as an asexual identity is excluded. The concept of *responsive desire* matters clinically: many women do not begin an encounter with spontaneous desire but develop it once arousal is under way, so an assessment of the adequacy of sexual stimulation is part of the diagnosis, not an afterthought. Around 30 percent of women report chronic low desire, but only a fraction of those experience the personal distress the criteria demand.

RULE **Distress in the woman is the gate, not the frequency of sex.** Low desire, low arousal, or a mismatch with a partner is a disorder only when it persists for about six months and causes clinically significant distress in the woman herself; a desire discrepancy alone, or an asexual identity, is not female sexual interest/arousal disorder.

PEARL

Ask about **responsive desire** before you label a woman as having low desire. If desire reliably arrives once she is aroused with adequate, wanted stimulation, the problem may be the context, the stimulation or the relationship rather than a dysfunction, and the treatment is couple-based, not pharmacological.

GOOD TO REMEMBER

- **Female sexual interest arousal disorder (the merged desire and arousal disorder):** at least three of six Criterion A indicators of reduced sexual interest or arousal, for at least approximately six months, causing distress in the woman; a desire discrepancy with a partner and an asexual identity are both excluded, and the disorder combines the old hypoactive desire and female arousal diagnoses.

10.3 Female orgasmic disorder

Delay, infrequency, absence, or reduced intensity of orgasm on almost all occasions. Female orgasmic disorder, historically called inhibited female orgasm or anorgasmia, is a marked delay in, marked infrequency of, or absence of orgasm, or a markedly reduced intensity of orgasmic sensations, experienced on almost all (roughly 75 to 100 percent) occasions of sexual activity for at least approximately six months and causing distress (DSM-5-TR 2022; Kaplan and Sadock CTP 2024). Two exclusions do the discriminating. A woman who reaches orgasm with clitoral stimulation but not during penile-vaginal intercourse does *not* meet the criteria, because clitoral-dependent orgasm is a normal variant, not a disorder. And where orgasm difficulty is the result of demonstrably inadequate sexual stimulation, the diagnosis is not made even though the woman may still need help. The lifelong subtype, present since the woman first became sexually active, can be specified further as "never experienced an orgasm under any situation," which is the classic indication for the directed-masturbation programme. Internationally, roughly 10 percent of women report never experiencing orgasm across their lifetime.

GOOD TO REMEMBER

- **Female orgasmic disorder (the diagnosis):** marked delay, infrequency, absence or reduced intensity of orgasm on about 75 to 100 percent of occasions, for at least approximately six months, with distress; a clitoral-only (non-coital) orgasm and orgasm difficulty from inadequate stimulation are both excluded, and the lifelong "never orgasmed" subtype is the target for directed masturbation.

10.4 Genito-pelvic pain penetration disorder, subsuming vaginismus and dyspareunia

One category built from four complaints, any one of which qualifies. Genito-pelvic pain/penetration disorder gathers the two older diagnoses of vaginismus and dyspareunia into a single category defined by persistent difficulty with one or more of: vaginal penetration during intercourse; marked vulvovaginal or pelvic pain during penetration attempts; marked fear or anxiety about that pain; and marked tensing or tightening of the pelvic-floor muscles on attempted penetration, for at least approximately six months with distress (DSM-5-TR 2022). Because these four so often drive one another (fear leads to guarding, guarding to pain, pain to more fear), DSM-5-TR reasoned it was cleaner to combine them, though the split remains useful clinically. The single most important step is not psychiatric at all: somatic causes of painful sex must be actively excluded, because a substantial minority of women presenting to sex-therapy clinics have identifiable pelvic pathology.

Vaginismus (historical term)

Involuntary spasm or tensing of the pelvic-floor and perivaginal muscles that prevents or makes painful any vaginal penetration; now the "penetration/tensing/fear" pole of genito-pelvic pain penetration disorder.

Dyspareunia (historical term)

Recurrent or persistent genital pain before, during or after intercourse; DSM-5-TR notes roughly 15 percent of North American women report recurrent painful intercourse. Somatic causes must be ruled out first.

Genitourinary syndrome of menopause

Oestrogen-deficiency vulvovaginal atrophy causing dryness and dyspareunia in peri- and post-menopausal women; the leading organic driver of acquired painful sex, and the one with a specific, effective treatment.

TRAP **Calling painful sex psychogenic before excluding an organic cause.** Dyspareunia and the pain-penetration disorder demand a genital and pelvic examination first: genitourinary syndrome of menopause, infections, vulvodynia, endometriosis, episiotomy scarring and dermatoses all cause it, and up to a third of sex-clinic attenders with the complaint have pelvic pathology. Rule out the organ before you formulate the mind.

INDIA

In Indian sexual-medicine and psychiatry practice, genito-pelvic pain/penetration disorder frequently presents not as "painful sex" but as **non-consummation of marriage**, often as a couple, sometimes with the man's erectile difficulty layered on, and typically laden with cultural expectation and shame. Neither licensed female-desire drug (flibanserin, bremelanotide) is marketed in India, so Indian management leans even harder on psychoeducation, couple therapy, graded dilators and pelvic-floor work; local oestrogen preparations for menopausal atrophy are, however, readily available generically. Frame the assessment for the couple, non-judgementally, and rule out organic pathology early.

GOOD TO REMEMBER

- **Genito-pelvic pain penetration disorder (subsuming vaginismus and dyspareunia):** persistent difficulty with any one of four (penetration, vulvovaginal or pelvic pain, fear of that pain, pelvic-floor tensing), for at least approximately six months with distress; it is the only female dysfunction with no generalized/situational specifier, and the first step is always to exclude an organic cause of the pain.

10.5 Biopsychosocial assessment and the multimodal management

Assess and treat biopsychosocially first; psychological and couple-based approaches lead. The ISSM (International Society for Sexual Medicine) and the general consensus frame female sexual dysfunction as biopsychosocial, so assessment and management run in parallel across relationship factors, mood and anxiety, medication effects, hormonal and genital contributors, and the woman's beliefs and knowledge about sex (ISSM; Kaplan and Sadock CTP 2024). Assessment is clinical, supported where useful by a rating instrument: the FSFI (Female Sexual Function Index), a nineteen-item scale across six domains, is the standard measure, with a validated cut-off at or below **26.55** flagging a woman at risk of sexual dysfunction (Rosen et al 2000; Wiegel et al 2005); the validated cut-off is carried in the text. Management is multimodal and stepwise: first, *psychoeducation* that corrects myths and reframes the response cycle; second, *treat the contributors*, which means optimising mood and anxiety, reviewing and where possible switching a culprit drug (antidepressant-induced dysfunction is developed in the Mood disorders: pharmacotherapy notes, and antipsychotic hyperprolactinaemia in the Schizophrenia: management, antipsychotics and adverse effects notes), and treating hormonal or genital pathology; third, *sex therapy*. The core behavioural method is sensate focus (Masters and Johnson), a graded programme of non-demand mutual pleasuring with intercourse initially interdicted, which lifts performance pressure and interrupts **spectatoring** (the anxious self-observation that sabotages arousal). Disorder-specific techniques layer on top: lifelong female orgasmic disorder is treated with directed masturbation, sometimes with a vibrator, plus Kegel exercises to build pelvic-floor awareness.

MODALITY	BEST SUITED TO	WHAT IT DOES
Psychoeducation	All three disorders	**Corrects myths, reframes the response cycle and responsive desire**
Treat the contributors	Acquired dysfunction of any kind	**Mood, anxiety, culprit drugs, hormonal and genital pathology**
Sensate focus (sex therapy)	Interest/arousal and orgasmic disorder, as a couple	**Non-demand pleasuring, intercourse banned early, ends spectatoring**
Directed masturbation and Kegels	Lifelong female orgasmic disorder	**Self-exploration to first orgasm; pelvic-floor awareness**
Pelvic-floor physiotherapy and graded dilators	Genito-pelvic pain/penetration disorder	**Desensitises penetration, retrains guarding; see 10.6**

The multimodal management of the female sexual dysfunctions, biopsychosocial and psychological-first; the full stepwise route is biopsychosocial-first (ISSM; Kaplan and Sadock CTP 2024).

3	6	26.55	100
FSIAD CRITERION A INDICATORS NEEDED, FROM A SET OF SIX	MONTHS MINIMUM DURATION FOR EVERY DYSFUNCTION	FSFI CUT-OFF FLAGGING FEMALE SEXUAL DYSFUNCTION	FLIBANSERIN BEDTIME DOSE (MG PER DAY)

MNEMONIC

PLISSIT

The escalating sex-therapy framework (Annon): **P**ermission (normalise and permit the sexual concern), **LI** Limited Information (targeted education), **SS** Specific Suggestions (concrete behavioural tasks such as sensate focus, dilators or directed masturbation), and **IT** Intensive Therapy (referral for in-depth psychotherapy). Most female sexual dysfunction is resolved at the first three, lighter levels, which is exactly why the drugs sit so far down the list.

GOOD TO REMEMBER

- **Multimodal management (guideline-anchored, ISSM, biopsychosocial):** assess and treat biopsychosocially, lead with psychoeducation, treat the contributors (mood, anxiety, culprit drugs, hormones), and use sensate focus as the core sex-therapy method, with directed masturbation for lifelong female orgasmic disorder; the FSFI (cut-off at or below 26.55) grades severity, and pharmacology is a narrow adjunct, not the first move.

10.6 The pain-penetration physiotherapy, local oestrogen, and the limited drug options

For pain and penetration, physiotherapy and graded dilators; for menopausal atrophy, local oestrogen; drugs are last and licence-limited. Genito-pelvic pain/penetration disorder has the most concrete physical management of the three: pelvic-floor physiotherapy and progressive vaginal trainers, in which the woman uses her own fingers or size-graduated dilators to desensitise penetration and unlearn the protective muscle guarding, ideally with a pelvic-floor physiotherapist, and combined with the psychological and sex-therapy work described above (Kaplan and Sadock CTP 2024). Where the driver is genitourinary syndrome of menopause, low-

dose local vaginal oestrogen (for example estriol or estradiol cream or pessary) is effective for the dryness and dyspareunia and is preferred over systemic hormone therapy for isolated urogenital symptoms (NICE NG23 menopause 2015; ISSM). Pharmacotherapy for low desire is genuinely limited: the two agents licensed anywhere, flibanserin (a 5-HT1A agonist and 5-HT2A antagonist, 100 mg once daily at bedtime) and bremelanotide (a melanocortin agonist, 1.75 mg subcutaneously on demand), are approved only for acquired, generalised hypoactive sexual desire disorder in *premenopausal* women, and both are covered in full, with their boxed warnings and cautions, in the dedicated flibanserin topic (Addyi FDA label 2015; Vyleesi FDA label 2019). PDE5 inhibitors are not established for female sexual dysfunction (results are inconsistent), and systemic testosterone for female low desire is off-label and unapproved in most jurisdictions; the overall pharmacological evidence base is weak, which is precisely why couple-based and psychological approaches remain the lead.

GOOD TO REMEMBER

- **Pain-penetration and oestrogen management (guideline-anchored):** genito-pelvic pain penetration disorder is treated with pelvic-floor physiotherapy and graded dilators plus the psychological work; menopausal dyspareunia (genitourinary syndrome of menopause) is treated with low-dose local vaginal oestrogen, preferred over systemic therapy for isolated urogenital symptoms (NICE NG23).
- **The limited drug options (guideline-anchored):** flibanserin (100 mg once daily at bedtime) and bremelanotide (1.75 mg subcutaneous, on demand) are licensed only for acquired, generalised hypoactive sexual desire disorder in premenopausal women; PDE5 inhibitors are not established and systemic testosterone is off-label. Full pharmacology sits in the dedicated flibanserin topic.

HOLD THIS

The female sexual dysfunctions are the DSM-5-TR trio, female sexual interest/arousal disorder (desire and arousal merged), female orgasmic disorder, and genito-pelvic pain/penetration disorder (vaginismus plus dyspareunia), each gated by about six months and distress; management is biopsychosocial-first (psychoeducation, sensate focus, dilators and pelvic-floor work, local oestrogen for menopausal painful sex), and the only licensed drugs treat premenopausal acquired generalised low desire alone.

11 · Dapoxetine and flibanserin

These two agents pair naturally as a compact pharmacology question: both are *repurposed serotonergic drugs licensed for a single sexual dysfunction*, one for the man and one for the woman, and each carries a small cluster of verified facts, a dose, a timing, a label restriction, and one signature caution, that the examiner can pull straight out. **Dapoxetine** is the short-acting, on-demand pill taken before sex for **premature ejaculation**; **flibanserin** is the daily bedtime pill taken for months for **hypoactive sexual desire disorder** in premenopausal women. Confuse their dosing rhythms and you lose the mark; hold the rhythm and the rest follows.

How to use this page. Learn each drug as a triad: what it is (mechanism and class), how it is dosed (the verified on-demand versus daily rhythm), and its one examinable caution. Then read the pair against each other, because the discriminator most often tested is the licensing restriction, on-

demand for **premature ejaculation** against acquired, generalised, **premenopausal** HSDD, and the single interaction that gets each drug into trouble.

11.1 Dapoxetine: the on-demand short-acting SSRI for premature ejaculation

The only agent licensed for on-demand treatment of premature ejaculation. Dapoxetine is a **short-acting SSRI** developed specifically for premature ejaculation, and it is the first and only drug approved for its **on-demand** treatment (Kaplan and Sadock CTP 2024; New Oxford Textbook of Psychiatry). The sexual-medicine and regulatory positions are uniform: an **on-demand SSRI** is the first-line pharmacological option for lifelong premature ejaculation (ISSM 2014; EAU male sexual dysfunction; AUA 2018), and the drug is licensed for this indication under the label recommendation of a **30 mg** starting dose taken **1 to 3 hours** before sexual activity (NICE ESNM40; Priligy SPC). It is titrated upward only if the starting dose is insufficient and tolerated, to a maximum **60 mg**, and it is never taken more than once every 24 hours. Benefit and risk are reappraised after the first 4 weeks or at least 6 doses.

Why the on-demand rhythm works. Unlike the long-acting SSRIs (paroxetine, sertraline, fluoxetine, citalopram), which delay ejaculation only when taken daily for a fortnight or more and are unsuitable as an as-needed drug, dapoxetine is absorbed and cleared rapidly, so a single pre-coital dose raises synaptic serotonin over the window that matters and then washes out. Its common adverse effects are the expected serotonergic ones, nausea, dizziness, headache and diarrhoea, together with an orthostatic, syncope-prone effect that drives its cardinal interaction rule (Priligy SPC). It is contraindicated in significant cardiac disease and in a history of mania or severe depression.

FEATURE	DAPOXETINE (VERIFIED)
Class	Short-acting, on-demand SSRI
Indication	Premature ejaculation (the only licensed on-demand agent)
Start dose (mg)	30, taken 1 to 3 hours before activity
Ceiling dose (mg)	60, only if 30 is insufficient and tolerated
Frequency	Not more than once every 24 hours
Review	Reappraise after 4 weeks or at least 6 doses
Signature caution	Do not combine with a PDE5 inhibitor (syncope); avoid in cardiac disease and in a mania or severe-depression history

Dapoxetine at a glance: the on-demand short-acting SSRI for premature ejaculation, with its verified label doses and the PDE5-inhibitor caution (ISSM 2014; NICE ESNM40; Priligy SPC).

PEARL

The pharmacokinetics are the point. A chronic SSRI blunts ejaculation through gradual receptor adaptation that takes days to build, which is why paroxetine and its peers must be taken every day off-label. Dapoxetine's rapid absorption and short half-life invert that logic: it acts within about an hour and clears quickly, so it can be swallowed only when needed, roughly 1 to 3 hours ahead. That single kinetic difference, not any special receptor trick, is what makes it the on-demand agent.

INDIA

Dapoxetine is heavily marketed in India: lead the generic, with Duralast and Sustinex the common brands, and it is also sold in sildenafil-dapoxetine and tadalafil-dapoxetine fixed-dose combinations. The verified caution runs against exactly those combinations, since the Priligy SPC advises against pairing dapoxetine with a PDE5 inhibitor because of syncope risk; keep the generic primary and confirm the exact product and strength locally before any prescribing use. Flibanserin has no established routine Indian presence, so it is examined as a name to recognise rather than a drug to prescribe here.

GOOD TO REMEMBER

- **Dapoxetine (guideline-anchored, ISSM 2014, NICE ESNM40, Priligy SPC):** the only agent licensed for on-demand premature ejaculation; a short-acting SSRI started at 30 mg taken 1 to 3 hours before activity, raised to a maximum 60 mg only if needed and tolerated, not more than once every 24 hours, and never combined with a PDE5 inhibitor because of syncope risk.

11.2 Flibanserin: the daily bedtime pill for premenopausal HSDD

A daily serotonergic agent for acquired, generalised HSDD in premenopausal women. Flibanserin (brand Addyi) is a 5-HT1A agonist and 5-HT2A antagonist that, in the prefrontal cortex, lowers serotonin while raising noradrenaline and dopamine activity; it was originally trialled as an antidepressant, failed, and was repurposed for desire (Kaplan and Sadock CTP 2024; Goodman and Gilman). It is one of the two FDA-approved agents (with bremelanotide) for acquired, generalised hypoactive sexual desire disorder (HSDD) in **premenopausal** women only, and its licensed dose is **100 mg** once daily at bedtime (Addyi FDA label 2015). Unlike dapoxetine it is a maintenance, not an as-needed, drug: it is taken every night for weeks, and it is discontinued after 8 weeks if there is no improvement.

Modest effect, three named cautions. The efficacy is real but modest, a small rise in satisfying sexual events and desire with reduced desire-related distress (Tasman; New Oxford Textbook of Psychiatry). Its adverse-effect and interaction profile is where marks sit: hypotension, syncope, somnolence, dizziness, nausea and dry mouth (Maudsley Prescribing Guidelines). The bedtime timing is deliberate, limiting daytime hypotension and sedation. It carries a boxed warning for severe hypotension and syncope with alcohol and with strong CYP3A4 inhibitors, so alcohol co-use and CYP3A4 interactions are the two cautions to state, alongside its CNS-depressant, sedating profile. Reassuringly, it appears safe in women already taking antidepressants (Maudsley Prescribing Guidelines).

FEATURE	FLIBANSERIN (VERIFIED)
Mechanism	5-HT1A agonist, 5-HT2A antagonist (lowers cortical serotonin, raises noradrenaline and dopamine)
Indication	Acquired, generalised HSDD in premenopausal women only
Dose (mg)	100 once daily at bedtime
Rhythm	Daily maintenance; stop at 8 weeks if no benefit
Effect size	Modest
Signature cautions	Alcohol and strong CYP3A4 inhibitors (hypotension, syncope); CNS depression and sedation

Flibanserin at a glance: the daily bedtime pill for premenopausal, acquired, generalised HSDD, with its modest effect and the alcohol, CYP3A4 and CNS-depression cautions (Addyi FDA label 2015; Maudsley Prescribing Guidelines).

GOOD TO REMEMBER

- **Flibanserin (guideline-anchored, Addyi FDA label 2015):** a 5-HT1A agonist and 5-HT2A antagonist for acquired, generalised HSDD in premenopausal women, dosed 100 mg once daily at bedtime, of modest effect, stopped at 8 weeks if no benefit; the examinable cautions are alcohol and strong CYP3A4 inhibitors (hypotension and syncope) plus its sedating, CNS-depressant profile.

11.3 Reading the pair: on-demand versus daily, and the label restrictions

Two rhythms, two label boxes, two cautions. The pair is designed to be discriminated. Dapoxetine is *on-demand and short-acting*, swallowed before a single act of sex for premature ejaculation, its trap being combination with a PDE5 inhibitor. Flibanserin is *daily and maintenance*, taken every bedtime for premenopausal HSDD, its trap being alcohol. The restriction most often tested on flibanserin is the population box: it is licensed only for *acquired* (not lifelong), *generalised* (not situational), *premenopausal* HSDD, so offering it to a postmenopausal woman or for a situational, relationship-bound loss of desire is off-label and off-target.

AXIS	DAPOXETINE	FLIBANSERIN
Target	Premature ejaculation (men)	**Acquired, generalised HSDD (premenopausal women)**
Class	Short-acting SSRI	**5-HT1A agonist, 5-HT2A antagonist**
Rhythm	On-demand, 1 to 3 hours before	**Daily, at bedtime**
Dose (mg)	30 start, up to 60 max	**100 once daily**
Signature caution	Not with a PDE5 inhibitor (syncope)	**Not with alcohol or strong CYP3A4 inhibitors (hypotension, syncope)**
Review point	After 4 weeks or 6 doses	**Stop at 8 weeks if no benefit**

The discrimination table for the pair; the contrast in dosing rhythm and licensed population is the highest-yield line, and the two kinetic profiles could hardly differ more (ISSM 2014; NICE ESNM40; Addyi FDA label 2015).

30	60	100	8
DAPOXETINE START DOSE (MG)	DAPOXETINE CEILING DOSE (MG)	FLIBANSERIN NIGHTLY DOSE (MG)	FLIBANSERIN REVIEW POINT (WEEKS)

RULE **The rhythm names the drug and the caution.** On-demand short-acting SSRI before sex means dapoxetine for premature ejaculation, caution the PDE5 inhibitor; daily bedtime 5-HT1A agonist for premenopausal, acquired, generalised HSDD means flibanserin, caution the alcohol.

TRAP **Prescribing flibanserin as an on-demand libido pill, or ignoring its label box.** It is a daily maintenance drug, not a pre-sex tablet, and it is licensed only for acquired, generalised HSDD in premenopausal women; offering it to a postmenopausal woman, for situational loss of desire, or without the alcohol and CYP3A4 warning is the classic error.

COMMON TRAP

Pairing dapoxetine with a PDE5 inhibitor. It is tempting when a man reports both premature ejaculation and erectile difficulty, and Indian fixed-dose combinations make it easy, but the Priligy SPC advises against the combination because of syncope risk. Treat the dominant complaint first and keep the two apart unless a specialist judges otherwise.

HOLD THIS

Dapoxetine is the on-demand short-acting SSRI for premature ejaculation, 30 mg (up to 60) taken 1 to 3 hours before sex and never with a PDE5 inhibitor; flibanserin is the daily bedtime 5-HT1A agonist / 5-HT2A antagonist for acquired, generalised, premenopausal HSDD, 100 mg nightly, of modest effect and never with alcohol.

12 · Paraphilic disorders

This topic is examined less on the exotic list of behaviours and more on one clean conceptual line: the difference between a **paraphilia**, an atypical sexual interest that is not in itself a disorder, and a **paraphilic disorder**, which the current nosology reserves for a paraphilia that

either causes the person *distress* or impairment or entails *harm*, or the risk of it, to another, usually non-consenting, person. Get that threshold right and most of the marks follow; miss it and you pathologise a private, harmless preference or, worse, treat a criminal charge as if the label alone made a diagnosis. The class also carries a genuine forensic and risk-assessment dimension the psychiatrist is asked to comment on, and a graded, guideline-anchored management answer that candidates rarely rehearse.

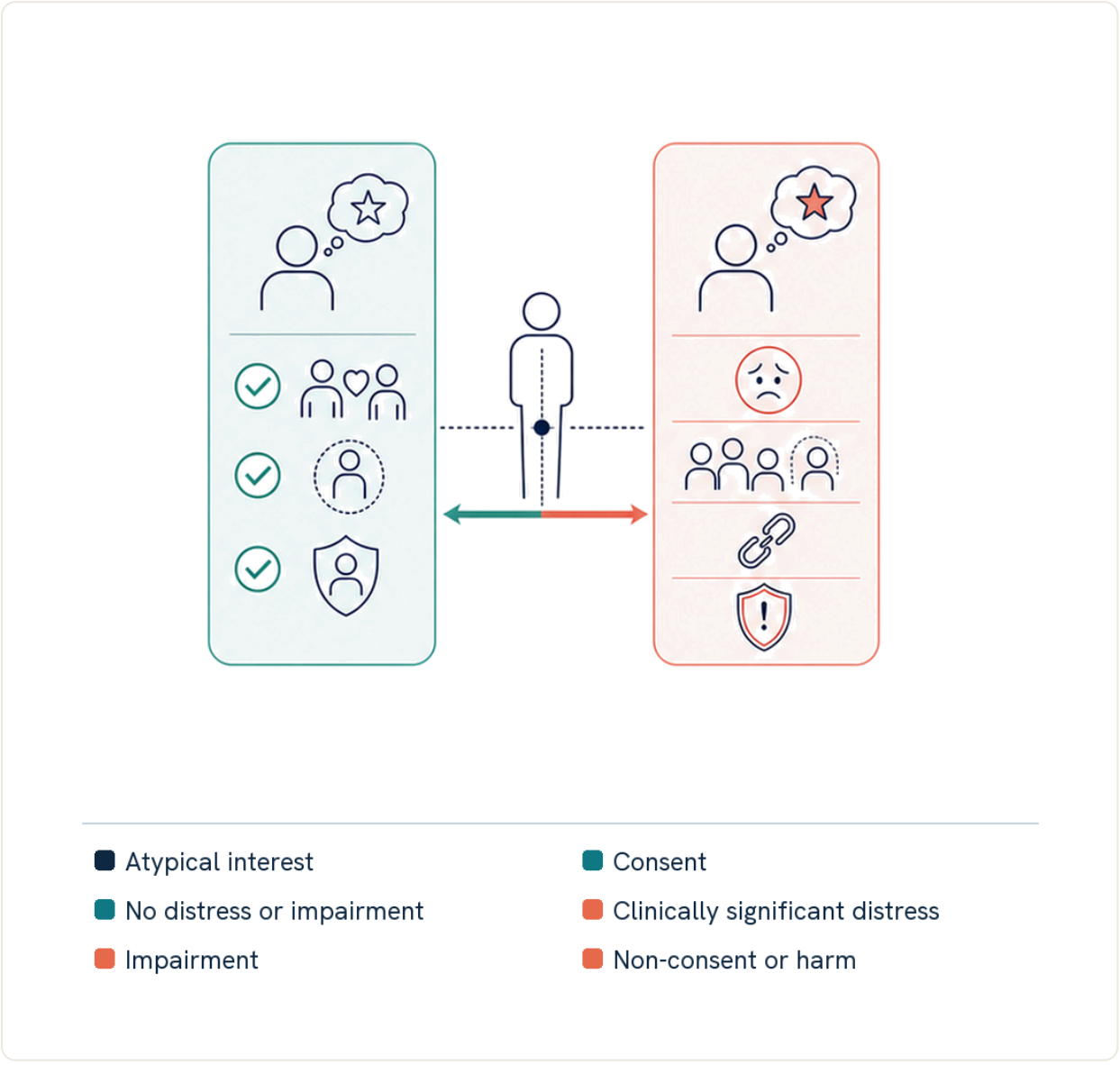


Fig 18.9 An atypical sexual interest is not by itself a disorder. A paraphilic disorder requires clinically significant distress or impairment, or behaviour involving a non-consenting person or substantial risk of harm.

How to use this page. First fix the paraphilia-against-disorder distinction and the shared criteria that gate every entity; then learn the eight named DSM-5-TR types and the sharp place where ICD-11 parts company; then the forensic frame, where the cardinal error is diagnosing from the offence rather than the sexual preference; and finally the **management of paraphilia**, psychological relapse-prevention first, with SSRIs and, for severe or high-risk cases, testosterone-lowering antiandrogen or GnRH-agonist treatment reserved for the top of the ladder. The combined map of the paraphilic and impulse-control classes is drawn in the accompanying figure

at the impulse-control block; refer to it there. The tone throughout is clinical, nosological, and non-graphic.

12.1 Paraphilia against paraphilic disorder: the consent, distress and harm threshold

An interest is not a disorder until it crosses a threshold. DSM-5 and DSM-5-TR define a paraphilia as "any intense and persistent sexual interest other than sexual interest in genital stimulation or preparatory fondling with phenotypically normal, physically mature, consenting human partners" (Kaplan and Sadock CTP 2024; DSM-5-TR 2022). The pivotal 2013 move was to separate that interest from the paraphilic disorder, defined as a paraphilia that is *currently causing distress or impairment to the individual*, or *a paraphilia whose satisfaction has entailed personal harm, or the risk of harm, to others*. In other words a paraphilia is a disorder only when criterion B is met: the person is distressed or impaired, or the interest is acted on with, or poses a risk to, a non-consenting person. This preserves the line between non-normative and pathological sexual behaviour without branding every unusual preference a mental illness. Across every named entity the shared gates are the same: the pattern is present for at least six months, and either causes clinically significant distress or impairment, or the urges have been acted on with a non-consenting person.

RULE **Distress, impairment, or harm to a non-consenting other is what makes a paraphilia a disorder.** The atypical interest alone is not diagnosable; you need criterion B, distress or impairment to the person, or personal harm or the risk of it to another who has not consented. Consent, distress and harm are the three words that carry the diagnosis.

GOOD TO REMEMBER

- **Paraphilic disorder (the defining criterion):** an intense, persistent atypical sexual interest present for at least six months that *either* causes the individual clinically significant distress or impairment *or* is acted on with, or risks harm to, a non-consenting person; without that criterion B threshold it is a paraphilia, not a disorder.

12.2 The named types, and where ICD-11 parts from DSM-5-TR

Eight named disorders in DSM-5-TR, grouped three ways. DSM-5-TR names eight specific paraphilic disorders, organised into anomalous *activity* preferences (voyeuristic disorder, exhibitionistic disorder, frotteuristic disorder), *algolagnic* disorders of pain and suffering (sexual masochism disorder and sexual sadism disorder), and anomalous *target* preferences (paedophilic disorder, fetishistic disorder, transvestic disorder), with residual "other specified" and "unspecified" categories replacing the old NOS label (Kaplan and Sadock CTP 2024; DSM-5-TR 2022). The activity-preference and sadism disorders require that the urges be acted on with a non-consenting person, or that they cause marked distress or impairment; the target-preference disorders can qualify on distress or impairment alone. Two age anchors are examined: for paedophilic disorder the individual must be at least 16 years of age and at least five years older than the prepubescent child, generally 13 years of age or younger; for voyeuristic disorder the individual must be at least 18 years of age. Course specifiers, "in a controlled environment" and "in full remission", apply to all except paedophilic disorder.

ICD-11 draws the line by consent, and drops three DSM entities. The ICD-11 "Paraphilic disorders" grouping is built explicitly around whether the arousal focus is on non-consenting others or on solitary or consenting behaviour. It lists exhibitionistic (6D30), voyeuristic (6D31), paedophilic (6D32), coercive sexual sadism (6D33) and frotteuristic (6D34) disorders, plus a catch-all for other paraphilic disorder involving non-consenting individuals (6D35), and a separate residual for paraphilic disorder involving solitary behaviour or consenting individuals (6D36), diagnosed only where there is marked distress and not merely because the behaviour is socially disapproved (ICD-11 CDDR). Crucially, ICD-11 *removed* fetishistic disorder, fetishistic transvestism and sadomasochism as named disorders, on the reasoning that private, consensual variants are not, by themselves, mental disorders. That DSM-keeps / ICD-drops split for fetishism and transvestism is a favourite discriminator.

DISORDER	CORE AROUSAL FOCUS	AGE OR DURATION ANCHOR	THE ONE THING TO ATTACH
Exhibitionistic disorder	Exposing one's genitals to an unsuspecting person	At least six months	**One of the three commonest offences in police records (with voyeurism and paedophilia)**
Voyeuristic disorder	Observing an unsuspecting person naked or in sexual activity	Individual at least 18 years of age	**The only paraphilia with a stated minimum age for the diagnosis**
Frotteuristic disorder	Touching or rubbing against a non-consenting person	At least six months	**Typically in crowded settings; from French "frotter", to rub**
Paedophilic disorder	Prepubescent child, generally 13 years of age or younger	Individual at least 16 years and at least five years older	**No course specifiers; the forensic core of the class**
Sexual sadism disorder	Physical or psychological suffering of another	At least six months	**ICD-11 names only the coercive, non-consenting form (6D33)**
Sexual masochism disorder	Being humiliated, beaten, bound or made to suffer	At least six months	**Often benign; asphyxiophilia is the dangerous specifier**
Fetishistic disorder	Non-living objects or a specific non-genital body part	At least six months	**Kept in DSM-5-TR; removed from ICD-11**
Transvestic disorder	Sexual arousal from cross-dressing	At least six months	**Kept in DSM-5-TR; removed from ICD-11. Not the same as gender incongruence**

The eight DSM-5-TR paraphilic disorders and their discriminators; ICD-11 retains only the five non-consenting-focused disorders plus two residual codes and drops fetishistic, transvestic and sadomasochism as named entities (Kaplan and Sadock CTP 2024; DSM-5-TR 2022; ICD-11 CDDR).

PEARL

Read the "in a controlled environment" and "in full remission" specifiers carefully. The absence of paraphilic behaviour in a prison or secure unit, where opportunity is removed, is *not* remission; it is simply a controlled environment. Full remission requires no acting on the urges with a non-consenting person and no distress or impairment for at least five years while in an *un*controlled setting, which is why a quiet custodial record cannot, on its own, be read as recovery.

GOOD TO REMEMBER

- **Exhibitionistic disorder (the criterion):** recurrent, intense arousal from exposing the genitals to an unsuspecting person for at least six months, acted on with a non-consenting person or causing distress or impairment; exhibitionism is one of the three commonest offences in police records.
- **Voyeuristic disorder (the discriminator):** arousal from observing an unsuspecting naked or sexually active person; the individual must be at least 18 years of age, the only paraphilia with a stated minimum diagnostic age, distinguishing it from adolescent curiosity.
- **Frotteuristic disorder (the criterion):** arousal from touching or rubbing against a non-consenting person, usually in a crowd, acted on or causing distress or impairment.
- **Paedophilic disorder (the criterion):** recurrent, intense arousal to a prepubescent child, generally 13 years of age or younger, with the individual at least 16 years of age and at least five years older than the child; it uniquely carries no course specifiers.
- **Fetishistic and transvestic disorder (the divergence):** both remain named DSM-5-TR disorders (objects or non-genital body parts; cross-dressing), but ICD-11 has removed them, treating private, consensual variants as non-disordered.

12.3 The forensic and risk-assessment dimension

A paraphilic disorder is a diagnosis; a sex offender is a legal category, and the two are not interchangeable. The term "sex offender" describes a person legally convicted of a sexual offence and says nothing about the presence or absence of a paraphilia; conversely a person with a paraphilia may never offend, obtaining gratification through fantasy alone (Kaplan and Sadock CTP 2024). The diagnosis rests on the individual's *sexual preference*, established through a comprehensive psychosexual evaluation, collateral history and, where used, objective measures, penile plethysmography (phallometry), visual reaction time and, in mandated settings, the sexual-history polygraph, since self-report is unreliable and there is no definitive test. Crossover between paraphilias is common, so a single presentation should prompt a review for the others. Risk is best estimated with structured actuarial instruments such as the Static-99R, which the evidence shows predict relative recidivism risk more accurately than unstructured clinical judgement, and clinicians must also weight the dynamic risk factors, deviant sexual interest, sexual preoccupation, poor self-regulation, intimacy deficits and offence-supportive attitudes.

TRAP **Diagnosing the paraphilia from the offence, or equating "sex offender" with a paraphilic disorder.** A man who has molested a child may have paedophilic disorder, but the same act can arise from intellectual disability, a manic episode, dementia or intoxication; you diagnose from the sustained pattern of sexual *preference*, not from the behaviour or the conviction alone.

WORKED EXAMPLE

A man is referred after exposing himself; he is distressed, describes a decade of recurrent urges to expose to unsuspecting strangers, and has acted on them repeatedly. That sustained pattern, with acting on the urges toward non-consenting others, supports exhibitionistic disorder. Contrast a first-ever episode of public undressing during a florid manic episode, with no prior deviant arousal: here the behaviour is a symptom of the mood disorder, and a paraphilic diagnosis would be wrong. Screen him for the other paraphilias, because crossover is the rule, and estimate risk with a structured actuarial tool rather than a gut impression.

12.4 Management principles: the graded, psychological-first ladder

The management of paraphilia is graded to severity and risk, and begins with psychological work. There is no evidence any paraphilic disorder can be "cured"; the realistic goal is control of behaviour and reduction of risk (New Oxford Textbook of Psychiatry). The World Federation of Societies of Biological Psychiatry (WFSBP) algorithm assigns treatment by severity: the less severe are managed with psychotherapy alone, while more severe or higher-risk presentations add pharmacotherapy on top (Kaplan and Sadock CTP 2024). The empirically supported psychological approach is structured cognitive-behavioural treatment, historically framed as relapse prevention, targeting the cognitive distortions (minimisations, justifications) and the offence cycle, and increasingly delivered through strength-based rehabilitation frameworks, the Good Lives Model and the Risk-Need-Responsivity model. Meta-analysis finds cognitive-behavioural treatment reduces reoffending more than didactic or purely psychodynamic work, and is comparable to antiandrogen treatment in effect; a non-judgemental, empathic therapist improves outcomes regardless of the programme's orientation.

MNEMONIC

PSYCHOTHERAPY → SSRI → ANTIANDROGEN → GnRH AGONIST

The WFSBP severity ladder for the management of paraphilia: cognitive-behavioural relapse-prevention for the less severe, an SSRI added as the first drug step, then a testosterone-lowering antiandrogen, and a long-acting GnRH agonist at the top for severe, treatment-refractory or high-risk cases. You climb only as severity and risk demand.

GOOD TO REMEMBER

- **Psychological management (guideline-anchored, WFSBP):** structured cognitive-behavioural relapse-prevention is first-line for less severe paraphilic disorders and the base of every plan; it targets cognitive distortions and the offence cycle, is comparable to antiandrogens in effect, and is now embedded in strength-based frameworks such as the Good Lives Model.

12.5 Pharmacological options: SSRIs, antiandrogens and GnRH agonists

Drugs work by dampening serotonergically driven urges or by lowering testosterone, and they escalate with severity. When medication is indicated, the first step is an SSRI, on the OCD analogy that enhanced central serotonergic tone reduces paraphilic arousal; it suits milder cases and those with prominent obsessive, compulsive urges, though the controlled evidence is limited

(Kaplan and Sadock CTP 2024). For more severe or higher-risk cases the strategy is to lower testosterone. The antiandrogens cyproterone acetate and medroxyprogesterone acetate are synthetic progestogens that reduce serum testosterone and thereby libido, erections and ejaculation; cyproterone acetate is used at **50 to 100 mg** per day and is licensed for male hypersexuality in some countries at 50 mg twice daily (Maudsley Prescribing Guidelines; Goodman and Gilman). At the top of the ladder, the long-acting GnRH agonists leuprolide and triptorelin produce a reversible chemical castration by exhausting the hypothalamic-pituitary axis; leuprolide is given as **7.5 mg** intramuscularly every month and triptorelin as 11.25 mg intramuscularly every 12 weeks, and they are generally better tolerated than the older antiandrogens (Maudsley Prescribing Guidelines; Kaplan and Sadock CTP 2024). Surgical castration is now nearly obsolete. All testosterone-lowering agents demand baseline and follow-up monitoring, testosterone, liver function, glucose and bone mineral density, given risks of osteopenia, weight gain, hyperglycaemia, gynaecomastia and, for cyproterone, meningioma.

STEP	AGENT	TYPICAL DOSE AND ROUTE	KEY POINT AND MONITORING
First drug	SSRI (e.g. sertraline, fluoxetine)	Standard antidepressant range, oral daily	**For milder or obsessive-type urges; evidence limited but low-risk**
Antiandrogen	Cyproterone acetate	50 to 100 mg oral, daily	**Lowers testosterone; watch LFTs, meningioma risk, feminisation**
Antiandrogen	Medroxyprogesterone acetate	Oral or intramuscular depot	**Progestogenic androgen-lowering; weight gain, glucose, thromboembolism**
GnRH agonist	Leuprolide	7.5 mg IM, monthly	**Chemical castration for severe or refractory cases; monitor bone density**
GnRH agonist	Triptorelin	11.25 mg IM, every 12 weeks	**Depot GnRH agonist; better tolerated than antiandrogens**

The pharmacological ladder for paraphilic disorders, escalated by severity and risk; doses are the verified Maudsley and Goodman and Gilman figures, and every testosterone-lowering agent needs testosterone, LFT, glucose and bone-density monitoring (Maudsley Prescribing Guidelines; Kaplan and Sadock CTP 2024; see gaps for paraphilia-specific dosing).

INDIA

The forensic frame is the genuine Indian anchor. Child sexual offences fall under the POCSO Act (Protection of Children from Sexual Offences Act, 2012), which also imposes a mandatory-reporting duty on the clinician, the practical face of the paedophilic-disorder risk assessment. Indian criminal law separately makes voyeurism a distinct statutory offence (introduced by the Criminal Law Amendment Act, 2013, and carried into the Bharatiya Nyaya Sanhita, 2023). India has *no* chemical-castration sentencing statute, and the Justice Verma Committee (2013) advised against castration as punishment, so testosterone-lowering treatment stays a consented clinical decision, not a court penalty. On availability, leuprolide is marketed in India as Lupride Depot and triptorelin as Decapeptyl; cyproterone acetate is available as an antiandrogen (confirm the exact standalone product and strength locally, see gaps). Keep the generic primary.

GOOD TO REMEMBER

- **Pharmacological management (guideline-anchored, WFSBP and Maudsley):** an SSRI is the first drug step for milder or obsessive-type urges; for severe or high-risk cases lower testosterone with an antiandrogen (cyproterone acetate at 50 to 100 mg per day) and, at the top, a long-acting GnRH agonist (leuprolide 7.5 mg IM monthly, triptorelin every 12 weeks), all with testosterone, LFT, glucose and bone-density monitoring; surgical castration is obsolete.

8	6	18	50 to 100
DSM-5-TR NAMED PARAPHILIC DISORDERS	MONTHS MINIMUM SYMPTOM DURATION	VOYEURISTIC DISORDER MINIMUM AGE (YEARS)	CYPROTERONE ACETATE DOSE (MG PER DAY)

HOLD THIS

A paraphilia becomes a paraphilic *disorder* only when it causes the person distress or impairment, or entails harm or the risk of harm to a non-consenting other, the consent-distress-harm threshold; you diagnose from the sexual preference, not the offence, and the management of paraphilia climbs from cognitive-behavioural relapse-prevention to SSRIs to testosterone-lowering antiandrogen or GnRH-agonist treatment for the severe and high-risk.

13 · Gender incongruence and gender-affirmative care

This is the topic where nosology and human rights meet, and the examiner wants to see that you can hold both. The single biggest fact is a reclassification: the eleventh revision of the international classification moved **gender incongruence** out of the mental disorders chapter altogether, so the modern, guideline-anchored position is that being transgender is *not* a mental illness. The management answer is not a drug at all but a stance, the gender-affirmative approach codified in the WPATH Standards of Care, and a clear sense of what the psychiatrist does and does not do within it. High-yield marks cluster on four things: the terminology (and the incongruence-versus-dysphoria distinction), the ICD-11 **depathologisation** contrasted with the DSM retention of a diagnosis, the affirmative-care pathway, and the Indian legal frame.

How to use this page. First fix the vocabulary, because half of the errors on this topic are vocabulary errors; then learn the two competing constructs, gender incongruence (the mismatch, no distress required) and gender dysphoria (the mismatch plus clinically significant distress); then

hold the two classifications side by side, ICD-11 having depathologised where DSM-5-TR retains a diagnosis; then anchor the affirmative-care pathway and the mental-health professional's bounded role; and finally the Indian statute. The one error this page is built to prevent is treating the identity itself as the pathology, when the guideline-anchored target of care is the distress, the comorbidity and the stigma, never the person's gender.

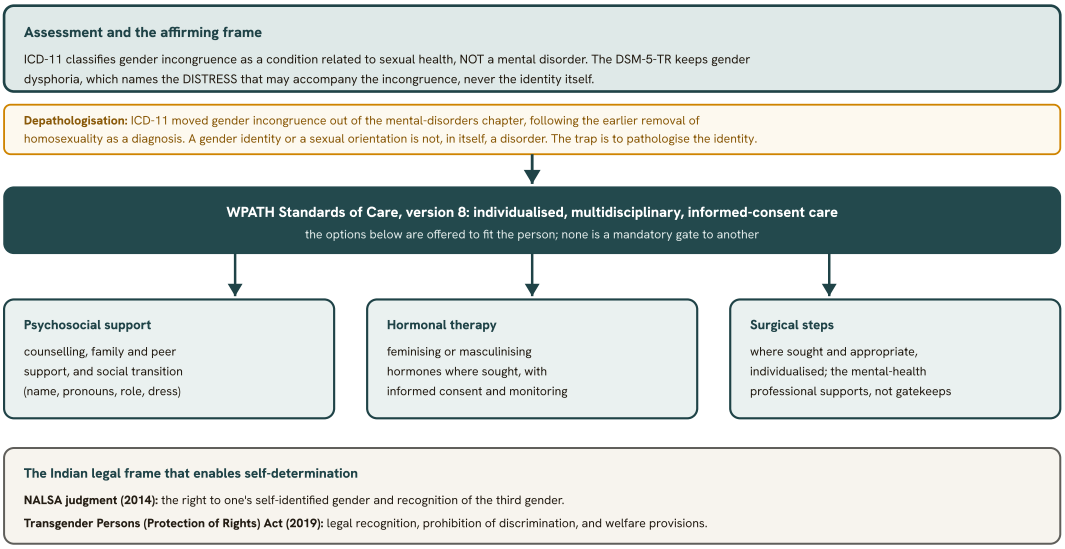


Fig 18.10 The gender-affirmative-care pathway. Care begins from an affirming frame: ICD-11 treats gender incongruence as a condition related to sexual health and not a mental disorder, having moved it out of the mental-disorders chapter just as homosexuality was removed as a diagnosis decades earlier, while the DSM-5-TR retains gender dysphoria to name the distress that may accompany incongruence rather than the identity itself. The WPATH Standards of Care, version 8, then set out an individualised, multidisciplinary, informed-consent model in which psychosocial support and social transition, hormonal therapy, and surgical steps are offered to fit the person, none a mandatory gate to another, and the mental-health professional supports rather than gatekeeps. In India this is underpinned by the NALSA judgment of 2014 and the Transgender Persons (Protection of Rights) Act of 2019.

13.1 The terminology: sex, gender identity and the umbrella terms

Separate sex, gender identity, gender expression and sexual orientation before anything else. The words are examined precisely, and conflating any two of them is the classic slip (Kaplan and Sadock CTP 2024). *Sex* refers to biological variables (genes, chromosomes, gonads, internal and external genital structures) that are male-typical or female-typical; sex assigned at birth is the sex recorded for an individual in infancy. *Gender* is the social category and role. Gender identity, a term coined by Robert Stoller in the mid-twentieth century, is a person's persistent inner sense of their own gender, which today is recognised as possibly male, female, both, in between or neither. Critically, gender identity says nothing about sexual orientation: whether a person experiences their gender as man or woman does not predict whom they are attracted to. Keep these four axes independent and most of the traps disappear.

Sex assigned at birth

The sex (male or female) recorded for a person at birth on the basis of observed anatomy; the reference point against which incongruence is later described.

Gender identity

A person's persistent internal sense of their own gender (Stoller); may be male, female, non-binary or another category, and is independent of sexual orientation.

Gender expression / gender role

The outward presentation of gender (dress, mannerisms, social role); the visible counterpart of the inner identity.

Transgender

Umbrella term (coined by Virginia Prince, early 1970s) for a person whose gender identity or expression differs from the sex assigned at birth; it is an identity, not a diagnosis.

Cisgender

A person whose gender identity aligns with the sex assigned at birth.

RULE **Identity is not orientation, and neither is a diagnosis.** Gender identity (who I am), gender expression (how I present), sex assigned at birth, and sexual orientation (whom I am drawn to) are four independent axes; being transgender or cisgender tells you nothing about a person's sexual orientation, and neither is, in itself, a disorder.

13.2 Gender incongruence versus gender dysphoria: where distress enters

Incongruence is the mismatch; dysphoria is the mismatch plus clinically significant distress. This one distinction earns marks repeatedly. **Gender incongruence** is a marked and persistent mismatch between a person's experienced or expressed gender and the sex assigned at birth. It is a description, not a pathology, and by itself it requires no distress. **Gender dysphoria** is the term the DSM uses for the aversive distress that *some* people with that incongruence experience; it is defined by the presence of clinically significant distress or impairment, and that distress, not the identity, is what a clinician treats (Kaplan and Sadock CTP 2024; DSM-5-TR 2022; ICD-11). The move from "gender identity disorder" to "gender dysphoria" in DSM-5 was deliberately made to strip the word "disorder" from the label and to shift clinical focus from identity to distress. Much of that distress is now understood through *gender minority stress*, the chronic strain of stigma, misgendering and discrimination, which is linked to elevated rates of depression, anxiety and suicidality; affirmation and the reduction of stigma are correspondingly protective. The population-level and public-health dimension of that suicide risk is developed in the Community psychiatry and public health notes; here the point is simply that distress is contingent and modifiable, not intrinsic to being transgender.

PEARL

A memorable way to hold the pair: **incongruence** is a noun of fact (the two do not match), **dysphoria** is a noun of feeling (and it hurts). You can have the first without the second, and a large proportion of transgender people do. The clinician's business is the second.

13.3 The ICD-11 depathologisation: out of the mental disorders chapter

ICD-11 renamed transsexualism as gender incongruence and moved it out of mental disorders entirely. This is the headline reform. In the eleventh revision (ICD-11), the WHO replaced "transsexualism" with gender incongruence and, for the first time, removed the diagnosis

from the Mental and Behavioural Disorders chapter, relocating it to a new chapter, "Conditions related to sexual health" (ICD-11; New Oxford Textbook of Psychiatry). This is the formal **depathologisation** of gender diversity: the reclassification keeps a diagnostic code, so that people can still access publicly funded and insured gender-affirming care, while explicitly stating that gender incongruence is *not* a mental disorder. The adolescent-and-adult category (gender incongruence of adolescence and adulthood, code HA60) requires a marked and persistent incongruence between experienced gender and assigned sex, shown by at least two of the four indicators (discomfort with one's sex characteristics, a desire to be rid of them, a desire for those of the experienced gender, and a desire to be treated as the experienced gender), continuously present for at least several months, and it cannot be assigned before the onset of puberty. Notably, unlike the DSM, ICD-11 requires *no* distress or dysfunction criterion at all.

GOOD TO REMEMBER

- **Gender incongruence, ICD-11 (the criterion anchor):** a marked, persistent mismatch between experienced gender and sex assigned at birth, at least two of the four indicators, continuously present for at least several months, not assignable before puberty; there is NO distress criterion. It sits in "Conditions related to sexual health," not the mental disorders chapter, so it is explicitly not a mental disorder.

13.4 The DSM-5-TR retention of gender dysphoria, and the contrast

DSM-5-TR keeps a diagnosis, gender dysphoria, gated by distress; ICD-11 does not. DSM-5-TR (DSM-5-TR) renamed gender identity disorder as gender dysphoria but, unlike ICD-11, retains it as a diagnosis within the manual. The adolescent-and-adult diagnosis requires at least two of the six criteria (a marked incongruence between experienced gender and one's sex characteristics, a strong desire to be rid of those characteristics, a desire for those of the other gender, a desire to be the other or an alternative gender, a desire to be treated as such, and a conviction of having the typical feelings of that gender), present for at least approximately six months, plus a mandatory Criterion B of clinically significant distress or impairment (DSM-5-TR 2022). There are four DSM diagnoses in the family (gender dysphoria in adolescents and adults, in children, other specified, and unspecified), with a "with a disorder of sex development" specifier and a "post-transition" specifier, the latter letting a person retain the diagnosis needed to access ongoing hormones after transition. The examiner's favourite contrast is captured below.

FEATURE	ICD-11 GENDER INCONGRUENCE	DSM-5-TR GENDER DYSPHORIA
Chapter placement	Conditions related to sexual health (moved OUT of mental disorders)	**Retained as a diagnosis within the manual**
Former name	Transsexualism	**Gender identity disorder**
Distress required?	No distress or dysfunction criterion	**Yes, Criterion B distress or impairment is mandatory**
Adult criteria threshold	At least two of the four indicators, several months	**At least two of the six, at least approximately six months**
Core stance	Explicit depathologisation of gender diversity	**Destigmatised label, but still a diagnosis**

The single highest-yield table on this topic: ICD-11 depathologises by relocation and needs no distress; DSM-5-TR destigmatises the label but keeps a distress-gated diagnosis (ICD-11; DSM-5-TR 2022; Kaplan and Sadock CTP 2024).

GOOD TO REMEMBER

- **Gender dysphoria, DSM-5-TR (the criterion anchor):** at least two of the six criteria for at least approximately six months, PLUS Criterion B clinically significant distress or impairment; formerly gender identity disorder, retained as a diagnosis (four sub-types) with "with a DSD" and "post-transition" specifiers. The distress is the gate; the identity is not.

13.5 The historical precedent: the depathologisation of homosexuality

Gender incongruence is following the road homosexuality already travelled: out of the manuals. The reclassification of gender incongruence is best understood as the second act of a story whose first act was the removal of homosexuality from psychiatric classification. The American Psychiatric Association removed homosexuality as a disorder from its diagnostic manual in **1973** (a residual "ego-dystonic homosexuality" category persisted for a time and was later dropped), and the WHO's ICD followed, with ICD-11 finally clearing all such orientation categories out (Kaplan and Sadock CTP 2024). The enduring principle is the one to quote in a viva: a sexual *orientation* is a normal human variation, not a disorder. Historically, gender-diverse presentations were conflated with homosexuality and both were pathologised; the modern separation of gender identity from sexual orientation, and the depathologisation of each in turn, is the same corrective applied twice. Framing gender incongruence this way signals to the examiner that you grasp the trajectory of the whole field, not just one diagnostic row.

MNEMONIC

ORIENTATION IS NOT A DISORDER

The line to carry from the homosexuality precedent into the gender discussion: what a person *is* (their orientation, their gender identity) is not the illness. Distress, comorbidity and the effects of stigma may need care; the identity does not. The two depathologisations, homosexuality first and gender incongruence second, rest on this single principle.

13.6 The WPATH SOC-8 gender-affirmative care pathway

The affirmative-care standard is individualised, multidisciplinary and informed-consent based, with a flexible staged transition. The reference framework for management is the World Professional Association for Transgender Health Standards of Care, eighth version (WPATH SOC-8 2022), which adopts the ICD-11 gender incongruence diagnosis and frames gender-affirmative care as individualised, multidisciplinary and grounded in informed consent, deliberately moving away from mental-health assessment as a universal gatekeeping hurdle while still recommending mental-health support where it is needed (WPATH SOC-8 2022; Kaplan and Sadock CTP 2024). The pathway is staged and flexible, not a rigid ladder: fully reversible steps (living as, and being socially recognised as, one's experienced gender, a *social transition*) usually precede partially reversible steps (gender-affirming hormone therapy) which precede irreversible surgical steps. Importantly, version 8 removed the older requirement for a minimum period of living in the experienced gender role before hormones, and it individualises timing rather than fixing minimum ages. For genital surgery, SOC-8 suggests at least **12 months** of continuous gender-affirming hormone therapy (unless contraindicated) and **two** referral letters documenting persistent gender incongruence and the capacity to give fully informed consent; for adolescents seeking puberty suppression, one criterion is that the young person has reached Tanner stage 2. The full staged route, from social transition through the hormonal and surgical options with the mental-health professional sitting alongside rather than as a gate, is drawn in the accompanying figure. Not every person wants or reaches every step, and that is by design.

TRAP **Pathologising gender incongruence instead of affirming it.** The examiner's cardinal error here is to treat the gender identity as the disorder and reach for something that tries to change it (so-called conversion or reparative efforts, which are ineffective, harmful and legislatively banned in many places). The affirmative stance is the standard of care: affirm the identity, and treat only the distress, the comorbidity and the effects of stigma.

8	12	2	2014
THE CURRENT WPATH STANDARDS OF CARE VERSION (SOC-8, 2022)	MONTHS OF CONTINUOUS GENDER-AFFIRMING HORMONE THERAPY WPATH SUGGESTS BEFORE GENITAL SURGERY	REFERRAL LETTERS WPATH SOC-8 ASKS FOR BEFORE GENITAL SURGERY	THE NALSA JUDGMENT YEAR, AFFIRMING SELF-IDENTIFIED GENDER IN INDIA

GOOD TO REMEMBER

- **WPATH SOC-8 pathway (the guideline anchor):** individualised, multidisciplinary, informed-consent affirmative care; a flexible staged transition running fully reversible (social) then partially reversible (hormones) then irreversible (surgery); version 8 dropped the minimum "real-life" duration before hormones; genital surgery is preceded by about 12 months of continuous gender-affirming hormones and two referral letters documenting persistent incongruence and capacity to consent.

13.7 The role of the mental-health professional (and the endocrine overview)

The psychiatrist assesses readiness and capacity, treats comorbidity and supports; the psychiatrist does not initiate hormones. Within affirmative care, the mental-health

professional's role is bounded and specific: assessment of the person's readiness and capacity to give informed consent, accurate diagnosis and treatment of any co-occurring mental illness (which does not by itself preclude transition but should be stabilised so it will not compromise a safe transition plan), psychoeducation, and psychosocial support (WPATH SOC-8 2022; Kaplan and Sadock CTP 2024). Hormone therapy can be initiated on a referral from a qualified mental-health professional or another suitably trained health professional able to assess incongruence, eligibility and readiness, but the prescribing itself is endocrinology-led. On the endocrine overview only (prescribing detail is out of scope and belongs to the endocrinologist): feminising therapy combines an oestrogen with an anti-androgen, and masculinising therapy uses testosterone, with the Endocrine Society Clinical Practice Guideline (2017) as the standard specialist, monitored reference (Endocrine Society 2017). The psychiatrist may co-monitor mood and adherence during hormone use, but does not start or titrate the regimen.

GOOD TO REMEMBER

- **Mental-health professional's role (the guideline anchor):** assess readiness and capacity for informed consent, diagnose and treat comorbid mental illness (stabilise, do not exclude), give psychoeducation and psychosocial support, and refer; the psychiatrist does NOT initiate or titrate gender-affirming hormones, which are endocrinology-led (feminising = oestrogen plus anti-androgen; masculinising = testosterone; Endocrine Society 2017).

13.8 The Indian legal frame: NALSA and the Transgender Persons Act

India recognises the self-identified gender and a third gender in law. The Indian frame is genuinely examinable and must be verified rather than paraphrased loosely. In the NALSA judgment (National Legal Services Authority v Union of India, Supreme Court, 15 April 2014), the court recognised transgender persons as a "third gender" and affirmed the constitutional right to self-identified gender. This was followed by statute: the Transgender Persons (Protection of Rights) Act, 2019 (the Transgender Persons Act) provides the framework for legal recognition of a transgender identity, prohibits discrimination in areas such as employment, education and healthcare, and sets out welfare provisions (NALSA 2014; Transgender Persons (Protection of Rights) Act 2019). India also has long-standing traditional third-gender communities, the hijra being the most widely known, which the two-spirit and hijra examples in the standard texts cite as evidence that a strict male/female binary is not culturally universal. For an Indian candidate, pairing the affirmative-care clinical stance with the NALSA judgment and the 2019 Act is the complete, high-scoring answer.

INDIA

Weave the legal frame into any Indian answer on this topic. The clinical stance (affirm, do not pathologise) and the legal stance now point the same way: the 2014 **NALSA judgment** gave transgender persons the right to self-identified gender and third-gender recognition, and the 2019 Transgender Persons (Protection of Rights) Act turned that into anti-discrimination and welfare law. Culturally, the hijra community is India's own long-standing third-gender tradition. The psychiatrist works within this frame, offering affirmative, non-judgemental care and appropriate referral, not gatekeeping and never conversion approaches.

GOOD TO REMEMBER

- **Indian legal frame (the statute anchor):** the NALSA judgment (Supreme Court, 15 April 2014) recognised a third gender and the right to self-identified gender; the Transgender Persons (Protection of Rights) Act, 2019 gives legal recognition, prohibits discrimination and provides welfare measures. Both are verified; quote them by name and year.

HOLD THIS

Gender incongruence is the mismatch between experienced gender and sex assigned at birth and is NOT a mental disorder (ICD-11 moved it to "Conditions related to sexual health," needing no distress); gender dysphoria is the DSM-5-TR term for the distress that only some experience; management is the WPATH SOC-8 individualised, informed-consent, gender-affirmative pathway (social, then hormonal, then surgical steps, hormones endocrinology-led) with the psychiatrist treating distress and comorbidity, not the identity, all within the Indian frame of the NALSA judgment (2014) and the Transgender Persons (Protection of Rights) Act, 2019.

14 · Dhat syndrome and culture-bound sexual presentations

This topic is the Indian examiner's favourite in the sexual-and-somatic band, and it is tested as a discrimination-and-management task rather than a memory dump. **dhat syndrome** is the presentation in which a young man attributes fatigue, weakness, anxiety and a range of somatic and sexual symptoms to the loss of semen, and the marks turn on recognising it as a **culture-bound** presentation, placing it correctly in the nosology, reading it through a cultural formulation, and managing the semen-loss belief without confronting it. It is the most examinable member of a small family of culturally shaped sexual presentations that examiners like to pair.

How to use this page. Fix the cardinal feature and the semen-loss attribution first; then the Ayurvedic cultural roots and the prevalence and comorbidity in the Indian and South Asian setting; then the nosological status as a cultural concept of distress and the cultural formulation the whole topic turns on; then the related **culture-bound sexual presentations**, koro chief among them; and finally the non-confrontational psychoeducational management. The complaint usually crystallises around **semen-loss anxiety** tied to masturbation and nocturnal emission, and the single error this page is built to prevent is reading a Dhat presentation without the cultural formulation.

14.1 Dhat syndrome: the semen-loss attribution

A cluster of symptoms pinned on the loss of semen. dhat syndrome is a term coined in South Asia about half a century ago to account for young men who attribute diverse symptoms to the loss of semen (DSM-5-TR 2022). Despite the name it is not, in the modern reading, a discrete disease but a culturally shaped presentation: the patient reports anxiety, fatigue, weakness, weight loss, poor concentration, multiple somatic complaints, low mood and sexual difficulty such as erectile dysfunction or premature ejaculation, and attributes them all to the passage of *dhat*, a whitish discharge he notices in urine or after defecation and believes to be semen. The cardinal feature is the anxiety and distress about the perceived loss of semen in the absence of any identifiable physiological dysfunction. The belief commonly carries marked guilt and dysphoria,

and it typically fastens onto masturbation and nocturnal emission as the feared sources of loss (Companion to Psychiatric Studies).

RULE **The attribution is the disorder, not the discharge.** What defines Dhat syndrome is the distressing belief that semen is being lost and is causing the symptoms; the whitish urinary discharge is usually normal, so the target of assessment and treatment is the semen-loss belief, not a genitourinary lesion.

GOOD TO REMEMBER

- **Dhat syndrome (the presentation):** diverse somatic, anxious, depressive and sexual symptoms that the patient attributes to the loss of semen (dhat), a whitish discharge in urine or after defecation that he believes to be semen; the defining feature is the distressing preoccupation with semen loss in the absence of an identifiable physiological cause, not any single somatic symptom.

14.2 The cultural roots and the Indian and South Asian context

An Ayurvedic belief that semen is a precious, finite essence. The attribution rests on an old and widely held sociocultural belief: semen is regarded as an extremely precious bodily substance, distilled from many drops of blood, so its loss is felt to drain vitality and to cause weakness and sexual failure. The idea connects to dhatu, the word for semen in Ayurveda, counted as one of seven essential bodily fluids whose balance is held to maintain health (DSM-5-TR 2022). Because the belief is culturally normative rather than idiosyncratic, Dhat presentations are common wherever it is shared. The figures from the **indian context** and the wider South Asian setting are striking: **64 percent** of men attending psychiatric clinics in India for sexual complaints, and **30 percent** of men attending general medical clinics in Pakistan, have been described with the concept (DSM-5-TR 2022). It is most often seen in young men from lower socioeconomic backgrounds, though middle-aged men are also affected, and a parallel concern about white vaginal discharge (the leukorrhea variant) forms the female counterpart. Depression and anxiety are frequent companions, and the classic teaching is that a Dhat presentation should prompt an active search for a comorbid depressive or anxiety disorder rather than being taken as a stand-alone complaint.

Dhat
the whitish urinary or post-defecation discharge the patient believes to be lost semen

Dhatu
semen in Ayurveda, counted among the seven essential bodily fluids whose balance is held to maintain health

Leukorrhea variant
the parallel female concept that attributes symptoms to the loss of white vaginal discharge

64%	30%	7
DHAT CONCEPT IN INDIAN PSYCHIATRIC SEXUAL-COMPLAINT ATTENDERS	DHAT CONCEPT IN PAKISTANI GENERAL-MEDICAL ATTENDERS	DHATU, THE ESSENTIAL BODILY FLUIDS OF AYURVEDA

INDIA

Dhat is one of the commonest ways sexual and general distress reaches the Indian clinic, and it sits at the meeting point of the somatic symptom disorders, the sexual dysfunctions and depression. The examiner's expectation is that you name it as a culture-bound presentation, read it through the cultural formulation, search for and treat the comorbid depression, anxiety or sexual dysfunction, and address the semen-loss belief with psychoeducation rather than dismissal. Its wider transcultural frame, alongside the other culture-bound presentations, is developed in the Consultation-liaison, geriatric and transcultural psychiatry notes.

14.3 A cultural concept of distress, not a discrete disorder: the cultural formulation

A cultural explanation of distress, held in the DSM-5-TR glossary rather than the disorder list. DSM-5-TR does not classify Dhat as a discrete disorder; it lists it among the cultural concepts of distress in the Section III chapter on culture and psychiatric diagnosis, and specifically as a cultural causal explanation, the semen loss being the culturally recognised cause to which a range of somatic and psychological symptoms are attributed (DSM-5-TR 2022; Clinical Methods in Psychiatry, AIIMS 2024). ICD-10 placed it, with koro and the other geographically localised presentations, among the other specified neurotic disorders as a culture-specific or culture-bound syndrome (ICD-10). The practical consequence is the same in both systems: the presenting symptoms map onto ordinary diagnoses, a somatic symptom disorder, an illness anxiety disorder, a depressive or anxiety disorder, or a sexual dysfunction, while Dhat names the cultural idiom through which they are expressed. This is why the assessment must run through a cultural formulation. The Cultural Formulation Interview, the person-centred protocol in the same DSM-5 chapter, elicits the patient's own definition of the problem, its perceived cause and context, and his coping and help-seeking, so that the semen-loss explanatory model is understood rather than overwritten (DSM-5-TR 2022).

TRAP **Reading a Dhat presentation without the cultural formulation.** Taken at surface value the semen-loss belief can be mislabelled as a delusion, or the discharge chased as an organic genitourinary disease; the cultural formulation reframes it as a shared explanatory model and redirects assessment to the comorbid depression, anxiety or sexual dysfunction beneath it.

GOOD TO REMEMBER

- **Dhat as a cultural concept of distress (the nosological status):** DSM-5-TR holds Dhat in the Section III glossary of cultural concepts of distress as a cultural causal explanation (semen loss as the perceived cause), not as a codeable disorder; ICD-10 placed it among the other specified neurotic disorders as a culture-bound syndrome. The first step is a cultural formulation, after which the presenting symptoms are coded as the ordinary depressive, anxiety, somatic-symptom or sexual diagnosis they represent.

14.4 Related culture-bound sexual presentations: koro

Genital retraction and the fear of death. The related **culture-bound sexual presentations** are worth naming because examiners pair them with dhat syndrome, and koro is the classic partner (DSM-5-TR 2022). Koro is an episode of sudden, intense anxiety that the penis, or in the female form the nipples, breasts or vulva, is shrinking or retracting into the body, accompanied by a

belief that this will prove fatal. It is reported across Asia including India, and notably in Southeast Asia, where it can spread rapidly through a community in epidemic form, often built on the same culturally elaborated fears about nocturnal emission and masturbation. The Chinese counterpart, shen-k'uei or kidney deficiency, attributes weakness and sexual symptoms to semen loss much as Dhat does. The discriminator to hold is the object of the fear: koro fixes on genital retraction and imminent death, Dhat on the draining loss of a vital fluid, and both differ from body dysmorphic disorder, whose preoccupation is with perceived ugliness rather than shrinkage or depletion (body dysmorphic disorder is developed on the obsessive-compulsive spectrum in the Anxiety, OCD and trauma-related disorders notes).

PRESENTATION	CORE ATTRIBUTION OR FEAR	THE DISCRIMINATOR
Dhat syndrome	Symptoms attributed to loss of semen (dhat) in urine	**Fear of depletion of a vital fluid; South Asian; comorbid depression and anxiety common**
Koro	Penis, or nipples, breasts and vulva, retracting into the body	**Fear of genital retraction and death; can occur in epidemics**
Shen-k'uei (kidney deficiency)	Weakness and sexual symptoms attributed to semen loss	**Chinese counterpart of the semen-loss concept**
Body dysmorphic disorder	Preoccupation with a perceived defect in appearance	**Fear of ugliness, not depletion or retraction; obsessive-compulsive spectrum**

The culture-bound sexual presentations separated by the object of the fear; body dysmorphic disorder is set beside them as the appearance-based contrast (DSM-5-TR 2022).

PEARL

Separate the three by the *object of the fear*: **Dhat** fears the *loss* of semen (depletion of a vital fluid), **koro** fears the *retraction* of the genitals into the body and death, and **body dysmorphic disorder** fears the *appearance* of the body (perceived ugliness). Loss, retraction, ugliness.

GOOD TO REMEMBER

- **Koro (the presentation):** sudden intense anxiety that the genitals (the penis, or the nipples, breasts or vulva in women) are retracting into the body, with a belief that death will follow; it can occur in epidemics. The discriminator is the fear of genital retraction and death, which separates it from body dysmorphic disorder (perceived ugliness) and from Dhat syndrome (perceived semen loss).

14.5 Non-confrontational psychoeducational management

Correct the myth, treat the comorbidity, never confront. Management of Dhat syndrome is non-pharmacological and non-confrontational first. The core is counselling and psychoeducation directed at gently correcting the misconception about semen loss: explain, in the patient's own explanatory language, that the whitish discharge is not a dangerous drain of vitality, that occasional masturbation and nocturnal emission are normal and harmless, and pair this with straightforward sex education to allay the specific fears. Cognitive behavioural techniques fold easily into this model, addressing the catastrophic beliefs about depletion and the checking and

reassurance-seeking they drive. The second, equally important step is to identify and treat any comorbidity by the usual means, a depressive or anxiety disorder, a sexual dysfunction, or a hypochondriacal concern, reserving an antidepressant for a genuine comorbid depression or anxiety rather than for the semen-loss belief itself. Throughout, the stance stays respectful of the cultural model: the aim is to reframe the belief collaboratively, not to dismiss or ridicule it, since confrontation ruptures the alliance and drives the patient away.

GOOD TO REMEMBER

- **Management of Dhat syndrome (the first step):** non-confrontational counselling and psychoeducation that corrects the semen-loss myth and normalises masturbation and nocturnal emission, combined with sex education and, where useful, cognitive behavioural techniques; then treat any comorbid depression, anxiety or sexual dysfunction by the usual means, reserving antidepressants for a genuine comorbidity, not for the belief itself. The first move is psychoeducation within the patient's cultural model, never confrontation.

HOLD THIS

Dhat syndrome is a culture-bound presentation, not a disease: the patient attributes anxiety, fatigue, weakness and sexual symptoms to the loss of semen (dhat, a whitish urinary discharge he believes to be semen), so DSM-5-TR holds it as a cultural concept of distress rather than a codeable disorder; read it through the cultural formulation, search for and treat the comorbid depression, anxiety or sexual dysfunction, and manage the semen-loss belief with non-confrontational psychoeducation, never by confronting or pathologising it.

15 · Medication-induced sexual dysfunction

Sexual dysfunction is one of the most common, most under-reported and most adherence-wrecking adverse effects in all of psychiatric prescribing. Patients rarely volunteer it, quietly stop the drug, and relapse; the examiner therefore wants you to *ask about it, attribute it correctly, and manage it by a guideline ladder rather than by simply stopping treatment*. Two drug classes dominate the answer. **Antidepressant-induced sexual dysfunction** is a **serotonergic** problem of desire, arousal and orgasm; **antipsychotic-induced sexual dysfunction** is largely a **prolactin** problem driven by dopamine blockade. The mechanism you name decides the management you offer.

How to use this page. Hold each class as a triad: the clinical picture (which functions fail, how prevalent, whether reversible), the mechanism (serotonin versus hyperprolactinaemia), and the verified management ladder (watchful waiting, **dose reduction**, **switch** to a lower-liability agent, then an **adjunct**). The deep receptor pharmacology behind each antidepressant sits in the Mood disorders: pharmacotherapy notes, and the full antipsychotic-by-antipsychotic prolactin and receptor profile in the Schizophrenia: management, antipsychotics and adverse effects notes; this page is the clinical syndrome and its management.

15.1 Antidepressant-induced sexual dysfunction: the clinical picture, prevalence and PSSD

A serotonergic triad of reduced desire, delayed or absent orgasm, and erectile difficulty. Selective serotonin reuptake inhibitor (SSRI) treatment lowers sexual function so reliably that the SSRI sexual side effects carry their own teaching profile, clustering into three failures: reduced

libido, delayed or absent orgasm (anorgasmia and delayed ejaculation), and erectile difficulty in men with reduced lubrication in women (Kaplan and Sadock CTP 2024; Maudsley Prescribing Guidelines). It is a class effect of serotonergic antidepressants and it is *largely dose dependent* and *generally fully reversible* on stopping (Maudsley Prescribing Guidelines). Prevalence is high but agent-dependent: treatment-emergent sexual dysfunction reaches 70 to 80 per cent with venlafaxine, citalopram, paroxetine and fluoxetine, and is lower, 25 to 45 per cent, with imipramine, phenelzine, duloxetine, escitalopram and fluvoxamine (Kaplan and Sadock CTP 2024).

Post-SSRI sexual dysfunction is the one to flag. In a minority the sexual symptoms persist despite stopping the drug, a state termed post-SSRI sexual dysfunction (PSSD): decreased libido, erectile dysfunction, delayed ejaculation, anorgasmia, vaginal dryness and, in men, genital numbness and pleasureless orgasm (Maudsley Prescribing Guidelines). Its prevalence and pathophysiology remain uncertain, one estimate putting the risk at **1 in 216** patients treated; diagnosis rests on the medication history, the onset and profile of symptoms and the exclusion of other causes, and no definitive treatment exists (Maudsley Prescribing Guidelines). Examine it as a name to recognise and a caution to counsel, not a syndrome to over-diagnose.

FUNCTION AFFECTED	ANTIDEPRESSANT-INDUCED PATTERN (VERIFIED)
Desire	**Reduced libido (serotonergic; also driven by the depression itself)**
Arousal	**Erectile difficulty in men; reduced lubrication in women**
Orgasm	**Delayed or absent orgasm, delayed ejaculation, anorgasmia (the most drug-specific)**
Course	**Largely dose dependent; generally fully reversible on stopping**
Persistent variant	**Post-SSRI sexual dysfunction (PSSD): symptoms continue despite discontinuation**

The antidepressant-induced sexual dysfunction picture: a serotonergic desire, arousal and orgasm triad, dose dependent and usually reversible, with PSSD as the persistent exception (Kaplan and Sadock CTP 2024; Maudsley Prescribing Guidelines).

GOOD TO REMEMBER

- **Antidepressant-induced sexual dysfunction (criterion-anchored, Maudsley Prescribing Guidelines):** a serotonergic triad of reduced desire, delayed or absent orgasm and erectile or lubrication difficulty; highest rates (70 to 80 per cent) with venlafaxine, citalopram, paroxetine and fluoxetine, largely dose dependent and generally fully reversible.
- **Post-SSRI sexual dysfunction / PSSD (criterion-anchored):** the defining feature is persistence of the sexual symptoms despite the antidepressant being discontinued; prevalence and mechanism uncertain, risk estimated near 1 in 216 treated, no definitive treatment, diagnosis by history and exclusion.

15.2 Managing antidepressant-induced sexual dysfunction: the strategy ladder

Confirm the cause, then climb the ladder. The Maudsley ladder is a sequence, not a menu (Maudsley Prescribing Guidelines Table on sexual adverse effects; Kaplan and Sadock CTP 2024). First, *rule out other causes*: compare sexual functioning on the antidepressant against functioning *before the antidepressant*, not before the depressive illness, since untreated depression itself lowers desire, and screen for alcohol or substance use, diabetes, vascular disease and other medications such as diuretics and beta-blockers. Then, where the depression is stable, work upward: **watchful waiting** for spontaneous tolerance, then dose reduction, then a **switch**, then an **adjunct**.

Watchful waiting is weak; switching is the well-supported move. Spontaneous remission occurs in only a small minority (roughly 5 to 10 per cent) and can take 4 to 6 months, so it is the least effective option and suits milder cases. Dose reduction to the lowest effective dose is reasonable once the patient is in full remission. A short planned *drug holiday* (missing a dose or two before planned intimacy) may help shorter-half-life agents but is useless for fluoxetine given its long half-life, and it risks discontinuation symptoms, reduced adherence and relapse, so it is used cautiously. The best-supported strategy, when mood is stable, is to switch to a lower-liability antidepressant: bupropion, mirtazapine, vortioxetine, agomelatine or moclobemide, with agomelatine, bupropion and vortioxetine carrying the best evidence (Maudsley Prescribing Guidelines).

Add-ons, where a switch is not wanted. In men with antidepressant-related erectile difficulty, adding a PDE5 inhibitor (sildenafil has the strongest evidence, tadalafil also works) improves function on randomised-trial evidence (Nurnberg, JAMA 2003). Add-on bupropion is used, chiefly in women at higher doses (300 mg per day), but its evidence is more modest and mixed (see gaps). Transdermal testosterone has randomised support in women with serotonergic-antidepressant-emergent low libido and in men on serotonergic antidepressants with low or low-normal testosterone.

STEP	WHAT TO DO	VERIFIED DETAIL
1. Confirm cause	Compare with function before the drug, not before the illness; exclude other causes	**Depression itself lowers desire; screen alcohol, diabetes, vascular disease, diuretics, beta-blockers**
2. Watchful waiting	Await spontaneous tolerance in milder cases	**Only 5 to 10 per cent remit; can take 4 to 6 months; least effective**
3. Dose reduction	Lower to the lowest effective dose	**Reserve for patients already in full remission**
4. Switch	Move to a lower-liability agent (mood stable)	**Bupropion, mirtazapine, vortioxetine, agomelatine, moclobemide; best evidence agomelatine, bupropion, vortioxetine**
5. Adjunct	Add an agent without switching	**PDE5 inhibitor for male erectile difficulty (sildenafil best evidence); add-on bupropion or testosterone in selected cases**

The verified management ladder for antidepressant-induced sexual dysfunction; the ordering, and the switch targets, are the highest-yield lines, ordered as a clear algorithm (Maudsley Prescribing Guidelines).

GOOD TO REMEMBER

- **Switch strategy (guideline-anchored, Maudsley Prescribing Guidelines):** where mood is stable, the well-supported move for antidepressant-induced sexual dysfunction is to switch to bupropion, mirtazapine, vortioxetine or agomelatine (best evidence: agomelatine, bupropion, vortioxetine), after first excluding depression itself as the cause and trying watchful waiting or dose reduction.
- **Add-on PDE5 inhibitor (guideline-anchored):** for antidepressant-related erectile difficulty in men, adding sildenafil (the best-supported PDE5 inhibitor) improves function on randomised-trial evidence; keep the antidepressant and add the PDE5 inhibitor rather than sacrificing a working mood response.

15.3 Antipsychotic-induced sexual dysfunction: hyperprolactinaemia and the prolactin ladder

Dopamine blockade, then raised prolactin. Sexual dysfunction is an adverse effect of most antipsychotics; individual susceptibility varies and the effect is usually reversible (Maudsley Prescribing Guidelines). Two linked mechanisms operate: antipsychotics decrease dopaminergic transmission, which itself lowers libido, and the same dopamine blockade raises prolactin by removing tonic inhibition of its release, producing **hyperprolactinaemia**. Prolactin elevation suppresses the hypothalamic-pituitary-gonadal axis, giving sexual dysfunction, menstrual disturbance, infertility, breast enlargement and galactorrhoea in both sexes, and rarely delusions of pregnancy; long-term risks are reduced bone mineral density and a possible increase in breast-cancer risk. Note the nuance: hyperprolactinaemia is *a key factor but may explain only about 40 per cent* of antipsychotic-related sexual dysfunction, the rest coming from anticholinergic effects (impaired arousal), peripheral alpha-1 blockade (erection and ejaculation problems in men) and sedation or weight gain (reduced desire).

The prolactin ladder ranks the culprits. The propensity of an antipsychotic to cause sexual dysfunction tracks its facility to raise prolactin: risperidone is the worst, then haloperidol, then olanzapine, then quetiapine, then aripiprazole (Maudsley Prescribing Guidelines). Aripiprazole, a partial dopamine agonist, is relatively free of sexual adverse effects as monotherapy and even improves function when patients are switched to it. Group the agents by prolactin: prolactin-raising (risperidone, paliperidone, amisulpride, sulpiride and the typicals) versus prolactin-sparing (aripiprazole first, then quetiapine, olanzapine, clozapine and the newer partial agonists). Before you blame the drug, exclude other causes of a raised prolactin: pregnancy, stress at venepuncture, hypothyroidism, renal impairment and prolactinoma, sampling early in the morning.

PROLACTIN LIABILITY	ANTIPSYCHOTIC (VERIFIED LADDER)
Highest (worst for dysfunction)	**Risperidone, paliperidone, amisulpride, sulpiride, first-generation antipsychotics such as haloperidol**
Intermediate to low	**Olanzapine, then quetiapine**
Prolactin-sparing (least)	**Aripiprazole (partial agonist), also clozapine, brexpiprazole, cariprazine, asenapine**

The prolactin ladder underlying antipsychotic-induced sexual dysfunction, risperidone worst and aripiprazole least (Maudsley Prescribing Guidelines).

GOOD TO REMEMBER

- **Antipsychotic-induced sexual dysfunction (criterion-anchored, Maudsley Prescribing Guidelines):** largely driven by hyperprolactinaemia from dopamine blockade, worst with risperidone and the typicals and least with aripiprazole; but prolactin explains only about 40 per cent, so also consider anticholinergic, alpha-1-blockade and sedative contributions, and exclude pregnancy, hypothyroidism and prolactinoma before attributing a raised prolactin to the drug.

15.4 Managing antipsychotic-induced sexual dysfunction: switch or aripiprazole adjunct

Two verified routes: switch down the ladder, or add low-dose aripiprazole. Where a prolactin-raising antipsychotic is driving the problem through hyperprolactinaemia, the first choice is to **switch** to a prolactin-sparing agent, aripiprazole first, or to a lesser extent quetiapine or olanzapine, remembering that any switch carries a risk of destabilising the illness (Maudsley Prescribing Guidelines). Where switching is not feasible, add low-dose aripiprazole to the existing treatment: it lowers prolactin in a dose-dependent way, 3 mg per day is effective and 6 mg per day more so, with higher doses unnecessary, and a 2022 network meta-analysis confirmed aripiprazole near 5 mg per day (and vitamin B6 at 600 mg per day) as effective. This aripiprazole adjunct is the standard way to normalise prolactin in patients kept on a raising agent such as haloperidol or risperidone long-acting injection. Dose reduction of the offending antipsychotic, and treating modifiable bone-health risks, sit alongside these.

ROUTE	INDICATION	VERIFIED DETAIL
Switch	Prolactin-raising agent is the driver and switching is feasible	**Move to a prolactin-sparing agent (aripiprazole first; quetiapine or olanzapine to a lesser extent); watch for relapse**
Aripiprazole adjunct	Must stay on the current antipsychotic	**Add aripiprazole 3 to 6 mg per day; lowers prolactin dose-dependently; 5 mg per day confirmed by 2022 network meta-analysis**
Exclude first	Before either route	**Rule out pregnancy, hypothyroidism, renal impairment and prolactinoma; sample prolactin in the early morning**

The two verified management routes for antipsychotic-induced hyperprolactinaemic sexual dysfunction, switch or aripiprazole adjunct, with the dose that matters (Maudsley Prescribing Guidelines).

GOOD TO REMEMBER

- **Aripiprazole adjunct (guideline-anchored, Maudsley Prescribing Guidelines):** where a prolactin-raising antipsychotic must be continued, adding aripiprazole 3 to 6 mg per day normalises prolactin dose-dependently (5 mg per day confirmed by 2022 network meta-analysis); the alternative first-line move is to switch to a prolactin-sparing agent, aripiprazole itself being the least offending.

15.5 Assessing it: baseline, the ASEX scale, and the common traps

Ask directly, and measure at baseline. Sexual dysfunction is far commoner than spontaneous reports suggest, so direct questioning or a rating scale beats waiting for the patient to volunteer it (Maudsley Prescribing Guidelines). The most examinable instrument is the ASEX (Arizona Sexual Experience Scale, McGahuey and colleagues), a brief five-item scale covering sex drive, arousal, penile erection or vaginal lubrication, ability to reach orgasm, and satisfaction from orgasm over one week; each item scores 1 to 6 so the total runs from 5 to 30 (out of a possible 30), with higher scores meaning worse dysfunction (Clinical Methods in Psychiatry, AIIMS 2024). Its practical value is a *baseline*: a score before the drug lets you attribute a later change to the medication rather than to the illness. The ASEX form sits on the sexual-function scale plate with the male sexual dysfunctions.

1 in 216	**40%**	**3 to 6**	**5 to 30**
PSSD RISK ESTIMATE (MAUDSLEY)	ANTIPSYCHOTIC SEXUAL DYSFUNCTION VIA RAISED PROLACTIN	ARIPIPRAZOLE ADJUNCT DOSE (MG PER DAY)	ASEX TOTAL RANGE (HIGHER IS WORSE)

INDIA

The add-on PDE5 inhibitor for antidepressant-related erectile difficulty in men is everyday practice here: lead the generic sildenafil, with Manforce and Penegra the common Indian brands, and tadalafil (Tadacip, Megalis) as the alternative; keep the generic primary and confirm the product and strength locally before prescribing. Risperidone and the typicals, the worst prolactin raisers, are among the most-used antipsychotics in Indian public practice, so hyperprolactinaemic sexual dysfunction and galactorrhoea are common bedside findings, and low-dose aripiprazole augmentation is a familiar fix. The ASEX itself is taught in the AIIMS Clinical Methods text as the standard bedside scale for drug-induced sexual dysfunction.

RULE **Switch or spare, do not just stop.** For medication-induced sexual dysfunction the guideline move is to confirm the cause, try watchful waiting or dose reduction, then switch to a lower-liability agent (bupropion, mirtazapine, vortioxetine or agomelatine for antidepressants; a prolactin-sparing antipsychotic or an aripiprazole adjunct for antipsychotics), never abrupt cessation that risks relapse.

TRAP **Blaming the drug without a baseline or a prolactin work-up.** Reduced libido may be the untreated depression, not the SSRI, unless you compare with function before the drug; and galactorrhoea on an antipsychotic must not be pinned on the drug before pregnancy, hypothyroidism and prolactinoma are excluded. A parallel error is trying a drug holiday with fluoxetine, whose long half-life makes it useless.

COMMON TRAP

Reflexively stopping the antidepressant or antipsychotic when a patient reports a sexual side effect. Abrupt cessation trades a manageable adverse effect for a relapse of depression or psychosis. The verified sequence is to confirm the drug is the cause, optimise the dose, and switch or augment within the guideline ladder while keeping the psychiatric illness treated.

HOLD THIS

Medication-induced sexual dysfunction splits by mechanism: for the antidepressant, rule out depression as the cause, try watchful waiting or dose reduction, then switch to bupropion, mirtazapine, vortioxetine or agomelatine (or add a PDE5 inhibitor in men); for the antipsychotic it is largely hyperprolactinaemia, worst with risperidone and the typicals and least with aripiprazole, so switch to a prolactin-sparing agent or add low-dose aripiprazole 3 to 6 mg per day.

Psychosomatic medicine and consultation-liaison

16 · The psychosomatic concept

This topic teaches the idea that the whole somatic band rests on, the **psychosomatic concept**: the position that mind and body are one system, so that emotional life can shape the onset, course and outcome of frank physical disease and, conversely, that physical illness reshapes the mind. It is the conceptual hinge of the chapter, sitting between the disorders where the body *complains* without disease (somatic symptom disorder) and the consultation-liaison service that

meets the medically ill patient at the bedside. Examiners test it in three predictable ways: define **psychosomatic medicine** and its modern diagnostic label, state the organising model (Engel's biopsychosocial frame), and list the classical psychosomatic illnesses with the theorist who named them.

How to use this page. Fix the terminology first, then learn the one formal diagnosis this concept carries in DSM-5-TR, that being **psychological factors affecting other medical conditions** (F54), and hold its cardinal discriminator from somatic symptom disorder: PFAOMC requires a *genuine* medical condition that psychological or behavioural factors are worsening. Then internalise the **biopsychosocial model** as the frame, sketch the stress-illness pathways at concept level (the neuroendocrine, autonomic and immune routes), and finish with the seven classical conditions. The service model and the disease-specific psychiatric aspects, the psycho-oncology, HIV, endocrine, cardiac, transplant and surgical or intensive-care work, are developed in the Consultation-liaison, geriatric and transcultural psychiatry notes; here we teach only the concept.

16.1 What "psychosomatic" means, and the field of psychosomatic medicine

One word, from two Greek roots, badly misused by the lay ear. The term derives from *psyche*, soul or mind, and *soma*, body, and refers literally to how the mind affects the body (Kaplan and Sadock CTP 2024). The popular misreading, that a psychosomatic complaint is imaginary or "all in the head", is precisely the error the concept exists to correct: the suffering and the disease are real, and the psychological contribution is to their course, not to their reality. Psychosomatic medicine is the subspecialty that studies and treats this mind-body interface in the medically ill. Its nomenclature has moved twice, and both moves are examinable. First, the American classification retired the older label psychophysiological disorders (also called psychosomatic disorders) in 1980 and replaced it with the descriptive diagnosis psychological factors affecting other medical conditions. Second, in 2017 the subspecialty itself was formally renamed consultation-liaison psychiatry to align the field's name with its actual bedside practice, though the historic term survives in the journals and societies (the American Psychosomatic Society, the journal *Psychosomatic Medicine*).

THE THREE LABELS, AND WHAT EACH ONE IS

Psychosomatic medicine is the *field* (now practised as consultation-liaison psychiatry). **Psychophysiological / psychosomatic disorders** was the old *nosological* term, deleted from DSM in 1980. **Psychological factors affecting other medical conditions (F54)** is the current *diagnosis* that replaced it. Do not conflate the field, the obsolete category and the live diagnostic code; a viva can ask for all three in one breath.

16.2 Psychological factors affecting other medical conditions (F54): the DSM-5-TR diagnosis

The concept's one formal home in the manual. Psychological factors affecting other medical conditions is the diagnosis given when psychological or behavioural factors adversely affect a real, diagnosed medical condition (DSM-5-TR 2022). It rests on three criteria. **Criterion A** requires that a medical symptom or condition, other than a mental disorder, is actually present. **Criterion B** requires that psychological or behavioural factors adversely affect that condition in at least one

of four ways (below). **Criterion C** requires that those factors are not better explained by another mental disorder, such as panic disorder, major depressive disorder or post-traumatic stress disorder. Severity is then graded in **four** steps by how much harm the psychological factor does, from mild through to extreme. The whole diagnosis turns on Criterion A: there must be an underlying general medical condition for the psychological factor to act upon, which is exactly what separates it from the somatic disorders where no such disease is required.

CRITERION B ROUTE	WORKED ILLUSTRATION
The factor influences the course of the condition (a close temporal link to its onset, exacerbation or delayed recovery)	**A stressful period immediately preceding an asthma exacerbation**
The factor interferes with the treatment of the condition	**Poor adherence to antihypertensive medication**
The factor constitutes an additional well-established health risk	**Continued smoking despite established chronic lung disease**
The factor influences the underlying pathophysiology, precipitating or exacerbating symptoms or necessitating care	**Anxiety aggravating angina or an arrhythmia**

The four routes by which psychological or behavioural factors adversely affect a medical condition under Criterion B; any one route suffices (DSM-5-TR 2022).

Mild

Increases medical risk (for example, inconsistent adherence with antihypertensive treatment)

Moderate

Aggravates the underlying medical condition (for example, anxiety aggravating asthma)

Severe

Results in medical hospitalisation or an emergency-department visit

Extreme

Results in a severe, life-threatening risk (for example, ignoring the symptoms of a heart attack)

GOOD TO REMEMBER

- **Psychological factors affecting other medical conditions / F54 (the diagnosis):** Criterion A, a genuine non-psychiatric medical condition is present; Criterion B, psychological or behavioural factors adversely affect it by one of four routes (course, treatment, health risk, or pathophysiology); Criterion C, not better explained by another mental disorder; severity graded mild, moderate, severe or extreme. The single discriminator to hold is Criterion A, the requirement for a real underlying medical disease that the psychological factor worsens.

RULE **PFAOMC needs a real disease being worsened; somatic symptom disorder needs an excessive response to symptoms.** Diagnose psychological factors affecting other medical conditions only when a genuine medical condition (Criterion A) is present and psychological or behavioural factors are demonstrably harming its course, treatment, risk profile or pathophysiology.

TRAP **Reading PFAOMC as "the same as somatic symptom disorder".** They are mirror images: PFAOMC starts from a real medical condition made worse by the mind, whereas somatic symptom disorder starts from distressing bodily symptoms plus a disproportionate psychological response, with no medical disease required. The presence or absence of a genuine underlying condition sorts them.

16.3 The biopsychosocial model: the organising frame

Engel's answer to biomedical reductionism. The biopsychosocial model was developed and named by George Engel in **1977** as a deliberate alternative to the purely biomedical model of disease (developmental and general-medicine texts). Its fundamental purpose is anti-reductionist: it insists that biological, psychological and social domains all be accounted for in every case, regardless of how obviously "physical" a lesion appears, so that psychological and social contributors are never excluded by default. This is not a neutral mediator between three domains; it is a positive stance against biological, psychological and social reductionism alike, and it has since become the standard formulation frame across medicine, not psychiatry alone. For the psychosomatic concept it is the load-bearing frame: it is what lets a genuine coronary lesion, a depressive state and chronic occupational stress be held in one explanatory picture rather than forced into a single cause.

Biological domain

Genetic predisposition, neuroendocrine and physiological processes, the organ pathology itself and the drugs acting on it

Psychological domain

Mood, personality, coping style, health beliefs and behaviours, illness cognitions and the meaning of the illness to the person

Social domain

Family, work and financial context, social support, culture and access to care

PEARL

The biopsychosocial model is easy to *recite* and hard to *use*. In an exam formulation, do not list the three domains and stop; show the *interaction*, for example how a social stressor (job loss) drives a psychological state (depression) that changes a biological pathway (adherence and inflammation) to worsen a real disease. The interaction is the mark-earning part.

16.4 The stress-illness pathways, at concept level

Three biological roads from an emotion to an organ. The mechanism that gives the concept its credibility is that psychological stress reaches the body through well-mapped physiological systems, so the mind-body link is not mystical but neuroendocrine, autonomic and immune (Kaplan and Sadock CTP 2024; Tasman). The neuroendocrine road is the hypothalamic-pituitary-adrenal axis: perceived stress drives cortisol and other counter-regulatory hormones, which over time impair glucose handling, immune surveillance and healing. The autonomic road is sympathetic and adrenomedullary activation, releasing catecholamines that raise heart rate and blood pressure and can, in vulnerable coronary vessels, provoke ischaemia. The immune road is

captured by psychoneuroimmunology, the study of how psychological states, particularly depression and chronic stress, shift immune function and raise pro-inflammatory cytokines that are themselves implicated in cardiovascular and autoimmune disease. When these systems are activated repeatedly rather than briefly, the cumulative physiological cost is described as allostatic load, the wear-and-tear price of chronic adaptation. Hold the three roads by system, not by disease; the disease-specific detail belongs to the consultation-liaison chapter.

PATHWAY	PRINCIPAL MEDIATORS	ILLUSTRATIVE ORGAN CONSEQUENCE
Neuroendocrine (HPA axis)	Cortisol and counter-regulatory hormones	**Impaired glucose control, immunosuppression, delayed healing**
Autonomic (sympatho-adrenal)	Adrenaline and noradrenaline (catecholamines)	**Raised heart rate and blood pressure, coronary ischaemia in vulnerable vessels**
Immune (psychoneuroimmunology)	Pro-inflammatory cytokines, altered lymphocyte function	**Contribution to cardiovascular and autoimmune disease activity**

The three concept-level stress-illness pathways linking a psychological state to physical disease, each linking a psychological state to physical disease (Kaplan and Sadock CTP 2024; Tasman).

16.5 The classical psychosomatic conditions

Alexander's seven, and how the list outgrew them. Franz Alexander, styled the Father of Psychosomatic Medicine, originally described **seven** classical psychosomatic illnesses. His specificity hypothesis proposed that a specific unconscious emotional conflict, occurring in a person with a genetically predetermined vulnerable organ, produces a specific physical disease. The seven he named are the classic viva list, easiest to hold as the mnemonic below. The specificity hypothesis has not survived as a literal theory, but it seeded the field, and as biopsychosocial causation became clearer the roster of illnesses in which psychological factors matter grew until the list of psychosomatic illnesses is virtually endless. That expansion is exactly why the modern manual abandoned a fixed list of "psychosomatic diseases" for the general, mechanism-neutral diagnosis of psychological factors affecting other medical conditions.

ALEXANDER'S CLASSICAL PSYCHOSOMATIC ILLNESSES	SYSTEM
Bronchial asthma	**Respiratory**
Ulcerative colitis	**Gastrointestinal**
Peptic ulcer	**Gastrointestinal**
Neurodermatitis (atopic dermatitis)	**Dermatological**
Thyrotoxicosis	**Endocrine**
Rheumatoid arthritis	**Musculoskeletal or autoimmune**
Essential hypertension	**Cardiovascular**

The seven classical psychosomatic illnesses described by Franz Alexander, the anchor list for the specificity hypothesis.

MNEMONIC

PURE ANT

A study aid for Alexander's seven: **P**eptic ulcer, **U**lcerative colitis, **R**heumatoid arthritis, **E**ssential hypertension, **A**sthma (bronchial), **N**eurodermatitis, **T**hyrotoxicosis. Seven letters, seven organs; recite the mnemonic and name the theorist (Alexander) and his mechanism (the specificity hypothesis) alongside it.

GOOD TO REMEMBER

- **Alexander's classical psychosomatic illnesses (the anchor list):** bronchial asthma, ulcerative colitis, peptic ulcer, neurodermatitis, thyrotoxicosis, rheumatoid arthritis and essential hypertension (PURE ANT); the discriminator to attach is the specificity hypothesis, that a specific emotional conflict in a genetically vulnerable organ yields a specific disease, a theory now historical but foundational.
- **George Engel, 1977 (the model):** the biopsychosocial model, requiring the biological, psychological and social domains all be accounted for, is the organising frame of the psychosomatic concept and the standard formulation frame across medicine.

7	1977	4
ALEXANDER'S CLASSICAL PSYCHOSOMATIC ILLNESSES	ENGEL'S BIOPSYCHOSOCIAL MODEL	PFAOMC SEVERITY GRADES (DSM-5-TR)

INDIA

The psychosomatic concept is not a Western import for the Indian resident; the canonical Indian textbook is itself the source that names Franz Alexander the Father of Psychosomatic Medicine, sets out the specificity hypothesis and Engel's 1977 model, and lists the seven classical illnesses, so this is examined from the Indian syllabus directly. It also lands with unusual force in Indian practice, where psychological distress is very commonly first voiced as bodily symptoms and where most of these patients are met not in a psychiatry clinic but on a general-hospital ward through the consultation-liaison service; the wider transcultural frame of somatic idioms of distress, including the culture-bound presentations, is developed in the Consultation-liaison, geriatric and transcultural psychiatry notes.

HOLD THIS

The psychosomatic concept holds mind and body as one system: its live diagnosis is psychological factors affecting other medical conditions (F54), which requires a REAL medical condition (Criterion A) that psychological or behavioural factors adversely affect, and is therefore the mirror image of somatic symptom disorder, not a synonym; Engel's 1977 biopsychosocial model is its organising frame, the HPA, autonomic and immune systems are its mechanisms, and Franz Alexander's specificity hypothesis gave the seven classical illnesses (PURE ANT).

17 · Consultation-liaison psychiatry and the disease-specific aspects

The interface discipline, mapped here and taught elsewhere. **Consultation-liaison psychiatry** is the branch of clinical psychiatry that works at the border between psychiatry and the rest of medicine, seeing the psychological problems of patients who are physically ill and

advising the teams that look after them. It matters to the examiner as a named model of care and as a pattern: the same short list of psychiatric problems (delirium, depression, anxiety, self-harm-related presentations and substance withdrawal) recurs across every medical and surgical setting, and each physical illness carries its own psychiatric signature. This note is a compact map. It names the field, its service model and its disease-specific reach, and hands the full teaching to the canonical home.

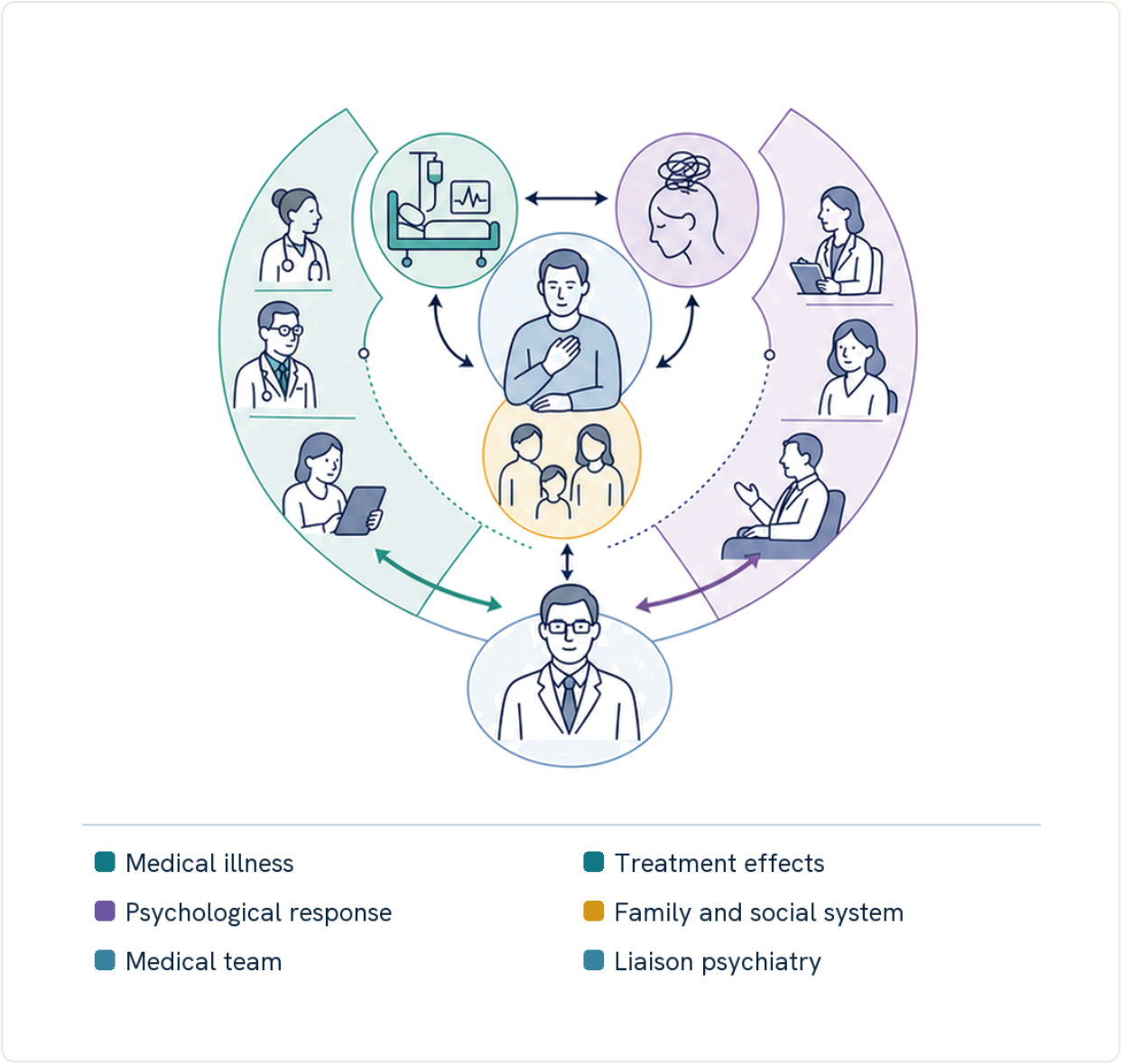


Fig 18.11 Consultation-liaison psychiatry connects medical illness and treatment effects with the patient's psychological response, mental state, family and social system while coordinating care with the medical team.

This is a naming and cross-reference note, not the full teaching. The principles of consultation-liaison psychiatry and the working service model, psycho-oncology and the psychiatric aspects of chronic medical illness, the psychiatric aspects of HIV, endocrine disease and cardiac disease, and the psychiatric aspects of organ transplantation and the surgical and critical-care settings are all developed in *the Consultation-liaison, geriatric and transcultural psychiatry notes*; the acute triage of an actively suicidal patient is in *the emergency psychiatry chapter*. What follows is only where each piece belongs and the one or two facts worth carrying across.

17.1 The principles of consultation-liaison psychiatry and the C-L service model

Consultation versus liaison. Lipowski, in 1971, defined the field as the clinical, teaching and research work of psychiatrists in the non-psychiatric parts of a general hospital. The two words name two activities. *Consultation* is patient-focused: a referral arrives, the psychiatrist answers a specific question and writes back. *Liaison* is team-focused: the psychiatrist teaches and works alongside the medical or surgical team so that psychological care is built into the ward, achieving **integration of care** rather than a single integrated clinician. Six service models are described worldwide, and which one a service runs is largely a question of resources. The commonest reasons a consult is requested are delirium, self-harm and suicide-related presentations, substance withdrawal, disturbed behaviour on the ward, an uncertain diagnosis and the psychological reaction to physical illness; the acute management of the actively suicidal patient is handled compassionately in *the emergency psychiatry chapter*.

C-L SERVICE MODEL	WHO OR WHAT IS THE FOCUS
Consultation model	**The patient is the focus; the consultant answers a specific referral question and hands back a note (the default model in India)**
Liaison model	The consultee and the clinical team are the focus; ongoing teaching and joint care integrate psychiatry into the ward
Bridge model	The C-L psychiatrist is embedded at a primary-care teaching site and trains primary-care physicians
Hybrid model	The psychiatrist sits as a member of a multidisciplinary team
Autonomous psychiatric model	The C-L psychiatrist is unaffiliated to any department and is hired directly by primary-health-care services
Postgraduate training model	A physician is trained in a mental-health setting for one to two years

The six C-L service models (AIIMS Handbook of Consultation-Liaison Psychiatry, 2020); India defaults to the consultation model, with the hybrid model emerging at tertiary centres.

RULE **Delirium until proven otherwise.** New behavioural or cognitive disturbance in a medical or surgical inpatient is delirium, the single commonest reason for a general-hospital psychiatric referral, until an organic cause is found and corrected; screen and treat the physical cause before reaching for a psychiatric label.

GOOD TO REMEMBER

- **The C-L service model (the organising principle):** consultation-liaison psychiatry (Lipowski, 1971) provides psychiatric consultation to the medically and surgically ill and liaises with the treating team, integrating care rather than taking it over; six service models run worldwide (consultation, liaison, bridge, hybrid, autonomous and postgraduate-training), and the first discipline on any referral is to answer the referral question and exclude delirium before attributing a new disturbance to psychiatric illness.

6	~20%	0.15-3.6%	79%
C-L SERVICE MODELS WORLDWIDE	DELIRIUM AMONG GENERAL-HOSPITAL INPATIENTS	INDIAN GENERAL-HOSPITAL REFERRAL RATE	UPPER PSYCHIATRIC-MORBIDITY RATE IN INPATIENT SAMPLES

INDIA

In India, consultation-liaison psychiatry is still practised largely as part of general adult psychiatry rather than a formal subspecialty, and general-hospital psychiatric referral rates are strikingly low, spanning roughly **0.15 to 3.6%** against the Western figure near **10%**. Formal C-L units exist at only a few centres such as AIIMS New Delhi, PGIMER Chandigarh and NIMHANS Bengaluru; most settings run the consultation model, with informal liaison delivered through the National Mental Health Programme and its District Mental Health Programme outreach. The examinable point is that scaling C-L care in a low-resource system starts with the consultation model, layering hybrid and collaborative-care models on as capacity grows.

17.2 Psycho-oncology, chronic medical illness, and the psychiatric aspects of HIV, endocrine disease and cardiac disease

Each illness has a psychiatric signature. **Psycho-oncology** covers the mental health of cancer patients and families: adjustment reactions, depression and demoralisation, anxiety around procedures and prognosis, delirium in advanced disease, and the communication and palliative-care skills that carry it. The psychiatric aspects of **chronic medical illness** are bidirectional, physical illness raising the risk of depression and anxiety while those disorders worsen adherence and outcome. The psychiatric aspects of HIV run from HIV-associated neurocognitive disorder through depression, mania and the neuropsychiatric effects of the infection and its treatment. Endocrine disease is the classic organic mimic: hyperthyroidism presents with anxiety, depression or mania and hypothyroidism with apathy, cognitive slowing, depression and the historical "myxoedema madness". In cardiac disease the link is prognostic, depression is both a risk factor for and a poor prognostic marker after coronary artery disease and myocardial infarction. Every one of these is developed in *the Consultation-liaison, geriatric and transcultural psychiatry notes*; the point to carry is the pattern, not the detail.

TRAP **Do not normalise depression in the physically ill.** Depression in the medically ill is common, more than twice general-population rates, and a poor prognostic marker in cardiac disease, so it is screened and treated, not written off as an understandable reaction to being unwell.

17.3 Organ transplantation, the surgical setting and the ICU

The high-stakes settings. Organ transplantation brings the psychiatrist in twice: before, for a structured evaluation of the candidate's capacity, adherence, substance use and psychosocial support, and after, for delirium, steroid-induced mood change and immunosuppressant neurotoxicity. The surgical setting turns on preoperative anxiety, postoperative delirium and questions of capacity and consent. The ICU is dominated by delirium, which is very common in critically ill and ventilated patients, alongside sedation-related states and the longer post-intensive-care syndrome of cognitive, mood and stress symptoms after discharge. These settings, and the disease-specific detail above, are taught in full in *the Consultation-liaison, geriatric and*

transcultural psychiatry notes; this note only fixes their address and the recurring theme that delirium is the thread running through all of them.

HOLD THIS

Consultation-liaison psychiatry (Lipowski) works at the medicine-psychiatry interface, providing consultation to the medically and surgically ill and liaising to integrate care through six service models (India mostly runs the low-referral consultation model); its disease-specific reach, psycho-oncology and chronic medical illness, the psychiatric aspects of HIV, endocrine disease and cardiac disease, and the transplantation, surgical and ICU settings, is developed in the Consultation-liaison, geriatric and transcultural psychiatry notes, and the working rule at the bedside is delirium-first, treat the depression, and hand back a clear, actionable note.

Impulse-control disorders

18 · The impulse-control disorders

This is a small, self-contained class that examiners love precisely because it is compact and rule-bound. An **impulse-control disorder** is defined by a single repeating engine: a failure to resist an impulse, drive or temptation to perform an act that is harmful to the person or to others, a rising sense of *tension or affective arousal* before the act, and *pleasure, gratification or relief* at the moment of doing it. Learn that tension-relief cycle once and it carries most of the marks across all four entities. The modern nosology regroups these behaviours: ICD-11 collects four named disorders under an ICD-11 impulse-control grouping, while DSM-5-TR scatters them, placing intermittent explosive disorder, pyromania and kleptomania in "Disruptive, impulse-control and conduct disorders" and handling compulsive sexual behaviour differently again.

How to use this page. Take each entity as a keyword with one defining criterion and one management line. Fix the shared tension-relief template first; then the four disorders, intermittent explosive disorder (impulsive aggression), kleptomania (impulsive stealing), pyromania (deliberate fire-setting) and compulsive sexual behaviour disorder; then the sharp discriminators that separate each from its "ordinary" mimic, and the graded, psychological-first management. The combined map of the paraphilic and impulse-control classes is drawn in the accompanying figure, which sits with this block; refer to it for how these entities relate to the paraphilias. The tone throughout is clinical and non-graphic.

MNEMONIC

TENSION → ACT → RELIEF

The shared engine of every impulse-control disorder: mounting *tension* or affective arousal, an impulsive *act* the person cannot resist, then *relief*, pleasure or gratification. Present this cycle and you have named what unifies intermittent explosive disorder, kleptomania, pyromania and compulsive sexual behaviour disorder, and what separates them from goal-directed, premeditated behaviour.

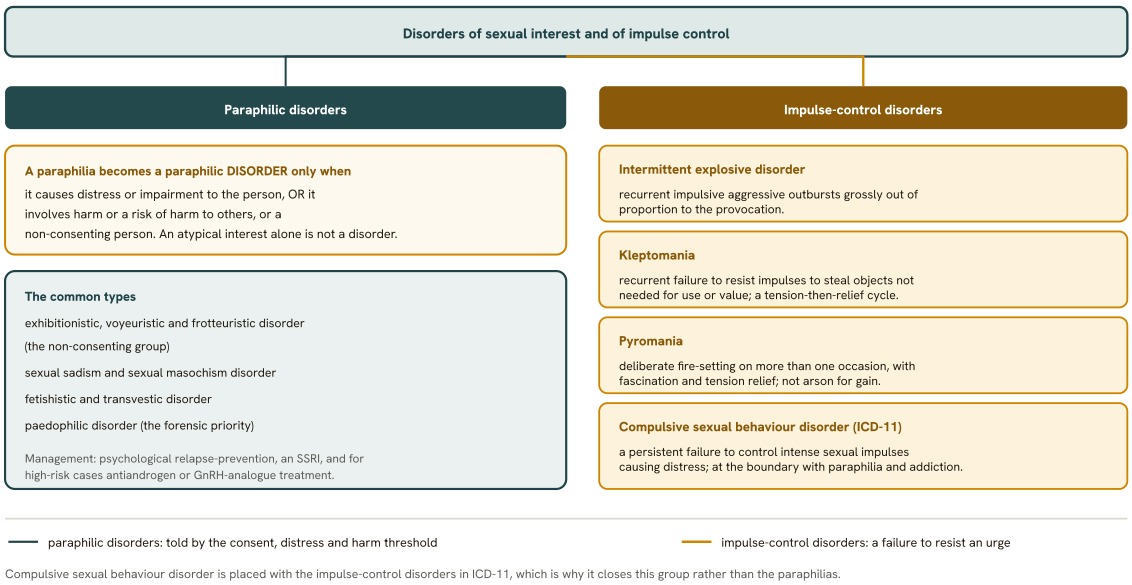


Fig 18.12 The paraphilic and impulse-control disorders. The two groups share a theme of behaviour driven by an urge, but they are recognised differently. A paraphilia becomes a paraphilic disorder only when it causes the person distress or impairment or entails harm or risk of harm to others or a non-consenting person, so an atypical interest by itself is not a disorder; the common types run from the non-consenting exhibitionistic, voyeuristic and frotteuristic disorders through sexual sadism and masochism, fetishistic and transvestic disorder, to paedophilic disorder as the forensic priority. The impulse-control disorders, intermittent explosive disorder, kleptomania and pyromania, are each a recurrent failure to resist an urge with a tension-then-relief cycle, and ICD-11 adds compulsive sexual behaviour disorder here, at the boundary with the paraphilias and with the addiction model.

18.1 Intermittent explosive disorder: impulsive aggression out of proportion to provocation

Recurrent, impulsive aggressive outbursts grossly out of proportion to the trigger. The core of intermittent explosive disorder is recurrent impulsive aggression, that is, aggressive outbursts that are impulsive or anger-based and grossly out of proportion, in intensity or duration, to the provocation (DSM-5-TR 2022; Kaplan and Sadock CTP 2024). DSM-5-TR operationalises the frequency two ways: verbal aggression (temper tantrums, tirades, verbal arguments) or non-damaging, non-injurious physical aggression occurring **twice weekly** on average over a 3-month period (Criterion A1), *or* three behavioural outbursts causing damage, destruction or physical injury within a 12-month period (Criterion A2). The magnitude is grossly out of proportion to the provocation (Criterion B); the outbursts are *not premeditated* and are not committed to achieve a tangible objective such as money, power or intimidation (Criterion C); and the chronological age is at least **6 years** (Criterion E). Outbursts have a rapid onset, little prodrome, and typically last under 30 minutes.

CRITERION	AGGRESSION TYPE	FREQUENCY THRESHOLD
A1	Verbal, or physical without damage or injury	Twice weekly on average, over a 3-month period
A2	Physical, causing damage, destruction or injury	Three outbursts within a 12-month period

The two frequency routes to the intermittent explosive disorder diagnosis; either the frequent low-grade route (A1) or the infrequent destructive route (A2) satisfies Criterion A (DSM-5-TR 2022).

RULE **The aggression is impulsive, not instrumental.** Intermittent explosive disorder is diagnosed only when the outbursts are impulsive or anger-based and are not premeditated and not aimed at a tangible objective; that is what separates it from the proactive, predatory aggression of conduct disorder and antisocial personality disorder.

GOOD TO REMEMBER

- **Intermittent explosive disorder (the criterion):** recurrent impulsive aggressive outbursts grossly out of proportion to provocation, either verbal or non-injurious aggression twice weekly over a 3-month period, or three destructive or injurious outbursts within a 12-month period; not premeditated, not for tangible gain, age at least 6 years.

Management: serotonergic pharmacotherapy plus cognitive-behavioural work. Because low central serotonergic function is linked to impulsive aggression, the drug evidence centres on SSRIs, and fluoxetine carries the single positive double-blind, placebo-controlled trial in intermittent explosive disorder (Coccaro and colleagues), dosed into the standard antidepressant range up to **60 mg** per day; across five controlled trials SSRIs reduce impulsive aggression, though under a third of patients reach full remission (Kaplan and Sadock CTP 2024). Where impulsivity is high, mood-stabilising anticonvulsants, divalproex sodium and valproate, reduce aggressive acts, with the largest effect in the most impulsive patients; the deeper pharmacology sits in the Mood disorders: pharmacotherapy notes. On the psychological side, cognitive-behavioural therapy targeting anger, hostile appraisals and the outburst cycle has a positive randomised trial (McCloskey and colleagues, twelve weekly sessions, group and individual formats), with gains sustained at follow-up.

GOOD TO REMEMBER

- **Intermittent explosive disorder management (guideline and evidence-anchored):** an SSRI is the drug of choice, fluoxetine having the one positive controlled trial (up to 60 mg per day); anticonvulsant mood stabilisers such as divalproex suit high trait impulsivity; and manualised cognitive-behavioural therapy for anger and impulse control is the evidence-based psychotherapy.

18.2 Kleptomania: the impulse to steal what is not needed

Recurrent failure to resist stealing objects not needed for use or value. Kleptomania is the recurrent failure to resist impulses to steal objects that are *not needed for personal use or for their monetary value* (Criterion A); the individual feels a rising subjective tension before the theft (Criterion B) and pleasure, gratification or relief at the moment of committing it (Criterion C); and the stealing is not done to express anger or vengeance and is not a response to a delusion or hallucination (Criterion D) (DSM-5-TR 2022). This is **impulsive stealing** driven by the tension-relief cycle, not by want: the objects are typically of little value to a person who could have paid for them, and are often given away, discarded, hoarded or secretly returned. It is distinct from ordinary theft, which is goal-directed, planned, and motivated by the value or usefulness of the item.

TRAP **Reading everyday shoplifting as kleptomania.** Most theft is ordinary, planned and motivated by the object's value; kleptomania is rare and defined by stealing things the person does not need or want, driven by mounting tension and relief. Equally, do not miss it in reverse, a patient who steals trinkets they discard, feels shame and cannot stop, is not simply "a thief".

GOOD TO REMEMBER

- **Kleptomania (the criterion):** recurrent failure to resist impulses to steal objects not needed for personal use or monetary value, with rising tension before and gratification or relief after the theft, not for anger, vengeance or in response to a delusion; the tension-relief cycle and the pointlessness of the object separate it from ordinary, goal-directed theft.

Management: an opioid antagonist and cognitive-behavioural therapy. There is no licensed drug, and the controlled evidence is thin, but the standout pharmacological signal is the opioid antagonist naltrexone, which reduces the urge to steal and stealing behaviour in trial data, plausibly by dampening the reward and relief that reinforce the act; SSRIs give mixed results and are used on the obsessive-compulsive-spectrum rationale (Kaplan and Sadock CTP 2024). The evidence-based psychotherapy is cognitive-behavioural therapy, classically covert sensitisation and imaginal desensitisation to the urge.

GOOD TO REMEMBER

- **Kleptomania management (evidence-anchored):** the opioid antagonist naltrexone has the best pharmacological support for reducing stealing urges; SSRIs are second-line with mixed evidence; and cognitive-behavioural therapy, particularly covert sensitisation and imaginal desensitisation, is the psychotherapy of choice. No agent is formally licensed.

18.3 Pyromania: deliberate fire-setting with fascination and relief

Purposeful, repeated fire-setting driven by fascination, not gain. Pyromania is **deliberate fire-setting** on more than one occasion (Criterion A), preceded by tension or affective arousal (Criterion B), with a *fascination with, interest in, curiosity about or attraction to* fire and its situational contexts, its paraphernalia, uses and consequences (Criterion C), and pleasure, gratification or relief when setting fires or witnessing their aftermath (Criterion D) (DSM-5-TR 2022). The diagnosis is exclusionary: the fire-setting must *not* be done for monetary gain, as an expression of sociopolitical ideology, to conceal criminal activity, to express anger or vengeance, to improve one's circumstances, in response to a delusion or hallucination, or as a result of impaired judgement; and it is not diagnosed if better explained by conduct disorder, a manic episode or antisocial personality disorder (Criteria E and F). This is what separates pyromania from arson, which is fire-setting for an external purpose such as profit, revenge or concealment.

GOOD TO REMEMBER

- **Pyromania (the criterion):** deliberate, purposeful fire-setting on more than one occasion, with pre-act tension, a fascination with fire, and relief on setting or watching it; not for monetary gain, ideology, concealment, anger or in response to a delusion; the intrinsic fascination and tension-relief, and the absence of external motive, separate it from arson.

Management: psychological, with no established drug. There are no controlled trials and no approved medication for pyromania; scattered case reports of SSRIs, naltrexone, topiramate and mood stabilisers are inconclusive (Kaplan and Sadock CTP 2024). The mainstay is cognitive-behavioural therapy combined with fire-safety education, an approach with the best support, especially in younger fire-setters where structured cognitive-behavioural programmes outperform education alone.

GOOD TO REMEMBER

- **Pyromania management (evidence-anchored):** no drug is licensed and pharmacotherapy evidence is only anecdotal; the first-line and best-supported treatment is cognitive-behavioural therapy paired with structured fire-safety education, targeting the antecedents of fire-setting and the fascination that reinforces it.

18.4 Compulsive sexual behaviour disorder: the ICD-11 impulse-control entity

A persistent failure to control intense, repetitive sexual impulses, classed with the impulse-control disorders. Compulsive sexual behaviour disorder (ICD-11 code 6C72) is a persistent pattern of failure to control intense, repetitive sexual impulses or urges resulting in repetitive sexual behaviour, over an extended period, at least six months (ICD-11 CDDR). The behaviour becomes a central life focus to the neglect of health, care and responsibilities; the person makes repeated unsuccessful efforts to reduce it; continues despite adverse consequences (relationship, financial, legal or health) and even when deriving little satisfaction; and the pattern causes marked distress or significant impairment. It is the ICD-11 successor to ICD-10 excessive sexual drive, the older label for **hypersexuality**, and it is deliberately placed among the impulse-control disorders. DSM-5-TR, by contrast, does *not* recognise it; a proposed "hypersexual disorder" was rejected for DSM-5 for want of evidence.

PEARL

Two boundaries are the whole exam answer. Against *paraphilia*: in compulsive sexual behaviour disorder the sexual interest itself is typically normative and it is *control* that fails, whereas a paraphilia is defined by an *atypical arousal focus*. Against *addiction*: ICD-11 declined to call this a behavioural addiction, reserving that grouping for gambling and gaming alone, and located it with the impulse-control disorders instead, so "sex addiction" is not an ICD-11 diagnosis. Crucially, distress arising *only* from moral or religious disapproval of one's own sexual behaviour does not qualify.

GOOD TO REMEMBER

- **Compulsive sexual behaviour disorder (the criterion):** a persistent, at-least-six-month failure to control intense, repetitive sexual impulses producing repetitive sexual behaviour that becomes a central focus, resists control and continues despite adverse consequences or little satisfaction, causing marked distress or impairment; classed as an ICD-11 impulse-control disorder, not a paraphilia and not a behavioural addiction, and not diagnosed on moral or religious distress alone.

DISORDER	THE IMPULSE RESISTED AND FAILED	TENSION THEN RELIEF	THE DISCRIMINATOR FROM ITS "ORDINARY" MIMIC
Intermittent explosive disorder	Impulsive aggressive outburst	Yes; anger or arousal, then release	**Impulsive, not pre-meditated and not for tangible gain (versus conduct disorder or antisocial aggression)**
Kleptomania	Stealing an unneeded, low-value object	Yes; tension, then grati-fication or relief	**Object not needed for use or value (versus ordinary, goal-direct-ed theft)**
Pyromania	Deliberate fire-setting	Yes; arousal, then relief on watching	**Fascination with fire, no external motive (versus arson for gain, revenge or concealment)**
Compulsive sexual be-haviour disorder	Repetitive sexual behaviour	Often to modulate neg-ative affect	**Control fails over a normative interest (versus a paraphilia's atypical arousal focus; not an addiction in ICD-11)**

The four ICD-11 impulse-control disorders share one engine, the tension-relief cycle, and each is separated from a common mimic by a single discriminator (DSM-5-TR 2022; ICD-11 CDDR; Kaplan and Sadock CTP 2024).

INDIA

The genuine Indian anchor is the medico-legal interface. Kleptomania, pyromania and impulsive aggression frequently surface in forensic settings, but the disorder is not, in itself, a legal defence: the insanity defence under Indian law, Indian Penal Code Section 84 (the M'Naughten rules, re-enacted in the Bharatiya Nyaya Sanhita 2023), acquits only where unsoundness of mind rendered the person incapable of knowing the nature of the act or that it was wrong or contrary to law. Most people with an impulse-control disorder retain that knowledge, so they are usually held criminally responsible for the theft, the fire-setting or the assault; the diagnosis bears on mitigation and sentencing, not automatic exculpation. The clinician's task is to distinguish the disorder from the crime (kleptomania from theft, pyromania from arson) and to say so honestly. Drug choices here, SSRIs, naltrexone and mood stabilisers, are the same generics used across the mood and obsessive-compulsive chapters; entity-specific Indian brand equivalents were not confirmable in the available sources, so the generic name stays primary.

4
ICD-11 NAMED IMPULSE-CONTROL DISORDERS

6
INTERMITTENT EXPLOSIVE DISORDER MINIMUM AGE (YEARS)

3
DESTRUCTIVE OUTBURSTS (PER 12-MONTH PERIOD, CRITERION A2)

HOLD THIS

Every impulse-control disorder is a failure to resist an impulse harmful to self or others, with **tension before and relief after**; ICD-11 names four, intermittent explosive disorder, kleptomania, pyromania and compulsive sexual behaviour disorder, and you diagnose each by the tension-relief cycle and the *absence* of an external, goal-directed motive, managing them psychologically first (cognitive-behavioural therapy) with an SSRI, fluoxetine or naltrexone as the drug adjunct.

Suicide and self-harm

19 · Suicide risk assessment

This is the topic on which the whole chapter closes, the *Defence of life* that the master mnemonic seeded at the outset, and it is examined as a skill rather than as a fact-list. The task is a **suicide risk assessment**: a compassionate, structured clinical interview that gathers the patient's suicidal thinking and behaviour, weighs the **risk factors** against the **protective factors** and the current mental state and social context, and then translates that synthesis into a plan for care and **safety**. It is emphatically *not* a numerical prediction of who will die, and the single most important idea on the page is that no instrument, and no clinician, can predict individual suicide reliably; the assessment exists to guide management, not to forecast an outcome.

How to use this page. Fix the vocabulary first (ideation, plan, intent, attempt, self-harm), then the two halves of the balance, the static and dynamic risk factors and the protective factors, then the framing of chronic against acute risk. After that, learn the three named aides in the way examiners want them, the Columbia Suicide Severity Rating Scale as the gold-standard structured interview, SAD PERSONS as a teaching aide with a stated limitation, and PHQ-9 item nine as a screen, and finally the two principles that bind the whole topic together: the limits of individual prediction, and the Indian statute that has recriminalised nothing and decriminalised the attempt. Throughout, hold the cardinal error the topic is built to prevent, treating a denied ideation as a cleared risk when the structured evaluation and the risk-and-protective balance say otherwise.

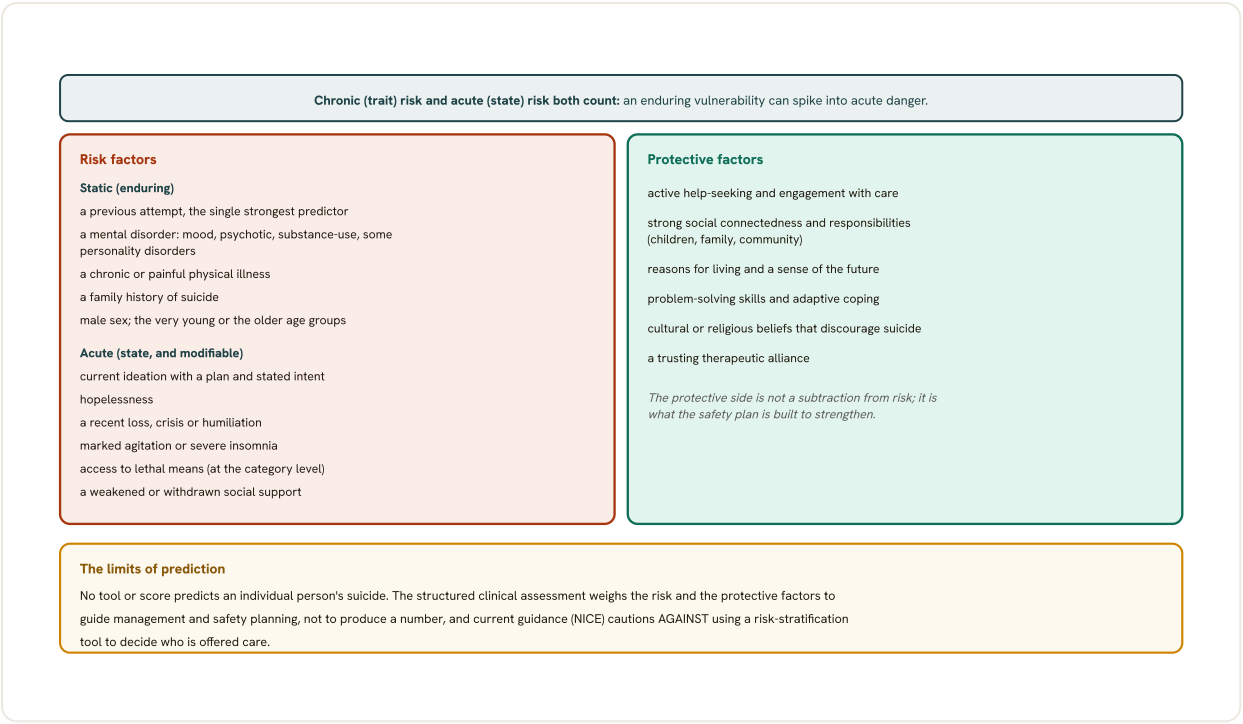


Fig 18.13 The balance of suicide risk and protective factors. A structured assessment weighs the two sides. The risk factors divide into static, enduring markers, of which a previous attempt is the single strongest, and acute, modifiable state factors such as current ideation with a plan and intent, hopelessness and a recent crisis, which is where intervention acts. The protective factors, from help-seeking and social connectedness to reasons for living and a therapeutic alliance, are not simply subtracted from risk; they are what a safety plan is built to strengthen. The decisive teaching point is the limit of prediction: no instrument forecasts an individual suicide, so the assessment guides care rather than generating a number, and current guidance discourages using a risk-stratification score to allocate treatment.

The Columbia Suicide Severity Rating Scale (C-SSRS): the screener structure

THE SCREENER ASKS, IN ESCALATING ORDER	WHAT IT MARKS
1. A wish to be dead, or to go to sleep and not wake up	ideation, lower
2. Non-specific active thoughts of ending one's life	ideation
3. Active thoughts with a general sense of acting, but no plan	ideation, rising
4. Active thoughts with some intention of acting	**high concern**
5. Active thoughts with a specific plan and intent	**highest ideation**
6. Behaviour: any preparatory act or attempt (asked of everyone)	**behaviour, highest**

Items 1 to 5 form an escalating ideation ladder and item 6 captures behaviour. The screener's own published triage points are: yes to item 1 or 2, low risk (behavioural-health referral at discharge); yes to item 3, moderate risk (behavioural-health consult); yes to item 4 or 5, high risk (patient safety precautions); yes to the behaviour item, high risk only if the behaviour fell within the past three months, otherwise moderate. The behaviour item is stated here in general terms, without method detail.

C-SSRS (Posner et al; Columbia Lighthouse Project); free for non-commercial clinical and research use with acknowledgement. Typeset here in structure only, safe-messaged, with the behaviour examples abstracted to "any preparatory act or attempt".

Fig 18.14 The Columbia Suicide Severity Rating Scale, shown as its structure. The screener walks up an ideation ladder, from a passive wish to be dead, through non-specific and then active thoughts, to active thoughts with intent and finally with a specific plan, and closes with a single behaviour question asked of everyone. It is used not to generate a number but to place where a person sits on that ladder: a positive answer at the second step already signals concern, and a positive answer higher up, or to the behaviour item, signals high risk needing immediate safety measures. It is presented here typeset and safe-messaged, with the behaviour examples abstracted so that no method detail appears.

SAD PERSONS: a teaching aide-memoire (out of a possible 10)

LETTER	ITEM (ONE POINT EACH)
S / A / D	male Sex; extremes of Age; Depression
P / E / R	Previous attempt; Ethanol or substance use; Rational thinking loss (psychosis)
S / O / N / S	Social supports lacking; Organised plan; No spouse or partner; Sickness (chronic illness)
Banding	**0 to 4 lower, 5 to 6 medium (consider admission), 7 to 10 high concern**

SAD PERSONS (Patterson et al, 1983). A teaching mnemonic, NOT a validated predictor of individual risk (Bolton 2012); use it to structure recall, never to clear a patient.

Over the last 2 weeks, how often have you been bothered by any of the following problems? *(Use "✔" to indicate your answer)*	Not at all	Several days	More than half the days	Nearly every day
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

Developed by Drs. Robert L. Spitzer, Janet B.W. Williams, Kurt Kroenke and colleagues, with an educational grant from Pfizer Inc. No permission required to reproduce, translate, display or distribute.

PHQ-9 item 9 is the single suicidality-screen item, scored 0 to 3 over two weeks; any score of 1 or more is a positive screen that prompts a full risk assessment. It is a screen, not a risk assessment.

PHQ-9 (Kroenke, Spitzer and Williams); PHQ family, no permission required to reproduce; free non-commercial educational use.

BECK SUICIDE INTENT SCALE (SIS): INTENT BEHIND AN ACTUAL ATTEMPT	STRUCTURE AND BAND
Part 1, objective circumstances (8 items): isolation, timing, precautions against discovery, acting to gain help, final acts, active preparation, a note, and communication of intent	each item scored 0 to 2
Part 2, self-report (7 items): expectation of fatality, conception of lethality, seriousness, attitude to living or dying, premeditation, reaction to survival, stated purpose	each item scored 0 to 2; total out of a possible 30
rated for a person who HAS made an attempt (distinct from the ideation scales)	**a commonly used categorisation (Pierce 1977): 0 to 3 low, 4 to 10 medium, 11 or more high intent; Beck did not fix a validated cut-off**

Beck Suicide Intent Scale (Beck, Schuyler and Herman, 1974); copyright the authors, permission required, so typeset here in summary with the verified structure rather than reproduced.

Fig 18.15 The suicide-risk aides. SAD PERSONS is a ten-point mnemonic that helps a trainee remember the domains to ask about, banded 0 to 4 lower, 5 to 6 medium and 7 to 10 high concern; it is explicitly a teaching aide and not a validated predictor of an individual's risk, so it structures recall but never clears a patient. PHQ-9 item 9 is the single screening question for suicidality, positive at a score of 1 or more, which prompts, rather than replaces, a full assessment. The Beck Suicide Intent Scale is the instrument for a person who has already made an attempt, rating the objective circumstances and the self-reported intent across fifteen items for a total out of a possible 30, with the widely quoted Pierce bands recorded as a common categorisation rather than a Beck-validated cut-off. All are presented safe-messaged, without method detail.

19.1 The vocabulary of suicidality

Precise terms, arranged along a continuum from thought to act. A defensible assessment begins with clean definitions, because the examiner marks the discrimination between them and because muddled terms produce muddled clinical decisions (Kaplan and Sadock CTP 2024; Clinical Methods in Psychiatry, AIIMS 2024). **Suicidal ideation** is thinking about, considering or planning ending one's life, and it ranges from a passive wish to be dead to active, specific thoughts. A **plan** is a formulated method and set of circumstances for acting. **Intent** is the subjective determination to act on those thoughts, the will to die, and it is separable from both ideation and plan. A **suicide attempt** is a non-fatal, self-directed, potentially injurious act carried out with at least some intent to die. **Self-harm**, in the sense used by the self-harm guideline, is any act of self-injury or self-poisoning irrespective of intent or motive, so it is the broadest term and deliberately does not assume a wish to die; non-suicidal self-injury is the subset undertaken with no suicidal intent. The clinician's job is to place the patient on the continuum, ideation, then plan, then intent, then behaviour, because escalation along it is one of the things that raises acute concern.

GOOD TO REMEMBER

- **The suicidality continuum (the terminology):** ideation (passive wish to active thought) → plan (a formulated method) → intent (the will to act) → attempt (a self-directed potentially injurious act with some intent to die); self-harm is the umbrella term for any self-injury or self-poisoning regardless of intent, so it does not by itself imply a wish to die. The discriminator to hold is that intent is separable from ideation and plan and must be asked about in its own right.

19.2 What a structured evaluation is, and is not

A weighing interview, not a checklist score. The guideline-anchored method is a **structured evaluation** through a clinical interview that explores the patient's suicidal thinking and its history, the current mental state, the psychosocial context and the balance of risk and protective factors, and that arrives at a clinical judgement about care and safety (NICE-aligned, NG225 2022). It is structured in that it systematically covers the same domains every time so that nothing high-yield is missed, but it is not a tally of ticked boxes producing a risk number. Asking directly and calmly about suicidal thoughts is a core skill and, contrary to a persistent myth, does not plant the idea or increase risk; a graded set of questions, moving from low mood to thoughts that life is not worth living, to active thoughts, plan and intent, is the safe and validated way in. The cardinal trap sits precisely here: a patient may deny ideation, yet when the static and dynamic risk load is high and protective factors are thin, a bare verbal denial cannot be treated as a cleared risk. Denial is one data point among many, not the end of the assessment.

WORKED EXAMPLE

A man in his forties is seen after a recent attempt was medically managed. He now says, flatly, "no, I am not thinking of anything like that, I just want to go home." Against that single denial sits a strong static load (a prior attempt, current severe depression) and a heavy dynamic load (marked hopelessness, agitation, a job loss the week before, living alone), with few protective factors and poor engagement. Taking the denial at face value and discharging him would be the cardinal error. The structured evaluation, weighing the whole balance rather than the last sentence spoken, keeps him in active care with a collaborative safety plan; the denial is noted, not trusted as an all-clear.

TRAP **Treating a denied ideation as a cleared risk.** A verbal "no" does not neutralise a high risk-and-protective balance. When the structured evaluation shows heavy static and dynamic loading with thin protection, the denial is one data point; the assessment, not the last answer, governs the safety plan.

19.3 Static risk factors: the fixed background

Historical, slow-changing markers that set the baseline. Static (distal, largely unchangeable) risk factors describe the population a patient belongs to and raise the baseline against which the current state is read (Kaplan and Sadock CTP 2024). The single strongest of them is a *previous suicide attempt*; a prior attempt and a current major depressive episode are together described as the two strongest predictors of future suicide, and the first attempt materially raises the risk of a later one. Mental illness is the next great pillar: mood disorders (unipolar and, with the highest risk, bipolar), schizophrenia and other psychoses, and substance use disorders including alcohol all carry substantially elevated risk, and psychological-autopsy data find a diagnosable mental disorder in the large majority of those who die. Chronic, disabling or painful physical illness adds independently, especially when depression is also present. A family history of suicide or of psychiatric disorder raises risk, partly heritable and partly environmental. Demographic markers (for example male sex for completed suicide, older age, social isolation, single or bereaved status) are statistically real but weak in the individual case, which is exactly why they must never be used alone.

STATIC (DISTAL) RISK FACTOR	WHY IT RAISES BASELINE RISK	THE POINT TO HOLD
Previous suicide attempt	Strongest single historical predictor	**Prior attempt plus current depression are the two strongest predictors**
Mental illness	Mood disorder, psychosis, substance use disorder all elevate risk	**Bipolar and severe depression carry the highest mood-disorder risk**
Chronic pain or physical illness	Disabling, painful or fatal disease, amplified by depression	**Independent contributor, greatest when depression co-occurs**
Family history	Family history of suicide or psychiatric disorder	**Part heritable, part environmental transmission**
Demographics	Male sex (completion), older age, isolation, single or bereaved	**Statistically real but weak alone; never a stand-alone basis**

The static background factors that set baseline risk, mapped in the accompanying figure against the dynamic and protective factors (Kaplan and Sadock CTP 2024).

RULE **Prior attempt is the strongest static factor.** A previous suicide attempt, with current major depression, is among the two strongest predictors of future suicide; every assessment asks explicitly about past attempts and never discounts them because the method was medically minor.

19.4 Dynamic risk factors: the modifiable foreground

Current, changeable states that drive acute concern and are the levers of intervention. Dynamic (proximal, modifiable) factors are what shift a patient from their chronic baseline into a period of heightened risk, and because they can change they are where treatment acts (Kaplan and Sadock CTP 2024; NICE NG225 2022). *Hopelessness* is the pre-eminent dynamic factor, more tightly linked to eventual suicide than depressed mood itself, which is why it is asked about and rated directly. *Current suicidal ideation with a plan and stated intent* is the most immediate marker, and escalation along the ideation continuum is itself a warning. *Agitation, severe anxiety and insomnia* raise near-term risk, particularly in a depressive or mixed mood state. A *recent loss or interpersonal crisis* (bereavement, separation, humiliation, job or financial loss, legal trouble) commonly precedes an act. *Access to lethal means* is a dynamic factor named only at the category level, because reducing that access is one of the most effective things a clinician and family can do. *Social isolation and disconnection*, and recent discharge from inpatient or emergency care, complete the picture, the transition period after any care contact being a recognised window of elevated risk.

GOOD TO REMEMBER

- **Dynamic risk factors (the modifiable foreground):** hopelessness (the pre-eminent one), current ideation with plan and intent, agitation or severe anxiety and insomnia, a recent loss or crisis, access to means (named at category level only), isolation, and the high-risk period just after any care contact. The point to hold is that these are the treatable levers; the assessment targets them, and reducing access to means is framed positively as putting time and distance between a person and a crisis.

19.5 Protective factors: the other half of the balance

Reasons and connections that buffer risk and must be actively sought. A one-sided hunt for risk is a poor assessment; the protective factors are weighed alongside and are themselves things to strengthen (Kaplan and Sadock CTP 2024; Clinical Methods in Psychiatry, AIIMS 2024). The best-evidenced are *help-seeking* and a willingness to engage with care; *social connectedness and support*, a partner, family, friends or community; concrete *reasons for living*, which can be elicited directly and are the object of the Reasons for Living Inventory; *responsibilities to others*, notably dependent children; *religious or cultural beliefs* that frame suicide as unacceptable; and *active engagement with treatment* with a therapeutic alliance the patient values. Protective factors are not fixed either; they are dynamic, they can erode in a crisis, and part of management is deliberately building and mobilising them. Crucially, protection does not cancel risk arithmetically; a patient with strong reasons for living and a high acute risk is still at high acute risk, so protective factors qualify the plan rather than override the concern.

PEARL

Asking directly about suicide does *not* plant the idea or raise risk, a myth worth retiring on sight. A graded approach works best: start with mood, move to whether life feels worth living, then to active thoughts, then plan, then intent, and, just as deliberately, ask what has kept the person going, their reasons for living, so the interview surfaces the protective half of the balance rather than only the risk half.

19.6 Chronic and acute risk

Two time-frames, held separately, because they call for different responses. Risk is not a single dial; the useful clinical framing separates **chronic and acute risk** (Kaplan and Sadock CTP 2024). *Chronic (baseline) risk* is the long-standing, trait-like elevation carried by the static factors, a history of attempts, an enduring mental illness, a personality vulnerability; it changes slowly and is managed over the long term through treatment of the underlying disorder and durable supports. *Acute (state) risk* is the near-term elevation driven by the dynamic factors, a surge of hopelessness, an intensifying ideation, a fresh loss, agitation, intoxication; it changes fast and demands an immediate response. The two combine: a patient may be chronically high-risk yet acutely settled, or chronically moderate yet acutely dangerous because of a proximal crisis, and it is the person at chronic *and* acute elevation who is of greatest immediate concern. Documenting both, and stating what specifically has changed to raise the acute component, is what makes an assessment defensible and actionable.

DIMENSION	CHRONIC (BASELINE) RISK	ACUTE (STATE) RISK
Driven by	Static, trait-like factors	**Dynamic, modifiable factors**
Time-course	Slow-changing, long-standing	**Fast-changing, near-term**
Typical content	Past attempts, chronic illness, vulnerability	**Rising hopelessness, ideation with intent, recent crisis, agitation**
Response	Long-term treatment and durable support	**Immediate safety plan, closer care, mobilise supports**

Chronic and acute risk are documented as two separate axes; the person elevated on both warrants the most immediate response (Kaplan and Sadock CTP 2024).

19.7 The Columbia Suicide Severity Rating Scale (C-SSRS)

The gold-standard structured interview, an ideation-severity ladder plus a behaviour subscale. The Columbia Suicide Severity Rating Scale (C-SSRS; Posner and colleagues, 2011) is a clinician-administered interview widely regarded as the gold-standard instrument for assessing and monitoring suicidality, free for clinical use and available in many languages and versions (a lifetime-recent baseline version, a since-last-visit version for follow-up, and a brief screener for non-specialists) (Clinical Methods in Psychiatry, AIIMS 2024). Its power for the exam is its structure. The *ideation-severity subscale* is an ordered ladder of five levels of increasing severity: a wish to be dead; non-specific active suicidal thoughts; active thoughts with some general consideration of how one might act but no worked-out plan and no intent; active ideation with some intent to act but without a specific plan; and active ideation with both a specific plan and intent. A separate *behaviour subscale* records the spectrum of suicidal behaviour, from preparatory acts through interrupted and aborted attempts to an actual attempt, together with a general rating of its severity, and one further category captures self-injurious behaviour without suicidal intent. It structures the interview and tracks change over time; it does not, and is not meant to, output a probability that a given person will act.

C-SSRS IDEATION LEVEL	WHAT IT CAPTURES (NO METHOD SPECIFICS)	THE ESCALATION IT MARKS
Level one	Wish to be dead	**Passive; a wish not to be alive, without active thoughts**
Level two	Non-specific active suicidal thoughts	**Active thoughts of ending one's life, no method, plan or intent**
Level three	Active ideation with general thought of acting	**Some consideration of how one might act, no worked-out plan, no intent**
Level four	Active ideation with some intent	**Some intent to act, still without a specific plan**
Level five	Active ideation with plan and intent	**Both a specific plan and intent present; the top of the ladder**

The C-SSRS ideation-severity ladder, described without method detail; the full instrument is reproduced in the accompanying scale plate (Posner 2011; AIIMS Clinical Methods 2024).

GOOD TO REMEMBER

- **C-SSRS (the instrument):** the gold-standard clinician-administered interview for assessing and monitoring suicidality, comprising eleven categories in all, five ordered ideation-severity levels (from a wish to be dead up to active ideation with a specific plan and intent), five behaviour categories, and one for self-injurious behaviour without suicidal intent. The discriminator to hold is that it structures and tracks the assessment but is explicitly not a predictor of who will act.

19.8 SAD PERSONS and PHQ-9 item nine: two teaching aides

A mnemonic best used to teach, and a single screening item, each with clear limits. Two further aides appear in every viva, and each must be quoted with its caveat (Patterson and colleagues, 1983; Kroenke and Spitzer, 2001). The SAD PERSONS scale is a ten-item mnemonic of classic risk factors, scored out of a possible ten, devised as a memory aid and teaching tool. Its examinable weakness is decisive: it is *not* a validated predictor of individual suicide, it performs poorly at discriminating who will act, and it must never be used to decide who receives care or admission; it earns its place as a way to remember factors, not to grade risk. The PHQ-9 depression questionnaire carries item nine, which asks about "thoughts that you would be better off dead, or of hurting yourself in some way," scored 0 to 3 over the past two weeks. It is a widely used single-item screen: any endorsement is a positive flag that must trigger a full structured suicide risk assessment, but on its own it screens rather than assesses, and it neither confirms risk nor grades it. Both aides feed the interview; neither replaces it, and the reproduced forms sit in the accompanying scale plate.

MNEMONIC

SAD PERSONS

Sex (male), **A**ge (older), **D**epression; **P**revious attempt, **E**thanol or substance use, **R**ational-thinking loss (psychosis), **S**ocial supports lacking, **O**rganised plan, **N**o spouse (isolation), **S**ickness (chronic illness). Ten items, one point each, scored out of a possible ten. Hold it for what it is: a teaching aide that lists risk factors, explicitly not a validated instrument for predicting an individual's risk or for rationing care.

GOOD TO REMEMBER

- **SAD PERSONS (the aide):** a ten-item risk-factor mnemonic scored out of a possible ten; its defining limitation is that it is not validated to predict individual suicide and must not be used to allocate care, so it teaches factors rather than grades risk.
- **PHQ-9 item nine (the screen):** a single item on death and self-harm thoughts, scored 0 to 3 over two weeks; any positive answer mandates a full structured suicide risk assessment. It screens, it does not assess or grade risk.

19.9 The limits of individual-risk prediction

No instrument predicts individual suicide; the assessment guides care, it does not forecast. This is the intellectual centre of the topic and its most heavily tested principle. Suicide is, at the

level of the individual, a rare and fluctuating event, and the evidence is consistent that no scale, algorithm or clinical judgement reliably identifies which person will act; this is the **limits of prediction** (Kaplan and Sadock CTP 2024; NICE NG225 2022). Two practical consequences follow. First, risk-assessment and stratification *tools* must not be used to predict future suicide or self-harm, nor to decide who is offered treatment or admission; a global "low, medium, high" label must not drive clinical decisions. Second, the field has moved from prediction toward a prevention-oriented *suicide risk formulation*, which summarises the gathered data into four judgements that inform action rather than forecast an event: the patient's *risk status* (relative to a comparison group), their *risk state* (relative to their own baseline or other time-points), the *resources* they can draw on in crisis, and the *foreseeable changes* that could raise risk (Pisani, Murrie and Silverman 2016). The purpose of the assessment is to identify modifiable, treatable factors and to shape a safety-focused plan, not to generate a number.

FROM PREDICTION TO PREVENTION-ORIENTED FORMULATION

The traditional model sorted patients into low, medium and high risk and stopped there, which both over-labels and mis-directs care. The prevention-oriented formulation instead asks four action-linked questions, risk status, risk state, available resources and foreseeable changes, and uses the answers to build management and a collaborative safety plan. Stratifying into fixed categories to allocate care is discouraged precisely because it borrows a predictive authority the data do not support, while diverting attention from the modifiable factors that treatment can actually change.

GOOD TO REMEMBER

- **Limits of prediction (the governing principle):** no tool or clinician reliably predicts individual suicide; risk-stratification scores must not be used to predict or to ration care. The assessment identifies modifiable factors and drives a safety plan, and the field favours a prevention-oriented formulation (risk status, risk state, resources, foreseeable changes) over a low-medium-high label.

19.10 From assessment to safety: the management link

The assessment earns its keep only when it produces a safety plan and the right level of care. A risk assessment is a means to safety, not an end; the guideline-anchored next steps are a collaborative safety plan, means-restriction counselling framed positively, a disposition matched to need, and treatment of the driving disorder (NICE NG225 2022; WHO LIVE LIFE 2021). The Stanley-Brown Safety Planning Intervention is the standard collaborative tool, built *with* the person: recognise personal warning signs, use internal coping strategies, use social contacts and settings that provide distraction, identify people who can help, list professionals and crisis or helpline contacts, and make the environment safer by reducing access to means. Means restriction, counselled as putting time and distance between a person and a crisis and involving family where appropriate, is the single most robustly evidenced lever and is always framed positively and never punitively. The level of care, community follow-up, crisis-team involvement or admission, is matched to assessed need and safety, with rapid follow-up after any emergency contact because the transition period is high-risk. Where a driving disorder is present, its

treatment is itself anti-suicidal, and two agents carry specific evidence: lithium in mood disorders and clozapine in schizophrenia; their pharmacology, dosing and monitoring sit in the Mood disorders: pharmacotherapy notes and the Schizophrenia: management, antipsychotics and adverse effects notes, and the acute triage of the actively suicidal patient in crisis is developed in the emergency psychiatry chapter.

GOOD TO REMEMBER

- **Safety planning and means restriction (the management step):** the guideline first move after assessment (NICE NG225 2022) is a collaborative safety plan (the Stanley-Brown components) plus positively framed means-restriction counselling, then a level of care matched to need with rapid follow-up. Means restriction is the highest-yield lever; drugs treat the driving disorder (lithium in mood disorders, clozapine in schizophrenia, both with specific anti-suicidal evidence) and supplement, never replace, the plan.

19.11 India: the Mental Healthcare Act 2017 and the decriminalised attempt

The statute every Indian candidate must quote precisely. The pivotal Indian provision is Section 115 of the Mental Healthcare Act 2017 (VERIFIED against the Act and Indian Kanoon). It provides that any person who attempts to commit suicide is presumed, unless proved otherwise, to have severe stress, and shall not be tried or punished for it, effectively overriding the old Section 309 of the Indian Penal Code that had criminalised the attempt. The Act goes further and places a duty on the appropriate government to provide care, treatment and rehabilitation to a person under such severe stress, so as to reduce the risk of recurrence. The clinical translation is humane and examinable: a person who attempts suicide is presumed to be suffering, not offending, and is owed care rather than a charge. This reframes the clinician's role at the bedside toward compassionate assessment and safety planning, in keeping with the safeguarding, non-judgemental tone the whole topic demands.

INDIA

India carries a large share of the world's suicide deaths, and suicide is among the leading causes of death in young Indian adults, a burden that makes competent assessment a public-health priority; it is stated here without any reference to means. The legal frame is the anchor: **Section 115** of the Mental Healthcare Act 2017 decriminalised the attempt through a presumption of severe stress and a duty of care, superseding Section 309 of the Indian Penal Code, and this is reinforced by national helpline infrastructure such as Tele MANAS. The Indian Psychiatric Society endorses the shift from punishment to care. The population-level and public-health suicide-prevention deep dive, including the WHO LIVE LIFE strategy and gatekeeper programmes, is developed in the Community psychiatry and public health notes.

RULE **The attempt is decriminalised, not the person blamed.** Under Section 115 of the Mental Healthcare Act 2017 a person who attempts suicide is presumed to be under severe stress and shall not be punished, and the state owes them care to reduce recurrence.

5	10	4
C-SSRS IDEATION-SEVERITY LEVELS	SAD PERSONS ITEMS (SCORE OUT OF A POSSIBLE TEN)	PREVENTION-ORIENTED FORMULATION JUDGEMENTS

HOLD THIS

A suicide risk assessment is a compassionate **structured evaluation** that weighs static and dynamic risk factors against protective factors and separates **chronic and acute risk**, using the C-SSRS ideation ladder to structure the interview and PHQ-9 item nine to screen, while remembering that SAD PERSONS is only a teaching aide and that **no instrument predicts individual suicide**, so stratifying into low-medium-high to ration care is discouraged; the assessment exists to drive a collaborative safety plan and means restriction, a denied ideation is never a cleared risk, and in India the attempt is decriminalised by Section 115 of the Mental Healthcare Act 2017.

20 · Epidemiology and aetiology of suicide

This is a CORE topic in the suicide band, and it is examined as two linked demands: state the **epidemiology of suicide** responsibly, and explain the **aetiological models** that make sense of it. The marks turn on framing the burden without sensationalising it, knowing the demographic and clinical risk patterns, placing the Indian picture with its student and agrarian dimensions accurately, and holding the three complementary explanatory frames: the individual-level **stress-diathesis model** that integrates the field, Durkheim's sociological typology, and Joiner's interpersonal theory. Throughout, the register stays compassionate, non-judgemental and means-free.

How to use this page. Fix the vocabulary and the spectrum first; then the global **suicide burden** and who is most at risk; then the Indian context and the legal frame set by the Mental Healthcare Act; and finally the aetiology, working from the integrating stress-diathesis model out to the sociological and interpersonal theories. The one idea to carry off the page is that suicide is best read as an enduring vulnerability meeting an acute stressor, never as a simple reaction to circumstances.

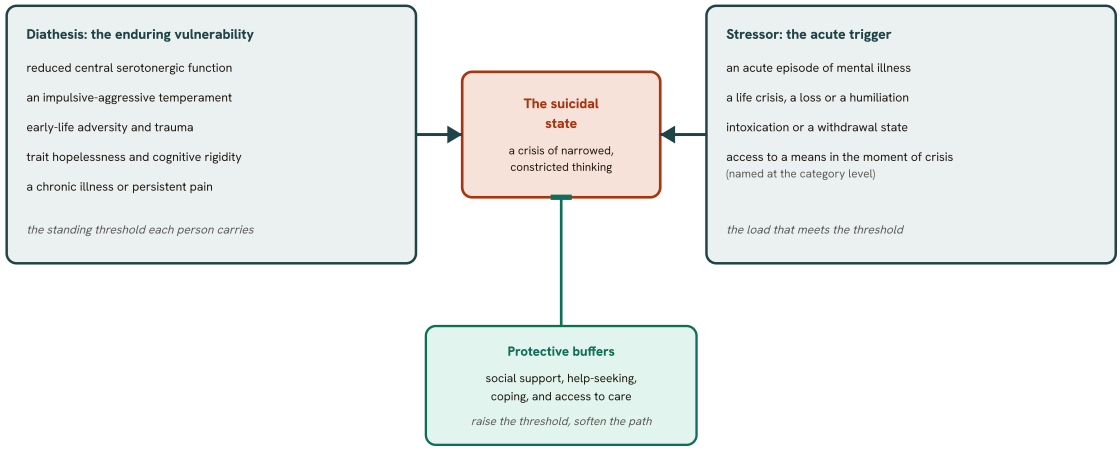


Fig 18.16 The stress-diathesis model of suicidal behaviour. Suicidal crises are best understood not as a simple product of a stressor but as the meeting of two things. Each person carries a standing diathesis, an enduring vulnerability made of reduced serotonergic function, impulsive-aggressive temperament, early adversity, trait hopelessness and chronic illness, which sets the threshold at which a crisis can occur. An acute stressor, an episode of illness, a loss or humiliation, or intoxication, then supplies the load that may meet that threshold, producing the suicidal state of narrowed, constricted thinking. Protective buffers, social support, help-seeking, coping and access to care, raise the threshold and soften the path. The model explains why an identical stressor tips one person and not another, and it shows where prevention and care can act, on the acute stressor and on the buffers.

20.1 The vocabulary and the spectrum of suicidal behaviour

Precise terms, because the examiner marks them. Suicidal phenomena form a spectrum, and the words are not interchangeable (Shorter Oxford Textbook of Psychiatry; Companion to Psychiatric Studies). Suicide is death caused by a self-directed act undertaken with at least some intent to die. Suicidal ideation ranges from a passive wish to be dead to active, planned thinking. A suicide attempt is a non-fatal self-directed act with some intent to die. Older literature used deliberate self-harm and parasuicide for intentional self-injury that need not carry a wish to die, and the acute triage of these presentations belongs to the emergency psychiatry chapter. The clinical point is that intent, not the medical severity of the act, defines where a presentation sits, and that the assessment stays needs-based and safety-focused rather than a graded checklist.

Suicidal ideation

thoughts of ending one's life, from a passive wish to be dead through to active planning

Suicide attempt

a non-fatal self-directed act carried out with some degree of intent to die

Suicide

death from a self-directed act undertaken with at least some intent to die

Deliberate self-harm

intentional self-injury that may or may not carry a wish to die; assessed for needs and safety, not by severity alone

20.2 The global suicide burden

A common, largely preventable cause of death. The **epidemiology of suicide** is examined first as scale. The World Health Organization reports that more than one in every hundred deaths worldwide is a suicide, and that suicide is the fourth leading cause of death among people aged 15 to 29 (WHO). More than three-quarters of suicides occur in low- and middle-income countries, so the **suicide burden** falls disproportionately on the settings with the least specialist provision (WHO; New Oxford Textbook of Psychiatry). The responsible way to state this in an exam is as a public-health problem that is common, unevenly distributed and amenable to prevention, keeping to counts and rates and never to method or graphic detail. The population and public-health approach to lowering these figures, including the highest-yield lever of reducing access to lethal means, is developed in the Community psychiatry and public health notes.

12	>1 in 100	4th	3
INDIA SUICIDE RATE PER 100,000 POPULATION (NCRB, 2021)	OF ALL DEATHS WORLDWIDE ARE SUICIDE (WHO)	LEADING CAUSE OF DEATH WORLDWIDE AT AGES 15 TO 29 (WHO)	COMPONENTS IN JOINER'S INTERPERSONAL THEORY

20.3 Who is most at risk: demographic and clinical patterns

Distal markers and the one proximal driver. Risk is patterned. Internationally more men die by suicide, while non-fatal self-harm is reported more often among women, a divergence usually called the gender paradox; part of the difference in case-fatality between groups reflects differences in the methods used and in help-seeking, which is one reason reducing access to lethal means is protective (Shorter Oxford; New Oxford). Risk rises at the extremes of adult age in many settings, and is higher among people who are unmarried, separated, widowed, socially isolated, unemployed or bereaved, and among those with chronic painful illness (Kaplan and Sadock CTP 2024). These are distal, largely fixed markers and they set the background rate. The single strongest proximal, and crucially modifiable, factor is active psychiatric illness: a mood disorder above all, and also alcohol and substance use, psychosis and personality disorder. Naming and treating that illness is where the epidemiology becomes clinical.

RULE **Treat the illness behind the statistic.** Active psychiatric illness, a mood disorder chief among them, is the strongest and most modifiable proximal risk factor for suicide; sociodemographic markers set the background rate, but the treatable target is the current disorder.

20.4 The Indian context

A rising rate, a young profile and a decriminalised act. India carries a large share of the global burden. Its national source is the National Crime Records Bureau (NCRB), whose annual Accidental Deaths and Suicides in India report is the primary dataset. The recorded suicide rate reached 12 per 100,000 (per lakh) population in 2021, up from about 10 per lakh in 2017, a steady year-on-year rise (NCRB, 2021). The majority of recorded deaths are among men, and the age profile skews young. Two dimensions are examined repeatedly and must be stated without sensationalising. The student dimension: NCRB records a marked and rising trend in suicides among students, widely linked to academic and examination stress. The agrarian dimension: the

farming sector, captured in NCRB's farmers and agricultural labourers category, is a recognised at-risk group tied to agrarian distress such as indebtedness and crop failure. The legal frame is a favourite: under Section 115 of the Mental Healthcare Act, 2017, a person who attempts suicide is presumed, unless proved otherwise, to be under severe stress and is not to be tried or punished, effectively overriding the old offence at Section 309 of the Indian Penal Code, and the appropriate government is placed under a duty to provide care and rehabilitation (Mental Healthcare Act 2017, Section 115).

INDIA

The Indian examiner expects three moves: the burden stated soberly from the NCRB source (a rate near 12 per lakh in 2021, up from about 10 per lakh in 2017), the two salient at-risk dimensions named (students, driven by examination and academic stress; and the farming sector, tied to agrarian distress), and the statute quoted precisely. Section 115 of the Mental Healthcare Act, 2017 decriminalises attempted suicide by presuming severe stress and directs the state toward care rather than punishment; the Indian Psychiatric Society has supported this reframing of the attempt as a signal of distress and a call for help.

GOOD TO REMEMBER

- **Section 115, Mental Healthcare Act, 2017 (the statute):** any person who attempts suicide is presumed, unless proved otherwise, to have severe stress and shall not be tried or punished, which in practice overrides Section 309 of the Indian Penal Code; the state carries a duty to provide care, treatment and rehabilitation. The first response to an attempt is compassionate assessment and care, not sanction.

20.5 Aetiological models: the stress-diathesis model as the integrating frame

An enduring vulnerability meeting an acute stressor. The **aetiological models** operate at three levels, and the individual-level frame that ties them together is the stress-diathesis model (associated with Mann and colleagues). It holds that suicidal behaviour arises when an acute state stressor acts on an enduring trait diathesis, and only when their combined load crosses a threshold (Kaplan and Sadock CTP 2024). The diathesis is the stable, trait-like vulnerability: a disposition to hopelessness and pessimism, impulsive-aggressive traits, a heritable component and the imprint of early-life adversity, associated at the biological level with reduced central serotonergic function. The stressor is the acute, state-dependent trigger: an episode of psychiatric illness, intoxication, or a humiliating interpersonal, financial or occupational crisis. The model earns its place because it explains what a stressor alone cannot: why the overwhelming majority of people exposed to severe adversity do not act, while the same stressor precipitates an act in a vulnerable individual. The accompanying figure sets the enduring diathesis and the acute stressor as two converging axes crossing a threshold, and it is the mental model to carry into any risk formulation.

TRAP **Reading a suicide as a simple reaction to circumstances.** Explaining an act by the precipitating stressor alone (a job loss, an exam failure, a relationship breakdown) misses the enduring diathesis and, with it, the treatable psychiatric illness that amplifies it; the stress-diathesis frame keeps both the vulnerability and the modifiable disorder in view.

GOOD TO REMEMBER

- **Stress-diathesis model (the defining structure):** suicidal behaviour emerges when an acute state stressor (a psychiatric episode, intoxication, a life crisis) acts on an enduring trait diathesis (hopelessness, impulsive-aggressive traits, reduced central serotonergic function, early adversity) and their combined load crosses a threshold. The discriminator from a purely social account is the enduring, trait-level vulnerability, which is why most people under severe stress do not act.

20.6 Sociological and interpersonal models: Durkheim and Joiner

The social frame: Durkheim's two axes. The sociological level was set by Durkheim, whose 1897 monograph argued that suicide rates track two social forces: the degree of social integration and the degree of social regulation (Shorter Oxford; Companion to Psychiatric Studies). Too little or too much of each yields a type. Low integration produces egoistic suicide, in a person cut off from the group and its shared meanings; excessive integration produces altruistic suicide, in which the self is sacrificed for the group or a cause. Low regulation, when the normative bonds that guide behaviour break down in times of upheaval, produces anomic suicide; excessive, oppressive regulation produces fatalistic suicide. The enduring value of the model is that it explains suicide as a social fact whose rate rises and falls with social conditions, not only as an individual event.

DURKHEIM TYPE	SOCIAL FORCE	THE DEFINING CONDITION
Egoistic	Integration	**Too little integration: the person is detached from the group and its shared meanings**
Altruistic	Integration	**Too much integration: the self is sacrificed for the group or a greater cause**
Anomic	Regulation	**Too little regulation: normative bonds break down amid social or economic upheaval**
Fatalistic	Regulation	**Too much regulation: life is over-controlled by oppressive rules or blocked futures**

Durkheim's four types arranged on the two axes of social integration and social regulation, each as a deficiency or an excess (Shorter Oxford; Companion).

PEARL

Hold Durkheim as a two-by-two: the *integration* axis gives **egoistic** (too little) and **altruistic** (too much); the *regulation* axis gives **anomic** (too little) and **fatalistic** (too much). Every type is a deficiency or an excess of one of the two forces.

The interpersonal frame: Joiner's desire and capability. At the psychological level, Joiner's interpersonal theory, the Interpersonal-Psychological Theory of Suicide, proposes that the desire to die arises from two interpersonal states: thwarted belongingness, the sense of being disconnected, excluded or alienated, and perceived burdensomeness, the belief that one is a burden on others (Kaplan and Sadock CTP 2024; DSM-5-TR 2022). Desire alone, however, is not enough for a serious attempt; the theory adds acquired capability, a fearlessness about pain, injury and death that is built up through repeated exposure to painful or provocative experiences. A near-lethal attempt requires all three: the desire (thwarted belongingness plus perceived burdensomeness) and the capability. The framework is clinically useful because it separates the wish from the ability to act, and because belongingness and burdensomeness are addressable in therapy.

MNEMONIC

DESIRE + CAPABILITY

Joiner's interpersonal theory needs both to converge on a serious attempt. DESIRE = thwarted **B**elongingness + perceived **B**urdensomeness (the two B's); CAPABILITY = the **acquired capability** to enact lethal self-harm, built by habituation to pain and fear. Wish plus ability, not wish alone.

GOOD TO REMEMBER

- **Durkheim's typology (the two axes):** suicide rates track social integration (egoistic = too little, altruistic = too much) and social regulation (anomic = too little, fatalistic = too much); each of the four types is a deficiency or excess of one force.
- **Joiner's interpersonal theory (the three components):** the desire to die comes from thwarted belongingness plus perceived burdensomeness, and a serious attempt additionally requires acquired capability (fearlessness about pain and death); all three must converge, which is why desire without capability, or capability without desire, does not produce a lethal act.

HOLD THIS

Suicide is an enduring diathesis (trait vulnerability: hopelessness, impulsive-aggressive traits, reduced serotonergic function, early adversity) meeting an acute stressor (a psychiatric episode above all, intoxication, or a life crisis) and crossing a threshold; epidemiology tells you who is at risk (men, the socially isolated, the young in India, students and those in agrarian distress, and anyone with active psychiatric illness), Durkheim explains the social rate through integration and regulation, and Joiner explains the individual act as desire (thwarted belongingness plus perceived burdensomeness) meeting acquired capability.

21 · Management of the suicidal patient and safety planning

This is the CORE management topic of the chapter, and it is examined as a sequence of clinical moves rather than a single fact. The **management of the suicidal patient** begins the moment the person is in the room: an engaging, non-judgemental relationship, a structured assessment that weighs risk against protective factors rather than a predictive score, a collaborative **safety plan**, a disposition matched to need, treatment of the disorder that is driving the risk, and active follow-up through the vulnerable weeks that come after. Get the order and the principles right

and the marks follow; the guideline spine here is NICE (NICE NG225 2022), which frames every step around compassion, needs and safety.

How to use this page. Fix the NICE position first, because it is the lead guideline and it sets two rules that reorganise older teaching: assess needs and safety through a person-centred interview, and do *not* use risk-stratification scores to predict future suicide or to decide who is offered care (NICE NG225 2022). Then learn the collaborative Safety Planning Intervention as the signature intervention, means restriction counselling framed positively, the level-of-care decision, the disorder-directed and anti-suicidal pharmacology, and the follow-up posture. The India anchor to carry is Section 115 of the Mental Healthcare Act, 2017. The acute triage of the person who is actively suicidal in the emergency room is developed in the emergency psychiatry chapter, and the population-level prevention deep dive sits in the Community psychiatry and public health notes. Throughout, the tone is safeguarding and the burden is stated without any reference to method.

Therapeutic stance

The engaging, warm, non-judgemental clinical posture that makes honest disclosure and collaboration possible; the vehicle every other step travels on.

Safety planning

A collaborative, prioritised written plan the person can use in a crisis, co-produced with the clinician; the Stanley-Brown Safety Planning Intervention.

Means restriction counselling

Working with the person and family to reduce access to lethal means, framed positively as putting time and distance between the person and a crisis.

Disposition

The level-of-care decision that matches the setting (community follow-up, crisis team, or admission) to assessed need and safety.

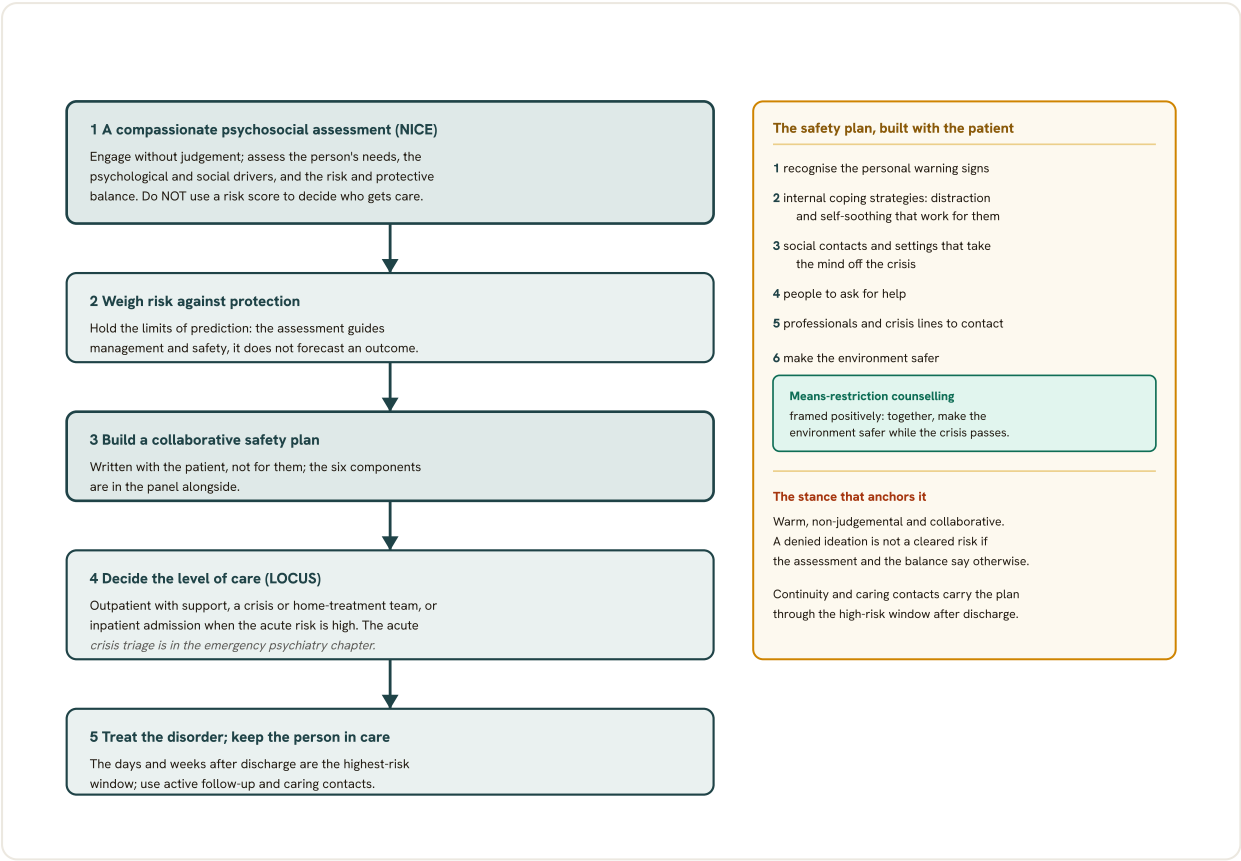


Fig 18.17 The management of the suicidal patient and safety planning. The pathway is anchored on a compassionate, non-judgemental psychosocial assessment, in the NICE tradition, that maps the person's needs and the drivers of their distress rather than reducing them to a risk score; guidance is explicit that a stratification score should not decide who receives care. The clinician then weighs the risk and protective balance, holding the limits of prediction, and builds a safety plan with the patient across its six components, from recognising warning signs to internal coping, social and professional contacts, and making the environment safer through means-restriction counselling framed positively. The level of care follows, from outpatient support through a crisis team to admission when acute risk is high, with the acute crisis triage taken up in the emergency psychiatry chapter. Because the period after discharge is the highest-risk window, active follow-up and caring contacts carry the plan forward.

21.1 The therapeutic stance: engage before you assess

A compassionate, non-judgemental relationship is the first intervention, not the preamble. The guideline foundation is that every person presenting after self-harm or with suicidal thoughts receives a compassionate, non-judgemental, needs-based assessment, regardless of the apparent medical seriousness of the act (NICE NG225 2022). The **therapeutic stance** means sitting with distress without recoiling from it, asking about suicidal thoughts directly and calmly (asking does not plant the idea), validating the pain that drives the thoughts, and conveying that help is possible. This stance is itself protective: it reduces the shame that keeps people from disclosing, and it is the precondition for an honest account of ideation, intent and access to means. NICE is explicit that the assessment is an intervention in its own right, an opportunity for engagement rather than a bureaucratic risk-scoring exercise. The clinician who leads with warmth gets the information the assessment depends on; the clinician who leads with a checklist often does not.

RULE **Engagement is the intervention, not the waiting room.** The compassionate, needs-based assessment is itself therapeutic (NICE NG225 2022); asking directly about suicidal thoughts does not increase risk, and the honest disclosure it earns is what every later step depends on.

GOOD TO REMEMBER

- **Therapeutic stance (the management step):** the guideline first move (NICE NG225 2022) is a compassionate, non-judgemental, needs-based assessment offered to everyone, whatever the medical severity of the act; ask about suicidal thoughts directly and calmly, treat the assessment as an engagement opportunity, and build the alliance before anything else.

21.2 Structured assessment and risk formulation, not a predictive score

Weigh risk against protective factors and current state; do not stratify to ration care. The examinable pivot of modern practice is that individual-level prediction of suicide is poor, risk fluctuates, and no tool reliably identifies who will act (NICE NG225 2022). The clinician therefore builds a **risk formulation** through a structured interview that weighs static and dynamic risk factors against protective factors, current mental state, intent and access to means, and the social context, and that arrives at a clinical judgement of current risk rather than a fixed low, medium or high label. NICE is unambiguous: do not use risk-assessment or stratification scales to predict future self-harm or suicide, and do not use their scores to determine who is offered treatment or admission. Structured instruments still have a role as aids to a thorough interview: the C-SSRS (Columbia Suicide Severity Rating Scale) is regarded as the gold-standard structured tool for assessing and monitoring suicidal ideation and behaviour, with five ideation levels of increasing severity (Clinical Methods in Psychiatry, AIIMS 2024); the older SAD PERSONS acronym scale and the ninth item of the PHQ-9 are screening aids; and SAFE-T (the Suicide Assessment Five-Step Evaluation and Triage) offers a five-step framework for structuring the interview and the disposition. All support, and none replace, the clinical formulation.

INSTRUMENT	WHAT IT IS	VERIFIED USE AND CAUTION
C-SSRS	Structured scale with five ideation levels of increasing severity, plus behaviour items	**Gold-standard aid (AIIMS 2024); supports, never replaces, the interview**
SAD PERSONS	Ten-item acronym-based screen, historically used in the emergency room	**A prompt only, not a substitute for clinical evaluation (AIIMS CL 2020)**
PHQ-9, the ninth item	Single screening item for thoughts of being better off dead or of self-harm	**A positive item triggers fuller assessment, never a decision on its own**
SAFE-T	Suicide Assessment Five-Step Evaluation and Triage framework	**Structures interview and disposition; a scaffold, not a predictive score**

Structured instruments as aids to the interview, with the NICE caution that scores must not predict risk or ration care (NICE NG225 2022); the reproduced forms sit with the suicide-risk assessment scales.

TRAP **Reading a denied ideation as a cleared risk.** A flat denial does not clear risk when the risk-and-protective balance, the collateral history and the mental state point the other way; formulate from the whole picture, and never let a global scale score or a single answer make the disposition (NICE NG225 2022).

GOOD TO REMEMBER

- **Risk formulation (the management step):** the guideline principle (NICE NG225 2022) is a structured, person-centred interview that weighs risk against protective factors, current state, intent and access to means, producing a clinical formulation rather than a predictive category; do not use stratification scores to predict or to ration care. The C-SSRS is the gold-standard structured aid but never a substitute for the interview.

21.3 Collaborative safety planning: the Safety Planning Intervention

Six prioritised steps the person can use in a crisis, co-produced not prescribed. The signature intervention is the Safety Planning Intervention (the Stanley-Brown Safety Plan), developed collaboratively for anyone at moderate to high risk when hospitalisation is not clinically indicated (Kaplan and Sadock CTP 2024; NICE NG225 2022). It is a written, personalised, prioritised ladder that the person moves down as distress rises: recognise personal warning signs; use internal coping strategies alone; draw on social contacts and settings that provide distraction; reach out to people who can be asked for help; contact professionals and crisis or helpline services; and make the environment safer by reducing access to lethal means. The plan is co-produced, kept where the person can find it, and reviewed and updated over time. Crucially it is a clinical instrument, not a promise: a signed no-suicide or no-harm contract has no evidence base and can falsely reassure the clinician, whereas the safety plan gives the person concrete, ranked actions and gives the clinician a structured way to involve family and services.

COMPONENT	WHAT IT LOOKS LIKE IN THE PLAN	THE POINT OF THIS RUNG
Recognise warning signs	The person's own thoughts, images, moods and situations that precede a crisis	**Catch the crisis early, at the person's own first signal**
Internal coping strategies	Things the person can do alone to take their mind off the crisis	**Self-soothing tried before anyone else is contacted**
Social contacts and settings	People and places that provide healthy distraction	**Distraction, not disclosure, at this rung**
People to ask for help	Family or friends the person can tell they are in crisis	**The first human help, when self-management is not enough**
Professionals and crisis contacts	Clinicians, crisis lines, helplines and emergency services	**The professional safety net, with numbers to hand**
Making the environment safer	Means restriction counselling, framed positively, with the person and family	**Time and distance between the person and a crisis**

The six components of the Safety Planning Intervention, a ranked ladder from internal coping to professional help ending in a safer environment (Stanley-Brown; NICE NG225 2022), laid out in the accompanying figure.

MNEMONIC

WISE-PS

The Safety Planning Intervention as a ranked ladder. **W**arning signs the person recognises; **I**nternal coping strategies used alone; **S**ocial contacts and settings for distraction; **E**nlist people to ask for help; **P**rofessional and crisis contacts; make the environment **S**afer through means restriction counselling. Six rungs, climbed only as far as each crisis needs.

RULE **A safety plan is a collaborative clinical act, not a contract.** The six-step Safety Planning Intervention is co-produced and works because the person descends a ranked ladder that ends in a safer environment; a signed no-suicide contract is not evidence-based and is not a substitute.

GOOD TO REMEMBER

- **Safety Planning Intervention (the management step):** the guideline-anchored intervention (Stanley-Brown; NICE NG225 2022; Kaplan and Sadock CTP 2024) is a collaborative, prioritised, written plan with six components, that being warning signs, internal coping, social contacts and settings for distraction, people to ask for help, professional and crisis contacts, and making the environment safer through means restriction. It is co-produced for moderate to high risk when admission is not indicated, and it replaces the discredited no-suicide contract.

21.4 Means restriction counselling: framed positively

Reduce access to lethal means, and frame it as time and distance, never as blame. The sixth rung of the safety plan is its own high-yield step. **Means restriction counselling** is a collaborative conversation about reducing access to lethal means, framed positively as putting time and distance between the person and a crisis so that an intense, often short-lived suicidal impulse can pass safely (NICE NG225 2022). The clinician works with the person, and where appropriate with family or carers, to make the immediate environment safer, at the category level of reducing access to lethal means rather than dwelling on any specific method. This is deliberately non-judgemental and non-alarming; it is offered as a shared act of care, not an accusation or a restriction imposed from outside. At the population level the same principle is the single highest-yield, most robustly evidenced suicide-prevention lever (WHO LIVE LIFE 2021), which is why the individual conversation matters so much; the population and public-health treatment of means restriction is developed in the Community psychiatry and public health notes.

GOOD TO REMEMBER

- **Means restriction counselling (the management step):** the guideline principle (NICE NG225 2022; WHO LIVE LIFE 2021) is to reduce access to lethal means, framed positively as putting time and distance between the person and a crisis, worked out collaboratively with the person and family and kept at the category level. It is the sixth safety-plan component and, at the population level, the highest-yield prevention lever.

21.5 Disposition: matching the level of care to need

Community, crisis team, or admission, decided by need and safety, not by a score. The **disposition** is the level-of-care decision, and it is matched to assessed need and safety rather than to a stratification label (NICE NG225 2022). The lowest-restriction option that keeps the person safe is preferred: outpatient management with a safety plan and social support where risk can be contained; a crisis resolution and home treatment team for intensive community support when risk is higher but hospitalisation can be avoided; and inpatient admission, voluntary wherever possible, when acute risk is high and cannot be managed safely in the community. Every step in the pathway includes rapid follow-up after any emergency contact and an active, documented handover, because the transition between services is itself a period of elevated risk. Where a person at imminent risk lacks capacity or declines care, admission may proceed under the relevant provisions of the Mental Healthcare Act, 2017. The acute triage of the person who is actively suicidal in crisis, the immediate **crisis intervention** in the emergency room, belongs to the emergency psychiatry chapter.

LEVEL OF CARE	WHEN IT FITS	THE SAFEGUARD THAT MUST TRAVEL WITH IT
Outpatient with support	Risk containable in the community, safety plan in place, supports available	**Rapid review and a documented follow-up appointment**
Crisis resolution / home treatment team	Higher risk needing intensive daily support, admission avoidable	**Frequent contact and a clear escalation route**
Inpatient admission	Acute risk high, cannot be kept safe in the community	**Voluntary where possible; least restriction that keeps the person safe**

The disposition ladder, from outpatient support to admission, chosen by assessed need and safety and not by a stratification score (NICE NG225 2022); sketched in the figure alongside.

WORKED EXAMPLE

A man in his forties is brought in by his wife after an episode of self-harm following job loss. Rather than reach for a scale score, the clinician spends the first minutes building rapport, then formulates: prominent hopelessness and recent loss on one side, a supportive spouse, help-seeking and no current intent on the other. Together they build a safety plan, moving through the man's own warning signs, a few internal coping steps, his brother as a first contact, and a crisis line; the last rung is a calm, positive conversation with the couple about making the home environment safer. Because risk is judged containable and support is strong, the disposition is outpatient management with a review within a few days and a crisis number in hand, rather than admission.

GOOD TO REMEMBER

- **Disposition (the management step):** the guideline principle (NICE NG225 2022) is to match the level of care, that being outpatient with support, a crisis or home-treatment team, or inpatient admission, to assessed need and safety at the least restriction that keeps the person safe; ensure rapid follow-up and an active handover at every transition, and take the immediate emergency-room crisis intervention to the emergency psychiatry chapter.

21.6 Treat the underlying disorder, and the anti-suicidal agents

The most durable risk reduction is treating the disorder that drives the risk. Suicidal risk usually sits on a treatable psychiatric disorder, most often a mood disorder, a psychotic illness, or a substance use disorder, and vigorous treatment of that disorder is central to management. Two agents carry a specific anti-suicidal effect that goes beyond simply treating the episode. Lithium reduces the risk of suicide and of death from any cause in mood disorders; the meta-analysis by Cipriani and colleagues, pooling 48 randomised controlled trials, established this signal, which is at least partly distinct from control of the mood episode itself (Cipriani 2013 BMJ), making lithium a specific reason to favour it in mood disorders carrying suicide risk. Clozapine is the only antipsychotic with a specific anti-suicidal indication; the International Suicide Prevention Trial showed it superior to olanzapine in reducing suicidal behaviour in schizophrenia and schizoaffective disorder at high risk (InterSePT, Meltzer 2003). Ketamine and intranasal esketamine produce a rapid, short-term fall in suicidal ideation as an adjunct within comprehensive care (the ASPIRE programme), but an effect on completed suicide is not established. The deep pharmacology of these agents lives elsewhere: lithium in the Mood disorders: pharmacotherapy notes, and clozapine in the Schizophrenia: management, antipsychotics and adverse effects notes.

AGENT	POPULATION AND EVIDENCE	WHAT TO HOLD
Lithium	Mood disorders; Cipriani 2013 BMJ, pooling 48 randomised trials	**Cuts suicide and all-cause death; effect partly independent of mood control**
Clozapine	Schizophrenia and schizoaffective disorder at high risk; InterSePT, Meltzer 2003	**Only antipsychotic with a specific anti-suicidal indication; beat olanzapine**
Ketamine / esketamine	Depression with acute suicidal ideation; the ASPIRE programme	**Rapid, short-term fall in ideation only; no proven effect on completed suicide**

The three anti-suicidal agents and the strength of their evidence; doses and full pharmacology sit in the mood and schizophrenia chapters, cross-referenced above.

GOOD TO REMEMBER

- **Lithium (the anti-suicidal drug):** reduces suicide and all-cause mortality in mood disorders, an effect partly distinct from mood control (Cipriani 2013 BMJ, 48 trials); favour it where a mood disorder carries suicide risk. Deep pharmacology in the Mood disorders: pharmacotherapy notes.
- **Clozapine (the anti-suicidal drug):** the only antipsychotic with a specific anti-suicidal indication, superior to olanzapine in high-risk schizophrenia and schizoaffective disorder (InterSePT, Meltzer 2003). Deep pharmacology in the Schizophrenia: management, antipsychotics and adverse effects notes.
- **Esketamine (the anti-suicidal drug):** rapid, short-term reduction in ideation as an adjunct (the ASPIRE programme); a reduction in completed suicide is not established, so it supplements rather than replaces comprehensive care.

21.7 Follow-up and continuity: the high-risk period after discharge

The weeks after an emergency contact or discharge are the most dangerous, so follow-up must be active. Management does not end at the plan or the discharge letter. Transitions between services and the period soon after discharge from inpatient care carry markedly elevated risk, so continuity of care with a prompt, actively arranged follow-up is essential rather than optional (NICE NG225 2022). The clinician ensures a named follow-up is booked before the person leaves, that the safety plan travels with them, and that the handover to community services is explicit and closed-loop. A low-cost, well-recognised adjunct in this window is the use of **caring contacts**, brief, non-demanding follow-up messages or letters that simply convey that the service is thinking of the person and remains available; they are offered as a supportive supplement to, not a replacement for, active clinical follow-up. The aim across the whole period is to keep the person connected to care exactly when disengagement is most dangerous.

6	5	4	115
SAFETY PLANNING INTERVENTION COMPONENTS	C-SSRS IDEATION LEVELS	WHO LIVE LIFE INTERVENTIONS	MENTAL HEALTHCARE ACT 2017 SECTION DECRIMINALISING THE ATTEMPT

PEARL

The post-discharge window is where a good inpatient stay is either consolidated or lost. Book the follow-up before discharge, send the safety plan out with the person, and treat any missed appointment in this window as a signal to reach out actively rather than to wait; caring contacts are the cheap, humane way to hold the thread.

GOOD TO REMEMBER

- **Follow-up and continuity (the management step):** the guideline posture (NICE NG225 2022) is that the period after an emergency contact or discharge is high-risk, so arrange prompt, active follow-up with an explicit closed-loop handover, send the safety plan with the person, and use caring contacts as a supportive adjunct. Disengagement is most dangerous exactly here, so continuity is a safety intervention.

21.8 India: Section 115 of the Mental Healthcare Act, 2017

The attempt is decriminalised, and severe stress is presumed. The India anchor for this topic is a statute, not a scale. Under Section 115 of the Mental Healthcare Act, 2017, any person who attempts suicide is presumed, unless proved otherwise, to have severe stress, and shall not be tried and punished for the attempt; this provision effectively overrides the older Section 309 of the Indian Penal Code (Mental Healthcare Act, 2017, Section 115). The same section places a duty on the appropriate government to provide care, treatment and rehabilitation to a person who has attempted suicide, to reduce the risk of a recurrence. For the clinician this reframes the encounter decisively: the person who has attempted suicide is a patient in severe distress owed care, not an offender, and the entire management sequence in this topic follows from that stance. The wider burden of suicide in India is substantial and is a public-health priority; it is stated here without any reference to method, and the population-level response is taken up in the Community psychiatry and public health notes.

INDIA

Section 115 of the Mental Healthcare Act, 2017 is the single most examinable India point on this topic: a person who attempts suicide is presumed, unless proved otherwise, to be under severe stress and shall not be tried or punished, effectively overriding Section 309 of the Indian Penal Code, and the government carries a duty to provide care, treatment and rehabilitation. The Indian Psychiatric Society has supported this decriminalisation. Read every suicidal presentation through this lens, that being distress owed care rather than conduct to be judged.

GOOD TO REMEMBER

- **Section 115, Mental Healthcare Act, 2017 (the statute):** a person who attempts suicide is presumed, unless proved otherwise, to have severe stress and shall not be tried or punished, effectively overriding Section 309 of the Indian Penal Code; the government has a duty to provide care, treatment and rehabilitation. The defining point is decriminalisation with a presumption of severe stress.

HOLD THIS

The management of the suicidal patient runs as a sequence: an engaging, non-judgemental therapeutic stance; a structured assessment that weighs risk against protective factors and current state, a formulation rather than a predictive score (and never a stratification score to ration care, NICE NG225 2022); a collaborative six-step Safety Planning Intervention ending in positively framed means restriction counselling; a disposition matched to need across outpatient support, crisis team, or admission; vigorous treatment of the underlying disorder, with lithium reducing suicide in mood disorders (Cipriani 2013 BMJ) and clozapine the only antipsychotic with a specific anti-suicidal indication (InterSePT, Meltzer 2003); and active follow-up through the high-risk post-discharge weeks with caring contacts. In India, Section 115 of the Mental Healthcare Act, 2017 presumes severe stress and decriminalises the attempt.

22 · Deliberate self-harm

This is the topic where a compassionate stance and a guideline become the same thing. Deliberate self-harm is any intentional self-poisoning or self-injury, carried out irrespective of motive and

irrespective of the degree of suicidal intent, so the term deliberately spans the person who wished to die, the person who did not, and every ambivalent state between. The examiner tests two moves: the clean *discrimination* between self-harm, non-suicidal self-injury and a suicide attempt, and the *management* that flows from a single landmark guideline. That guideline is NICE NG225 (Self-harm: assessment, management and preventing recurrence, 2022), and it reframed the field so decisively that the whole of **self-harm management** can be reconstructed from its two central positions: every episode earns a full, needs-based psychosocial assessment, and risk-stratification scores must never be used to predict future self-harm or to decide who receives care.

How to use this page. Fix the vocabulary first, then the relationship between self-harm and suicide (any self-harm raises future suicide risk, whatever the apparent medical seriousness), then the NICE NG225 stance as the lead: a **compassionate non-judgemental**, needs-based psychosocial assessment for every presentation, no risk score used to ration treatment, a collaborative safety plan, the carefully stated harm-minimisation debate, and continuity of care. Throughout, safe-messaging is absolute: the burden and the risk are stated without any reference to method, and access to means is named only at the category level. The accompanying management-and-safety-planning algorithm, drawn at the management topic, also maps the self-harm pathway, so this page refers to it generically rather than redrawing it.

22.1 What deliberate self-harm is, and what it is not

An umbrella term that spans intent, not a synonym for a suicide attempt. The defining feature of self-harm is that it is intentional self-poisoning or self-injury *regardless* of the person's motive or the degree of suicidal intent (NICE NG225 2022; Kaplan and Sadock CTP 2024). This is why the guideline prefers the bare term "self-harm" to the older "deliberate self-harm (DSH)": it refuses to assume a wish to die and refuses to grade the act by its apparent medical seriousness. Sitting inside that umbrella are two narrower ideas held apart by intent. Non-suicidal self-injury (NSSI) is intentional self-inflicted injury to the body undertaken with the expectation that it will cause only minor physical harm and with no intent to die, a distinct entity coded in the ICD-11 (MB23.E); it is frequently a means of regulating unbearable affect rather than an attempt to end life. A *suicide attempt*, by contrast, is a self-directed, potentially injurious act carried out with at least some intent to die, however ambivalent. The clinician's first task is therefore not to label the method but to establish where on this intent-spanning field the person stands, because that is what the assessment, never the score, then addresses.

TERM	DEFINING FEATURE	THE DISCRIMINATOR TO HOLD
Deliberate self-harm (self-harm)	Intentional self-poisoning or self-injury, irrespective of motive or suicidal intent	**The umbrella term; does not, by itself, imply a wish to die**
Non-suicidal self-injury (NSSI)	Self-inflicted bodily injury with the expectation of only minor harm and no intent to die (ICD-11 MB23.E)	**The subset explicitly without suicidal intent, often to regulate affect**
Suicide attempt	A self-directed, potentially injurious act with at least some intent to die	**Intent to die is present, however ambivalent or fleeting**

The terminology of self-harm, arranged by the single axis of suicidal intent; the umbrella and its two subsets separate cleanly on that axis (NICE NG225 2022; ICD-11 CDDR).

GOOD TO REMEMBER

- **Deliberate self-harm (the definition):** intentional self-poisoning or self-injury irrespective of motive or degree of suicidal intent, so it is the broadest term and spans intent rather than assuming it. The discriminator to hold is that NSSI is the intent-free subset (ICD-11 MB23.E, expectation of only minor harm, no wish to die) while a suicide attempt carries at least some intent to die; the act is never graded by its apparent medical seriousness.

22.2 The relationship to suicide

Self-harm and suicide are neither identical nor safely separable: any self-harm raises future suicide risk. The two are distinct in the moment, because self-harm can occur with or without suicidal intent, yet they are bound together over time (NICE NG225 2022; New Oxford Textbook of Psychiatry). The examinable principle is that any episode of self-harm, including an episode with no suicidal intent at the time, is among the strongest markers of later suicide, and the risk of suicide is substantially elevated in the period immediately after a presentation. This has an immediate clinical consequence that the guideline insists upon: the apparent medical triviality of an act carries no reassurance about future risk, so a superficial injury or an apparently minor act is not a lesser presentation and must not be triaged as one. A history of prior self-harm is likewise one of the strongest static risk factors weighed in any suicide risk assessment, a link developed in the assessment topic. The safeguarding reading is the humane one: a person who has harmed themselves has signalled distress and elevated risk, and is owed a full assessment and active care rather than a rapid discharge.

RULE **Any self-harm raises future suicide risk, whatever the method or medical seriousness.** An episode with no suicidal intent still marks elevated future risk; the triviality of the act never justifies a lesser response, and every presentation earns a full assessment.

GOOD TO REMEMBER

- **Self-harm and suicide (the relationship):** self-harm occurs with or without suicidal intent and is distinct from a completed attempt in the moment, yet any self-harm, including non-suicidal episodes, is among the strongest predictors of subsequent suicide and the risk is highest soon after a presentation. The point to hold is that apparent medical seriousness does not grade future risk.

22.3 The NICE NG225 lead: a needs-based psychosocial assessment for every episode

The single first move, for every presentation, is a compassionate needs-based psychosocial assessment. The leading position of NICE NG225 (2022) is that every person presenting after an episode of self-harm should receive a full **psychosocial assessment**, carried out in a compassionate non-judgemental manner, regardless of the apparent medical seriousness of the act and regardless of whether they are seen in an emergency department, in primary care or on a ward. The assessment is *needs-based*, not risk-scored: it explores the person's own needs, the psychological and social factors that drove and surround the episode (the precipitants, the mental state, the relationships, the losses, the supports), and the risks to their safety, and it does so as an engagement, not an interrogation. NICE is explicit that this assessment is itself therapeutic, an intervention in its own right rather than a gate to one, because being heard without judgement is what re-establishes safety and the willingness to accept help. This is the anchor of self-harm management, and every downstream step (the safety plan, the level of care, the aftercare) is built on it.

RULE **Every episode gets a full compassionate psychosocial assessment (NICE NG225).** Whatever the apparent medical seriousness and wherever the person is seen, the needs-based assessment of needs, psychosocial factors and safety is the guideline first move, and it is itself therapeutic.

PEARL

Treat the psychosocial assessment as an intervention, not a triage form. NICE NG225 frames the compassionate, unhurried, non-judgemental conversation as therapeutic in itself: it validates distress, rebuilds engagement, and is often the moment a person first accepts help. Asking directly and calmly about self-harm and suicidal thoughts does not plant the idea or raise risk, a myth worth retiring on sight.

GOOD TO REMEMBER

- **The psychosocial assessment (the management step, NICE NG225 2022):** a compassionate non-judgemental, needs-based assessment for every episode covering the person's needs, the psychological and social factors, and the risks, given regardless of the medical seriousness of the act. The guideline principle to hold is that it is itself an intervention, not a gateway that screens people out of care.

22.4 The critical position: risk-stratification tools must not gate care

Do not use a risk score to predict future self-harm, and never to decide who is offered treatment. This is the position on which NICE NG225 (2022) most sharply broke with earlier practice, and it is the single most heavily tested point in the topic. Risk-assessment and stratification tools and scales must not be used to predict future self-harm or suicide, and must not be used to determine who is offered treatment, admission or discharge. A global label of "low", "medium" or "high" risk must not drive any clinical decision, because such instruments perform poorly at identifying who will act at the individual level and, used as a gate, they systematically deny care to people who need it. What replaces the score is the person-centred assessment of the preceding subtopic: the individualised weighing of needs, psychosocial factors and safety. The

instruments may still have narrow uses, for structuring a conversation or prompting domains, but the moment a number is used to ration care the guideline has been broken.

APPROACH	WHAT IT DOES	NICE NG225 VERDICT
Needs-based psychosocial assessment	Weighs the person's needs, psychosocial context and safety, individually, every episode	**Endorsed as the standard for every presentation**
Risk-stratification tool or global score	Sorts the person into low, medium or high to predict future self-harm	**Must not be used to predict, nor to decide who is offered care or admission**

The reframe at the centre of NICE NG225: a needs-based assessment governs care, a stratification score never does (NICE NG225 2022).

TRAP **Using a risk-stratification score to withhold care.** Reading a "low risk" label off a scale and discharging on the strength of it is the cardinal error NICE NG225 forbids; the score does not predict the individual, and it must never decide who is offered treatment.

COMMON TRAP

A young person is seen after a first episode of self-harm, appears calm, and a stratification tool returns a "low" global score. Discharging on that number, without the compassionate needs-based assessment, is exactly the practice NICE NG225 was written to end: the calm presentation and the low score neither predict future risk nor address the psychosocial drivers of the episode. The person is instead offered a full psychosocial assessment, a collaborative safety plan and active follow-up. The number never governs the disposition.

GOOD TO REMEMBER

- **Risk-stratification tools (the critical NICE NG225 position):** do not use risk-assessment or stratification scores to predict future self-harm or suicide, and do not use them to decide who is offered treatment or admission. A low-medium-high label must not drive care; a person-centred assessment of needs and safety does. The trap to hold is treating a "low risk" score as a licence to discharge.

22.5 Safety planning and access to help

A collaborative safety plan, built with the person, plus positively framed means-restriction counselling. After the assessment, the guideline first move is a collaborative safety plan developed *with* the person, together with clear, concrete information on how to get help during a crisis (NICE NG225 2022). The standard structure is the Stanley-Brown Safety Planning Intervention, whose components map directly onto self-harm: recognise personal warning signs; use internal coping strategies; use social contacts and settings that provide distraction; identify people who can be asked for help; list professionals and crisis or helpline contacts; and make the environment safer by reducing access to means. Means restriction is named only at the category level and is always framed positively and collaboratively, as putting time and distance between the person and a crisis rather than as a punitive removal, and family or carers are involved where

appropriate. The plan is a living document, revisited and revised, not a form signed once, and giving the person a real route to help between contacts is part of what makes it work.

GOOD TO REMEMBER

- **Safety planning (the management step, NICE NG225 2022):** build a collaborative safety plan with the person (the Stanley-Brown components) and give clear crisis-access information; counsel on reducing access to means, framed positively as time and distance from a crisis, involving carers where appropriate. The guideline principle to hold is that the plan is collaborative and revisited, and means restriction is named only at the category level, never punitively.

22.6 The harm-minimisation debate, stated carefully

Harm minimisation is an adjunct considered only within a wider plan, for people who continue to self-harm, and its evidence and ethics remain contested. For a person who continues to self-harm despite treatment, an individualised harm-minimisation approach, aimed at reducing the frequency, severity and impact of episodes, may be *considered* as one part of a wider, individualised plan (NICE NG225 2022). It is never a first-line or stand-alone intervention, and it is offered only after, and alongside, a proper assessment and the attempt to treat the underlying difficulties. The guideline is careful, and so must the candidate be: the overarching aim always remains reducing and ultimately stopping self-harm, and the evidence base and the ethics of harm minimisation are genuinely contested, so it is stated as a considered, bounded option rather than an endorsed strategy. In an exam answer the safe formulation is to name it, place it firmly as an adjunct for continuing self-harm within a broader plan, and flag the contested evidence, without specifying techniques.

GOOD TO REMEMBER

- **Harm minimisation (the contested adjunct, NICE NG225 2022):** consider it only as part of a wider individualised plan for people who continue to self-harm, never as first-line or stand-alone; the aim stays reducing and stopping self-harm, and the evidence and ethics are contested. The principle to hold is that it is a bounded adjunct, not an endorsed strategy, and it is stated without specifying techniques.

22.7 Continuity of care, aftercare and the self-harm-focused intervention

The period after an episode is high risk; continuity of care and active handover are protective. Self-harm management does not end at the safety plan. NICE NG225 (2022) emphasises continuity of care and follow-up after every episode, because transitions between services, the move from an emergency department to community care, from a ward to home, from one team to another, are recognised periods of elevated risk that demand an active, named handover rather than a passive referral. Rapid follow-up after any emergency contact and a clear, agreed plan for who is responsible are the protective moves. Beyond immediate aftercare, the guideline supports offering a psychological intervention specifically tailored to self-harm, and, for adults with recurrent self-harm and emotional dysregulation, dialectical behaviour therapy has the strongest evidence; the specific modality and session structure are taken from the guideline itself and are flagged here rather than fixed. Where a driving disorder underlies the self-harm, treating it is part of care, and two agents carry specific anti-suicidal evidence, lithium in mood

disorders and clozapine in schizophrenia, whose pharmacology, dosing and monitoring sit in the Mood disorders: pharmacotherapy notes and the Schizophrenia: management, antipsychotics and adverse effects notes; the acute triage of the actively suicidal patient in crisis is developed in the emergency psychiatry chapter, and the population and public-health suicide-prevention deep dive in the Community psychiatry and public health notes.

GOOD TO REMEMBER

- **Continuity and aftercare (the management step, NICE NG225 2022):** ensure continuity of care and rapid follow-up after every episode, and treat every service transition as a high-risk period needing an active named handover. Offer a psychological intervention tailored to self-harm, with dialectical behaviour therapy best evidenced for adults with recurrent self-harm and emotional dysregulation; treat any driving disorder, using the anti-suicidal evidence for lithium and clozapine held in the mood and psychosis chapters.

22.8 India: the decriminalised attempt and the duty of care

A person who self-harms is presumed to be under severe stress and is owed care, not a charge. The Indian frame for any self-harm or attempt is Section 115 of the Mental Healthcare Act 2017 (verified against the Act and Indian Kanoon). It provides that any person who attempts to commit suicide is presumed, unless proved otherwise, to have severe stress, and shall not be tried or punished for the attempt, effectively overriding the old Section 309 of the Indian Penal Code that had criminalised it. The Act goes further, placing a duty on the appropriate government to provide care, treatment and rehabilitation to reduce the risk of recurrence. The clinical translation is exactly the safeguarding stance the whole topic demands: a person who has harmed themselves is suffering, not offending, and the bedside response is compassionate assessment and safety planning, not judgement. India carries a large share of the world's suicide burden, and self-harm is a common emergency presentation, a burden stated here without any reference to means; the Indian Psychiatric Society endorses the shift from punishment to care.

INDIA

The anchor is **Section 115** of the Mental Healthcare Act 2017: the attempt is decriminalised through a presumption of severe stress and a duty of care, superseding Section 309 of the Indian Penal Code. The clinical stance follows directly, compassionate assessment and a collaborative safety plan rather than a charge, reinforced by national helpline infrastructure such as Tele MANAS. The burden is real and large but is stated without method, in keeping with safe-messaging, and the population-level prevention strategy sits in the Community psychiatry and public health notes.

GOOD TO REMEMBER

- **Section 115, Mental Healthcare Act 2017 (the statute, India):** a person who attempts suicide is presumed to be under severe stress and shall not be punished, overriding Section 309 of the Indian Penal Code, and the state owes them care to reduce recurrence. The principle to hold is that self-harm is met with care, not criminal liability.

2022	0	2017
NICE NG225, THE LEADING SELF-HARM GUIDELINE	RISK-STRATIFICATION SCORES THAT MAY PREDICT SELF-HARM OR RATION CARE	MENTAL HEALTHCARE ACT, SECTION 115 (ATTEMPT DECRIMINALISED)

HOLD THIS

Deliberate self-harm is intentional self-poisoning or self-injury irrespective of intent, so it spans NSSI (no wish to die) and the suicide attempt alike, and any self-harm raises future suicide risk whatever its medical seriousness; **NICE NG225** makes the management a single stance, a compassionate non-judgemental needs-based **psychosocial assessment** for every episode, no risk-stratification score ever used to predict self-harm or to decide who is offered care, a collaborative safety plan with positively framed means restriction, harm minimisation only as a contested adjunct, and active continuity of care, while in India Section 115 of the Mental Healthcare Act 2017 presumes severe stress and owes the person care rather than a charge.

23 · Suicide prevention

This topic asks you to lift the gaze from the single patient to the population: not *how do I assess this person*, but *what actually lowers the suicide rate of a community*. The marks turn on holding one organising frame, the World Health Organization's **WHO LIVE LIFE** guide, and its four evidence-based interventions; on placing each intervention on the right tier of a three-level public-health model; on knowing which single lever carries the strongest evidence; and on stating the Indian frame, the **National Suicide Prevention Strategy** and the decriminalising statute, accurately. Throughout, the register stays compassionate, non-judgemental and free of any method detail, and **means restriction** is framed positively as putting time and distance between a person and a crisis.

How to use this page. Fix the public-health scaffold first (the three tiers and the universal, selective and indicated classification); then load the WHO LIVE LIFE four interventions as the spine; then the highest-yield population lever, means restriction; then the community tier (gatekeeper training, crisis lines and responsible media reporting) and the individual and pharmacological tiers; and finally the Indian national frame. The population and public-health deep dive, including the epidemiology behind these levers, is developed in the Community psychiatry and public health notes; this page is the prevention framework itself. The one idea to carry off the page is that the biggest gains in **suicide prevention** come not from better individual prediction but from population-level action that reduces access to lethal means.

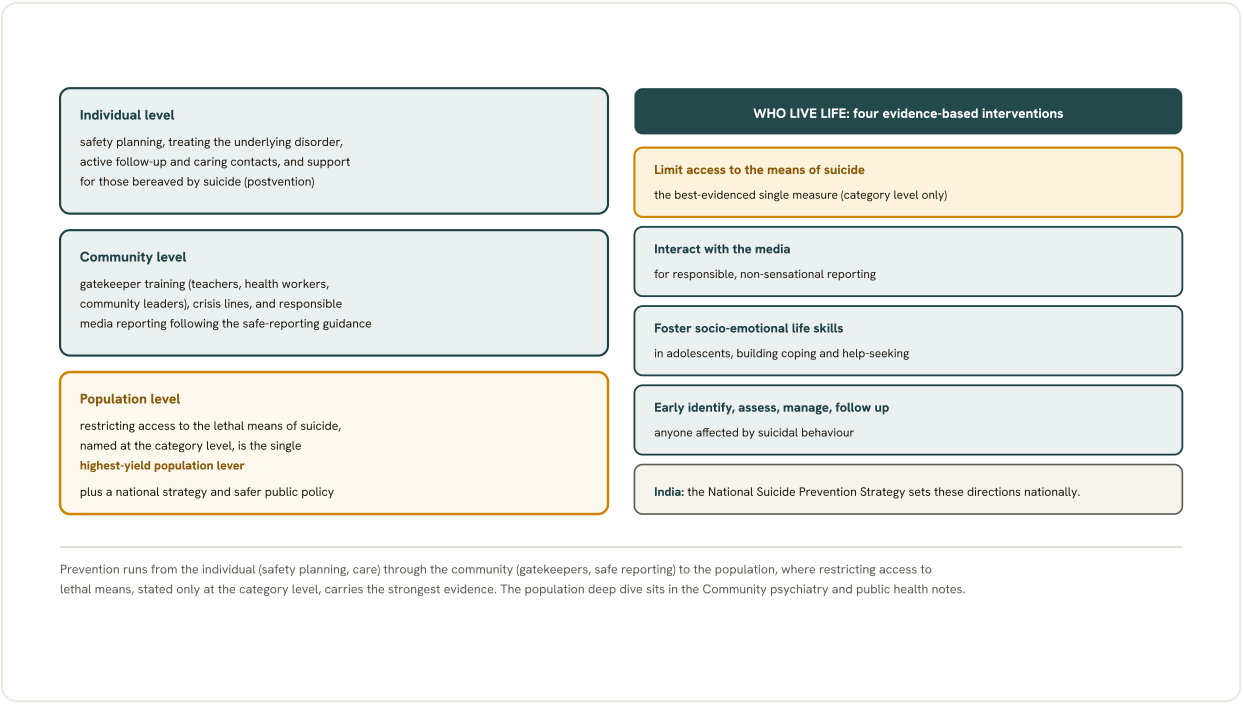


Fig 18.18 Suicide prevention. Prevention works across three levels. At the individual level it is safety planning, treatment of the disorder, active follow-up and caring contacts, and support for those bereaved. At the community level it is gatekeeper training, crisis lines and responsible, non-sensational media reporting. At the population level, restricting access to the lethal means of suicide, named only at the category level, is the single highest-yield lever, alongside a national strategy. The WHO LIVE LIFE framework gathers the four best-evidenced interventions, limiting access to means, engaging the media, fostering socio-emotional life skills in adolescents, and early identification and follow-up, and India expresses these through its National Suicide Prevention Strategy. The wider population and public-health treatment sits in the Community psychiatry and public health notes.

23.1 Prevention as a public-health task: the three tiers

From the clinic to the population. Because individual-level prediction of who will act is poor, prevention is best organised as a public-health task working across three tiers at once (New Oxford Textbook of Psychiatry; Kaplan and Sadock CTP 2024). The **individual tier** works with people already at risk or already affected: structured assessment, collaborative safety planning, follow-up and, above all, treating the underlying illness. The **community tier** works with at-risk groups and settings: gatekeeper training, crisis helplines, school-based life-skills programmes and responsible media reporting. The **population tier** works with everyone: reducing access to lethal means, reducing stigma, and the surveillance and strategy that underpin them. A complementary classification, borrowed from Gordon and used throughout the field, is universal, selective and indicated prevention: universal reaches a whole population regardless of risk (a canonical example is regulating access to hazardous means); selective targets a higher-risk subgroup (adolescents, farming communities); indicated targets identified individuals already showing warning signs. The two schemes map onto each other, and the examiner rewards the candidate who can place any given intervention correctly on the grid.

TIER	WHO IT TARGETS	EXEMPLAR INTERVENTIONS
Individual (indicated)	People already at risk or affected	**Structured assessment, collaborative safety planning, follow-up, treating the underlying disorder**
Community (selective)	At-risk groups and settings	**Gatekeeper training, crisis helplines, school life-skills, responsible media reporting**
Population (universal)	The whole population	**Means restriction (the highest-yield lever), stigma reduction, national strategy and surveillance**

The three-tier public-health model of prevention, aligned with the universal, selective and indicated classification (New Oxford; Kaplan and Sadock CTP 2024).

23.2 The WHO LIVE LIFE frame: four evidence-based interventions

The spine of every prevention answer. The World Health Organization LIVE LIFE implementation guide sets out four evidence-based interventions, and naming all four in order is the reliable way to structure an essay (WHO LIVE LIFE, 2021). They are: **L**imit access to the means of suicide; **I**nteract with the media for responsible reporting of suicide; foster socio-emotional **L**ife skills in adolescents; and **E**arly identify, assess, manage and follow up anyone affected by suicidal thoughts and behaviours. These four are supported by four foundational pillars (situation analysis, multisectoral collaboration, awareness-raising and capacity-building), underpinned in turn by adequate financing, surveillance, and monitoring and evaluation. The frame is deliberately cross-sectoral: it reaches beyond the health system into agriculture, media, education and regulation, which is precisely why it can move a population rate that clinical services alone cannot.

LIVE LIFE INTERVENTION	WHAT IT MEANS	TIER AND EVIDENCE
Limit access to means	Regulation reducing population access to lethal means	**Population; highest-yield, most robustly evidenced**
Interact with the media	Promote responsible, safe reporting; counter contagion	**Community; addresses the Werther effect**
Foster life skills	School-based socio-emotional and coping-skills programmes	**Universal, adolescent-directed**
Early identification and follow-up	Detect, assess, manage and actively follow up those affected	**Individual and clinical; gatekeeper-supported**

The four WHO LIVE LIFE interventions, each mapped to its prevention tier (WHO LIVE LIFE, 2021).

MNEMONIC

LIVE LIFE = LIMIT · INTERACT · LIFE-skills · EARLY

The four WHO interventions in order: **LIMIT** access to the means; **INTERACT** with the media for responsible reporting; foster **LIFE-skills** in adolescents; and **EARLY** identify, assess, manage and follow up. Four interventions on four pillars.

4	10%	1/3	48
WHO LIVE LIFE EVIDENCE-BASED INTERVENTIONS	NATIONAL SUICIDE PREVENTION STRATEGY TARGET REDUCTION IN SUICIDE MORTALITY BY 2030 (INDIA)	WHO GLOBAL TARGET REDUCTION IN THE SUICIDE RATE BY 2030	RANDOMISED TRIALS POOLED IN THE LITHIUM ANTI-SUICIDAL META-ANALYSIS (CIPRIANI, 2013)

GOOD TO REMEMBER

- **WHO LIVE LIFE (the four interventions):** Limit access to the means of suicide; Interact with the media for responsible reporting; foster socio-emotional Life skills in adolescents; Early identify, assess, manage and follow up. The guideline principle is that these four population and community levers, not better individual prediction, produce the largest fall in the suicide rate.

23.3 Means restriction: the single highest-yield lever

The one intervention with the strongest evidence. Of the four, restricting access to the means of suicide is the most robustly evidenced and highest-yield population-level intervention (WHO LIVE LIFE, 2021; New Oxford). It works because many suicidal crises are acute and ambivalent: putting time and distance between a person and a readily available lethal means allows the crisis to pass, and substitution to an equally lethal alternative is often incomplete. Canonical, method-free examples taught at the policy level are the regulation of highly hazardous pesticides in agriculture, limiting the pack sizes of commonly available over-the-counter medicines, and securing recognised structural hotspots with barriers. The accompanying figure sets the three prevention tiers in three levels with means restriction at the population base carrying the greatest population impact, and it is the mental model to reproduce. The full population and public-health case for this lever, with its epidemiological evidence, is developed in the Community psychiatry and public health notes.

RULE **Reducing access to lethal means is the highest-yield lever.** Across the whole toolkit, population-level means restriction has the strongest and most consistent evidence for lowering the suicide rate; it is the intervention to name first when asked what works.

TRAP **The substitution myth.** Assuming that a person prevented from one means will simply and inevitably find another is not borne out by the evidence; because crises are often transient and ambivalent, restricting access reduces deaths rather than merely displacing them.

GOOD TO REMEMBER

- **Means restriction (the guideline principle):** reducing population access to lethal means is the single highest-yield, most robustly evidenced suicide-prevention intervention (WHO LIVE LIFE, 2021). It is framed positively, as putting time and distance between a person and a crisis, and it acts at the population tier where clinical services cannot reach.

23.4 The community tier: gatekeeper training, crisis lines and responsible media

Widening the net beyond the clinic. The community tier equips non-specialists and shapes the information environment. Gatekeeper training equips frontline non-specialists (teachers, primary-care staff, community and religious leaders, helpline volunteers) to recognise warning signs and refer people at risk; it reliably improves skills and is highly acceptable in schools and workplaces, though a direct effect on completed suicide is harder to demonstrate and it works best as one component of a layered programme (Savita Malhotra; Dulcan). Crisis helplines and telephone or text lines provide accessible, immediate support at the point of distress. Responsible media reporting follows established safe-reporting guidance: avoid prominent or repetitive coverage, omit method and location detail, avoid framing suicide as a solution or romanticising it, and instead signpost help. This matters because sensational reporting can drive imitation, the Werther effect of copycat suicide, whereas coverage that models coping and recovery can be protective, the Papageno effect (New Oxford; Shorter Oxford). The acute triage of a person in active crisis who reaches these services belongs to the emergency psychiatry chapter.

PEARL

Hold the two named media effects as a mirror pair: the **Werther effect** is harm from irresponsible, sensational reporting (imitation and contagion); the **Papageno effect** is protection from responsible reporting that models coping and help-seeking. Responsible media reporting is the deliberate move from Werther toward Papageno.

GOOD TO REMEMBER

- **Gatekeeper training (the guideline role):** train non-specialists to identify and refer people at risk; it improves recognition and is highly acceptable, and it supports the early-identification intervention of WHO LIVE LIFE, but is delivered as part of a layered programme rather than as a stand-alone guarantee of reduced deaths.
- **Responsible media reporting (the guideline principle):** follow safe-reporting guidance (no method or location detail, no sensationalising or romanticising, signpost help); it shifts the population effect of coverage from the harmful Werther effect toward the protective Papageno effect.

23.5 The individual tier and the pharmacological prevention levers

Care, safety planning and the disorder-specific drugs that lower risk. At the individual tier, prevention means the early identification, assessment, management and active follow-up of people affected, with a collaboratively built safety plan (the Stanley-Brown Safety Planning Intervention components: warning signs, internal coping strategies, social contacts, people and professionals to call, and making the environment safer by restricting access to means) and rapid follow-up after any crisis contact, since transitions between services are a period of raised risk.

Two drugs carry a specific, evidence-based anti-suicidal effect and so act as pharmacological prevention levers. Lithium reduces the risk of suicide in people with mood disorders, a signal at least partly distinct from control of the mood episode itself, shown in the meta-analysis by Cipriani and colleagues pooling **48** randomised trials (BMJ, 2013); its full pharmacology is in the Mood disorders: pharmacotherapy notes. Clozapine is the only antipsychotic with a specific anti-suicidal indication, established by the International Suicide Prevention Trial in schizophrenia and schizoaffective disorder at high risk (InterSePT; Meltzer, 2003); its full pharmacology is in the Schizophrenia: management, antipsychotics and adverse effects notes. Treating the underlying disorder, and choosing an agent with an anti-suicidal signal where one exists, is itself prevention.

GOOD TO REMEMBER

- **Lithium (the guideline evidence):** favour lithium in a mood disorder carrying suicide risk; it reduces suicide and all-cause mortality versus placebo across 48 pooled randomised trials (Cipriani, BMJ 2013), an anti-suicidal effect at least partly independent of mood control.
- **Clozapine (the guideline indication):** clozapine is the only antipsychotic with a specific indication for reducing recurrent suicidal behaviour, in schizophrenia and schizoaffective disorder, established by the InterSePT trial (Meltzer, 2003).

23.6 The Indian national frame: strategy and statute

A first national strategy and a decriminalised act. India's prevention frame has two pillars the examiner expects. The first is the National Suicide Prevention Strategy, announced by the Ministry of Health and Family Welfare in 2022 as the country's first such strategy, with the stated goal of reducing suicide mortality by **10%** by 2030 against a 2019 baseline (a modest target beside the WHO Comprehensive Mental Health Action Plan aim of a **one-third** reduction in the suicide rate by 2030). Its actions are staged as immediate (within 1 to 3 years: advocacy for responsible media reporting, reducing access to a commonly used agrarian means through pesticide regulation, and strengthening surveillance and the mental-health workforce), intermediate (within 4 to 7 years: integrating mental health into general health care, training helpline workers, and reducing workplace stressors) and long term (within 8 to 10 years: destigmatisation, safer agricultural alternatives, and embedding well-being in education). The second pillar is the statute: under Section 115 of the Mental Healthcare Act, 2017, a person who attempts suicide is presumed, unless proved otherwise, to be under severe stress, and shall not be tried or punished, which effectively overrides the old offence at Section 309 of the Indian Penal Code, and the government carries a duty to provide care and rehabilitation. The Indian Psychiatric Society has supported this reframing of an attempt as a signal of distress and a call for help rather than a crime.

INDIA

Three moves win the Indian answer. Name the National Suicide Prevention Strategy (Ministry of Health and Family Welfare, 2022; the first national strategy) with its headline goal, a 10% reduction in suicide mortality by 2030. Quote Section 115 of the Mental Healthcare Act, 2017 precisely: attempted suicide is presumed to arise from severe stress and is not punished, overriding Section 309 of the Indian Penal Code, with a state duty of care. And weave in the two Indian dimensions the strategy targets, the agrarian sector (means regulation and safer farming) and students and adolescents (well-being curricula and life skills), consistent with the WHO LIVE LIFE emphasis on cross-sectoral action.

GOOD TO REMEMBER

- **National Suicide Prevention Strategy (the policy anchor):** India's first national strategy (Ministry of Health and Family Welfare, 2022); goal is a 10% reduction in suicide mortality by 2030 against a 2019 baseline, staged across immediate, intermediate and long-term actions spanning health, agriculture, media and education.
- **Section 115, Mental Healthcare Act, 2017 (the statute):** any person who attempts suicide is presumed, unless proved otherwise, to have severe stress and shall not be tried or punished (overriding Section 309 of the Indian Penal Code); the state must provide care, treatment and rehabilitation. The first response to an attempt is compassionate care, not sanction.

HOLD THIS

Prevention works in tiers (individual, community, population); the WHO LIVE LIFE guide gives the four evidence-based interventions (Limit access to means, Interact with the media for responsible reporting, foster Life skills, Early identify and follow up); of these, means restriction is the single highest-yield population lever; and the Indian frame is the National Suicide Prevention Strategy (2022, a 10% reduction goal by 2030) sitting on Section 115 of the Mental Healthcare Act, 2017, which decriminalises the attempt and mandates care.

24 · The neurobiology of suicidal behaviour

This is a short, high-yield topic that supplies the biological half of the picture built elsewhere in the chapter: it names the substrate of the enduring vulnerability, the **diathesis**, on which an acute stressor acts. Kaplan frames the **neurobiology of suicide** around a small number of recurring findings, and the examinable ones are three: a reduced central **serotonergic** function (indexed classically by low cerebrospinal-fluid 5-HIAA and tied to impulsive-aggressive and suicidal behaviour), a dysregulated stress axis (the **HPA axis**), and a set of emerging polyamine and inflammatory signals. The thread that binds them is the stress-diathesis (stress-vulnerability) model: these are trait-level, largely cross-diagnostic vulnerability markers, not tests that predict who will act (Kaplan and Sadock CTP 2024; New Oxford Textbook of Psychiatry).

How to use this page. Learn the serotonergic finding first, because it is the single most consistent and most examined; then the HPA-axis stress-response finding and what post-mortem study adds; then the newer polyamine and inflammatory signals and how the whole set constitutes the biological diathesis. The one idea to carry off the page is that these markers describe an enduring vulnerability and have limited value for predicting an individual, so the clinical task remains the

compassionate, structured assessment, and the tone throughout stays safeguarding and non-sensational.

24.1 Reduced central serotonergic function

The most consistent biological finding in the field. A decreased, dysregulated central serotonergic system in people who die by suicide and in those who attempt it, seen regardless of the psychiatric diagnosis, is a very strong correlate of suicidal behaviour and is described as one of the most consistent neurobiologic findings in psychiatry (Kaplan and Sadock CTP 2024). The classic in-vivo marker is a low concentration of the main serotonin metabolite, 5-HIAA (5-hydroxyindoleacetic acid), in the cerebrospinal fluid; central serotonergic function is also probed by the neuroendocrine fenfluramine challenge test and by PET of prefrontal metabolism (Tasman Psychiatry). Crucially, decreased central serotonin metabolism maps more tightly onto trait impulsive-aggression than onto any specific disorder: low CSF 5-HIAA is associated with impulsive, aggressive behaviour and with more medically serious, determined attempts, so it behaves as a trait vulnerability that raises the likelihood of an act when an acute episode and adverse circumstances coincide (Kaplan and Sadock CTP 2024).

MARKER OR METHOD	WHAT IT INDEXES	THE POINT TO HOLD
CSF 5-HIAA	The principal serotonin metabolite in cerebrospinal fluid	**Low CSF 5-HIAA marks reduced central serotonergic function and tracks impulsive-aggression**
Fenfluramine challenge	Prolactin response to a serotonin-releasing probe	**A blunted response signals reduced serotonergic responsiveness**
PET of prefrontal metabolism	In-vivo prefrontal serotonergic and metabolic activity	**Reduced prefrontal serotonergic and metabolic response**
Post-mortem 5-HT2A binding	Receptor-level change in the prefrontal cortex	**Altered 5-HT2A binding in the prefrontal cortex of those who died by suicide**

The measures of central serotonergic function used to demonstrate the core neurobiological finding; these findings form the diathesis axis of the stress-diathesis model (Tasman Psychiatry; Kaplan and Sadock CTP 2024).

RULE **Serotonergic hypofunction is the trait signal, not a diagnostic one.** Reduced central serotonergic function, indexed by low CSF 5-HIAA, is the most consistent biological correlate of suicidal behaviour and is cross-diagnostic, binding to impulsive-aggressive traits rather than to any single disorder.

GOOD TO REMEMBER

- **Reduced central serotonergic function (the core finding):** a decreased, dysregulated serotonergic system, marked by low CSF 5-HIAA and probed by the fenfluramine challenge and prefrontal PET, is one of the most consistent neurobiologic findings and correlates with suicidal behaviour irrespective of diagnosis. The discriminator to hold is that it is a trait-level marker tied to impulsive-aggression, more so than to any specific psychiatric disorder.

24.2 HPA-axis dysregulation: the stress response

The stress-response pathway that links life adversity to biology. The most studied pathway after the serotonergic one is the stress-response pathway mediated by the HPA axis (hypothalamic-pituitary-adrenal axis); disruption of this axis with altered glucocorticoid activity may increase the risk for suicidal behaviour (Kaplan and Sadock CTP 2024). The robust, exam-ready form of the finding is that HPA-axis hyperactivity, reflected in an abnormal dexamethasone suppression test (that is, non-suppression of cortisol), is a robust predictor of future completed suicide, primarily among patients in a major depressive episode. Post-mortem brain study of people who died by suicide adds the anatomy and the downstream chemistry: significant alterations in the prefrontal cortex and hippocampus (regions of emotion regulation and executive function), altered 5-HT2A binding, decreased BDNF (brain-derived neurotrophic factor, a neuroprotective signal), and dysregulated glutamatergic and GABA signalling. Taken together, the HPA-axis and neuroplasticity findings show how an enduring stress-response vulnerability is written into the brain.

TRAP **Reading a biomarker as a clinical predictor for the individual.** An abnormal dexamethasone suppression test or a low CSF 5-HIAA describes group-level risk and enduring vulnerability; these findings have limited practical value in the individual case, so the clinical decision still rests on the structured risk-and-protective assessment, never on a biological test.

GOOD TO REMEMBER

- **HPA-axis dysregulation (the stress-axis finding):** hyperactivity of the HPA axis, shown as cortisol non-suppression on the dexamethasone suppression test, is a robust predictor of future completed suicide, primarily in mood disorder; post-mortem study adds prefrontal and hippocampal change, altered 5-HT2A binding and reduced BDNF. The discriminator is that it is a stress-response vulnerability marker, robust at the group level yet of limited use for predicting an individual.

24.3 Polyamine and inflammatory signals, and the diathesis synthesis

The newer signals, and how the biology assembles into a diathesis. Beyond serotonin and cortisol, two emerging areas complete the compact picture. Changes in the polyamine system are reported alongside the serotonergic and HPA-axis changes as candidate substrates that make some individuals more vulnerable to suicidal behaviour (New Oxford Textbook of Psychiatry). Separately, a growing literature links inflammation, depression and suicide, drawing attention to neuroinflammation and the microbiome, and GABAergic signalling is a further active area (Kaplan and Sadock CTP 2024). Overlaying all of these, epigenetic mechanisms are the bridge from experience to biology: childhood adversity can alter, through DNA methylation and histone modification, the genes governing neurotrophic signalling and neurotransmission, and this is how early environment loads the diathesis. Assembled, the serotonergic hypofunction, the dysregulated HPA axis and these newer signals are precisely what the stress-diathesis (stress-vulnerability) model calls the diathesis: an enduring, partly heritable, partly experience-shaped trait vulnerability on which an acute stressor acts to produce an act (Kaplan and Sadock CTP 2024). Where a driving disorder is present, its treatment is itself anti-suicidal, and two agents

carry specific evidence whose pharmacology sits elsewhere: lithium in mood disorders, in the Mood disorders: pharmacotherapy notes, and clozapine in schizophrenia, in the Schizophrenia: management, antipsychotics and adverse effects notes.

INDIA

The biology gives a compassionate reading of the Indian statute. Because a suicidal act needs an enduring diathesis for an acute stressor to act upon, "severe stress" is a signal of suffering rather than of choice, which is exactly the presumption written into Section 115 of the Mental Healthcare Act 2017: a person who attempts suicide is presumed, unless proved otherwise, to be under severe stress and is not to be punished, and the state owes them care. The neurobiology and the law point the same way, toward assessment and care, not blame.

2	3	5-HT2A
STRESS-DIATHESIS COMPONENTS: AN ACUTE STRESSOR ACTING ON AN ENDURING DIATHESIS	CORE SYSTEMS STUDIED: SEROTONERGIC, HPA AXIS, NEUROPLASTICITY	THE SEROTONIN RECEPTOR ALTERED IN THE PREFRONTAL CORTEX POST-MORTEM

HOLD THIS

The neurobiology of suicidal behaviour is the biological **diathesis** of the stress-diathesis model: a reduced central **serotonergic** function (low CSF **5-HIAA**, tied to impulsive-aggression and cross-diagnostic, the single most consistent finding) plus a dysregulated **HPA axis** (cortisol non-suppression on the dexamethasone suppression test predicting completed suicide in mood disorder), with newer polyamine, inflammatory and epigenetic signals, all describing an enduring trait vulnerability that has limited value for predicting the individual, so care rests on the structured assessment, not a biological test.

25 · Anti-suicidal pharmacology

Why this topic sits apart. Almost every effective psychiatric drug lowers suicide risk indirectly, by lifting the depression, settling the mania or quietening the psychosis that drove the risk. The examinable heart of **anti-suicidal pharmacology** is narrower and sharper: two agents, and only two, carry a specific, trial-level anti-suicidal effect that is at least partly *distinct* from their control of the mood episode or the psychosis, and each maps to a single disorder group. Lithium reduces suicide and self-harm in mood disorders (Cipriani 2013 BMJ), and clozapine reduces recurrent suicidal behaviour in schizophrenia and schizoaffective disorder (InterSePT, Meltzer 2003, and an FDA indication). A third strand, ketamine and esketamine, is the emerging rapid option for suicidal ideation. The topic then closes on post-attempt management, the ordered clinical response after an act.



Fig 18.19 Anti-suicidal care is layered: establish immediate safety, make a collaborative safety plan, treat the underlying syndrome, reduce access to lethal means, mobilise support, ensure rapid follow-up and use evidence-based medication or somatic treatments when indicated.

How to use this page. Hold the set as two "specific-signal" drugs plus one "emerging" drug, then the ordered post-attempt sequence. For each drug learn three things: the disorder it applies to, the trial or evidence that anchors it, and the one line that names its status (a class effect for lithium, the only antipsychotic so indicated for clozapine). The deep pharmacology, the doses, serum levels and monitoring, lives in the mood-disorder and schizophrenia chapters and is cross-referenced here; this page is about the anti-suicidal *effect* and its evidence. Safe-messaging holds throughout: the discussion stays at the level of risk, evidence and care, never method.

25.1 Two specific signals against a disorder-directed background

Treating the disorder is itself anti-suicidal; two drugs add more. The default and most important principle is that reducing suicide risk pharmacologically means treating the underlying disorder effectively, because an untreated mood episode or active psychosis is itself the main driver of risk (Kaplan and Sadock CTP 2024). The examinable exception is that two agents carry a dedicated anti-suicidal effect that sits over and above symptom control and is tied

to one disorder group each: lithium in mood disorders and clozapine in schizophrenia and schizoaffective disorder. A third, newer strand, ketamine and esketamine, gives a rapid but short-term effect on suicidal ideation rather than on completed suicide. These two specific signals stand against the disorder-directed background so the exception is not mistaken for the rule.

AGENT	DISORDER GROUP	ANCHORING EVIDENCE	STATUS TO STATE
Lithium	Mood disorders (unipolar and bipolar)	Cipriani 2013 BMJ meta-analysis, 48 RCTs	**A class effect specific to lithium, not shared by other mood stabilisers; reduces suicide and death from any cause**
Clozapine	Schizophrenia and schizoaffective disorder	InterSePT (Meltzer 2003), 2-year RCT versus olanzapine	**The only antipsychotic with an anti-suicidal FDA indication; reduces recurrent suicidal behaviour**
Ketamine and esketamine	Major depression with acute suicidal ideation	ASPIRE programme (esketamine)	**Emerging adjunct; rapid, short-term fall in ideation, no proven effect on completed suicide**

The examinable core of anti-suicidal pharmacology: two specific signals plus one emerging option, each read as disorder, evidence, and status (Cipriani 2013 BMJ; InterSePT, Meltzer 2003; ASPIRE).

RULE **Only two agents carry a specific anti-suicidal signal.** Beyond treating the disorder, only lithium (in mood disorders) and clozapine (in schizophrenia and schizoaffective disorder) have a dedicated, trial-level anti-suicidal effect; for each, name the trial and the status.

TRAP **Assuming the benefit is class-wide.** Lithium's anti-suicidal effect is not reproduced by valproate, lamotrigine or carbamazepine, and clozapine's is not reproduced by other antipsychotics; InterSePT's comparator olanzapine is an effective drug yet was inferior, so do not assume any mood stabiliser or any antipsychotic delivers the same protection.

25.2 Lithium: the anti-suicidal effect in mood disorders

Lithium lowers suicide in mood disorders, and it behaves as a class-specific property. The lithium anti-suicidal effect is the best-established in the field. The meta-analysis by Cipriani and colleagues (BMJ 2013;346:f3646) pooled 48 randomised controlled trials and found that lithium reduced the risk of suicide and the risk of death from any cause compared with placebo, across unipolar and bipolar mood disorders (Cipriani 2013 BMJ). Two points make it examinable. First, the anti-suicidal signal is at least partly *distinct* from control of the mood episode itself, so it is a reason to favour lithium specifically when a mood disorder carries suicide risk, not merely a by-product of better mood control. Second, it looks like a **class effect of lithium**, seen with lithium and not clearly shared by the other mood stabilisers, which is why the choice of the mood stabiliser can matter for risk. The proposed substrate is a dampening of impulsive aggression, consistent with the serotonergic diathesis of suicidal behaviour, but the effect is claimed on the

outcome evidence, not on a mechanism. The deep pharmacology, the therapeutic range, monitoring and toxicity, belongs to the Mood disorders: pharmacotherapy notes; here the point is the effect and the trial that anchors it.

PEARL

The word to hold is *distinct*. If lithium only prevented suicide by preventing relapse, any equally good mood stabiliser would match it, but they do not. The anti-suicidal effect tracks lithium specifically and is partly separable from episode control, which is exactly why it changes the prescribing calculus in a mood disorder with suicide risk rather than being a footnote to relapse prevention.

GOOD TO REMEMBER

- **Lithium anti-suicidal effect (evidence-anchored, Cipriani 2013 BMJ):** lithium reduces the risk of suicide and of death from any cause in mood disorders, pooled across 48 randomised controlled trials; the effect is at least partly distinct from mood-episode control and is a class effect specific to lithium, not shared by the other mood stabilisers, so it favours lithium where a mood disorder carries suicide risk. Deep pharmacology in the Mood disorders: pharmacotherapy notes.

25.3 Clozapine: recurrent suicidal behaviour in schizophrenia

Clozapine reduces recurrent suicidal behaviour in schizophrenia, and it is the only antipsychotic licensed for it. The clozapine persistent suicidality data come from the International Suicide Prevention Trial (InterSePT; Meltzer et al, Archives of General Psychiatry 2003;60:82-91). It was a double-blind randomised comparison that enrolled roughly 980 patients with schizophrenia or schizoaffective disorder judged to be at high suicide risk, assigned them to clozapine or to olanzapine, and followed them for up to 2 years. Clozapine was superior in delaying recurrent suicidal behaviour, with fewer clozapine-treated patients requiring hospitalisation or rescue intervention to prevent suicide (InterSePT, Meltzer 2003). This underpins the FDA-approved indication for reducing the risk of recurrent suicidal behaviour in schizophrenia and schizoaffective disorder, the only antipsychotic to hold such an indication. As with lithium, the effect appears partly distinct from control of the positive symptoms, so a persistent suicide risk in schizophrenia is itself a recognised reason to move to clozapine. The deep pharmacology, the titration and the mandatory haematological monitoring, belongs to the Schizophrenia: management, antipsychotics and adverse effects notes.

GOOD TO REMEMBER

- **Clozapine persistent suicidality (guideline-anchored, InterSePT, Meltzer 2003, and the FDA indication):** clozapine reduces recurrent suicidal behaviour in schizophrenia and schizoaffective disorder, shown in the InterSePT 2-year randomised trial where it outperformed olanzapine, and it is the only antipsychotic FDA-indicated for reducing suicide risk. Persistent suicidality in schizophrenia is a recognised reason to move to clozapine; deep pharmacology and monitoring in the Schizophrenia: management, antipsychotics and adverse effects notes.

25.4 Ketamine and esketamine: the emerging rapid option

A rapid, short-term effect on suicidal ideation, not a proven effect on completed suicide. Ketamine and intranasal esketamine (Spravato) produce rapid, short-lived reductions in suicidal ideation, often within hours, which is what makes them of interest when ideation is acute (Kaplan and Sadock CTP 2024; Maudsley Prescribing Guidelines). Esketamine has been studied specifically in major depressive disorder with acute suicidal ideation or behaviour (the ASPIRE programme). The honest reading of the evidence is that it supports a rapid effect on *ideation*, as an adjunct within comprehensive care, whereas a reduction in completed suicide has not been established. So it functions as a bridge, buying time while definitive treatment and safety planning take hold, and never as a stand-alone answer to risk.

GOOD TO REMEMBER

- **Ketamine and esketamine (guideline-anchored, ASPIRE programme):** a rapid, short-term reduction in suicidal ideation, studied for esketamine in major depression with acute suicidal ideation or behaviour; it is an adjunct within comprehensive care that buys time, not a proven reducer of completed suicide and not a stand-alone treatment.

25.5 Post-attempt management: the ordered response

An ordered sequence, not a single drug. Post-attempt management is the structured response after an act, and it is examined as a sequence. First comes medical stabilisation of the physical consequences to medical fitness; only then, once the person is medically fit, a compassionate, non-judgemental psychosocial assessment of needs, context and safety, which every episode warrants regardless of the apparent medical seriousness of the act (NICE NG225 2022). This feeds a collaborative safety plan with means-restriction counselling framed positively, and, running underneath all of it, treatment of the underlying disorder, which is the main pharmacological lever against future risk and where the two specific agents above may enter. A recurring pitfall the guideline names is using a risk-stratification score to decide who is offered care; risk is assessed to guide a needs-based, collaborative response, not to ration it. The acute triage of the actively suicidal patient in crisis is covered in the emergency psychiatry chapter, and the population-level, public-health side of prevention in the Community psychiatry and public health notes.

STEP	THE ACTION	THE PRINCIPLE
Medical stabilisation	Treat the physical consequences of the act to medical fitness first	**Life and physical safety precede any psychiatric disposition**
Psychosocial assessment	Compassionate, non-judgemental assessment of needs, context and safety, every episode	**Needs-based, never a risk score (NICE NG225 2022)**
Safety plan and means counselling	Build a collaborative safety plan; counsel on reducing access to lethal means	**Means restriction is the highest-yield step, framed positively**
Treat the underlying disorder	Optimise treatment of the driving disorder; consider lithium or clozapine where indicated	**Effective disorder treatment is itself anti-suicidal**

The post-attempt management sequence, medical stabilisation then needs-based psychosocial assessment, safety planning and disorder treatment, with those post-attempt steps set in order (NICE NG225 2022).

INDIA

The statute frames post-attempt management compassionately. Under Section 115 of the Mental Healthcare Act, 2017, a person who attempts suicide is presumed, unless proved otherwise, to be under severe stress, and is not to be tried or punished, with a duty on the government to provide care, treatment and rehabilitation to reduce the risk of recurrence (Mental Healthcare Act 2017, Section 115). The clinical sequence and the law point the same way, toward assessment and care rather than blame. Both specific agents are available and used in India: lithium is inexpensive and widely prescribed, and clozapine is available with the mandatory haematological monitoring, so the anti-suicidal evidence is directly actionable here. The Indian Psychiatric Society position aligns with this care-first, means-restriction framing.

GOOD TO REMEMBER

- **Post-attempt management (guideline-anchored, NICE NG225 2022):** an ordered response, medical stabilisation of the physical consequences first, then a compassionate, non-judgemental psychosocial assessment of needs and safety in every episode, a collaborative safety plan with positively framed means-restriction counselling, and treatment of the underlying disorder, which is itself the main anti-suicidal lever. A risk-stratification score must never decide who is offered care. Acute crisis triage is in the emergency psychiatry chapter.

48	2	1
RANDOMISED TRIALS POOLED IN THE CIPRIANI LITHIUM META-ANALYSIS	INTERSEPT FOLLOW-UP (YEARS)	ANTIPSYCHOTIC WITH AN ANTI-SUICIDAL INDICATION (CLOZAPINE)

HOLD THIS

Beyond treating the disorder, only two drugs carry a specific anti-suicidal effect: **lithium** reduces suicide and all-cause death in mood disorders (Cipriani 2013 BMJ, 48 RCTs; a class effect specific to lithium) and **clozapine** reduces recurrent suicidal behaviour in schizophrenia and schizoaffective disorder (InterSePT, Meltzer 2003; the only antipsychotic so FDA-indicated); ketamine and esketamine cut ideation rapidly but not completed suicide; and post-attempt management runs medical stabilisation, then a needs-based psychosocial assessment and positively framed safety plan, then treatment of the underlying disorder.

Apply and consolidate

26 · Worked cases

This is the topic on which the whole chapter is *closed*, the point where the four rooms of the master mnemonic, the body that complains, the body that desires, the urge that acts and the life that must be protected, are walked through as reasoning rather than recited as fact. Everything before this page taught entities in isolation; here five **worked examples** put them back into the clinic, because the examiner rarely asks "define" and almost always asks "here is a patient, place them and defend the next step". A vignette is marked on two moves, the discrimination that names the frame and the guideline-anchored step that follows from it, so each case below is reasoned through both.

How to use this page. Read each case as a two-part act: first the diagnostic or discrimination reasoning that fixes the frame, then the management or safety step that the frame demands, with the cardinal error the case is built to catch called out in the open. The order tracks the arc, a somatic-symptom work-up, then the produced-symptom discrimination, then an erectile-dysfunction management case, then a gender-incongruence affirmative-care case, and finally a suicide-risk-assessment-and-safety-planning case, the last written under strict safe-messaging, with no method detail anywhere and a compassionate, safeguarding register throughout.

26.1 A somatic-symptom-disorder work-up

case: a woman in her late thirties has attended gastroenterology, cardiology and general medicine repeatedly over roughly eight months with abdominal pain, palpitations and fatigue; the investigations have been normal each time, yet she spends hours reading about serious illness, checks her pulse many times a day, has cut back her work, and cannot be settled by a normal review. She arrives at psychiatry surprised to be referred, insisting the trouble is physical.

The reasoning. Place her against the three DSM-5-TR criteria for somatic symptom disorder (DSM-5-TR 2022). Criterion A is met, there are distressing, disrupting somatic symptoms. Criterion C is met, the symptomatic state has persisted well beyond six months. The load-bearing move is Criterion B, the **positive psychological criterion**: her disproportionate and persistent thoughts about seriousness, her high health anxiety, and the excessive time and behaviour devoted to symptoms are all present, and any one of the three would suffice. The diagnosis is therefore secured by what she does and feels about the symptoms, not by the symptoms being

unexplained; even were an explanatory condition later found, the excessive response would still qualify her. Grade the burden with the PHQ-15 (fifteen items, each scored 0 to 2, a total out of a possible 30) and read Criterion B directly with the SSD-12 (a total out of a possible 48); the totals run out of a possible 48.

RULE **Diagnose on the positive criterion, not on a normal work-up.** Somatic symptom disorder is established by the excessive thoughts, feelings and behaviours of Criterion B alongside a distressing somatic symptom; whether the symptom is medically explained does not decide it.

WORKED EXAMPLE

The wrong turn is a fresh battery of tests to "reassure" her, which teaches the body to keep speaking. The right first move is physician-centred: a single named clinician, brief scheduled visits at a fixed interval rather than symptom-triggered ones, explicit validation that the symptoms and the distress are real, restriction of unnecessary investigation and referral, early treatment of any comorbid depression or anxiety, and a steady shift of the conversation from symptoms toward functioning. Cognitive behaviour therapy is the first-line psychotherapy, targeting the catastrophic reading of bodily sensations (IPS_CPG 2020). Drugs are not started for the somatic symptoms themselves.

GOOD TO REMEMBER

- **Somatic symptom disorder (the diagnosis):** Criterion A, distressing somatic symptoms; Criterion B, excessive thoughts, feelings or behaviours about them (the positive psychological criterion); Criterion C, a persistent symptomatic state beyond six months. The single discriminator is that Criterion B, not the absence of a medical explanation, defines it.
- **Physician-centred care (the management step):** the guideline first-line (IPS_CPG 2020), being a therapeutic alliance, validation of real symptoms, restriction of unnecessary tests and referrals, early treatment of comorbid mood or anxiety, and a shift toward functioning; the first move is the alliance, and antidepressants are not prescribed for medically unexplained somatic symptoms unless a specialist advises (WHO mhGAP 2016), reserved instead for a comorbid depressive or anxiety disorder or a dominant chronic-pain component.

If a conversion element sat within her presentation its bedside positive signs and management would be worked in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes; the consultation-liaison service model that most often meets such patients, and the transcultural reading of a Dhat-type presentation through a cultural formulation, are developed in the Consultation-liaison, geriatric and transcultural psychiatry notes.

26.2 A somatic-versus-factitious-versus-malingering discrimination

case: a man is referred with recurrent, dramatic and shifting symptoms that never quite match the objective findings, and the team is split on whether he is genuinely unwell, making himself unwell, or putting it on for a reason. The whole discrimination reduces to two questions asked in order: is the symptom *produced*, and if so, *why*.

The reasoning. The first question separates the genuine somatic disorders, whose symptoms are not intentionally produced, from the two feigned conditions, where they are. The second

question then splits the feigned pair on the incentive. If this man carries a pending compensation or medicolegal claim, shows disability far exceeding the objective findings, and is poorly cooperative with assessment and treatment, an **external incentive** is present and the frame is malingering, coded Z76.5 as a condition for clinical attention and expressly not a mental disorder; DSM-5-TR says it is *strongly suspected*, never confirmed, on any combination of its four pointers (DSM-5-TR 2022). If instead he consciously falsifies or induces signs, seeks procedures and admissions, and no external reward is in view, so that the motive is simply to occupy the sick role, the frame is factitious disorder imposed on self (F68.10), whose Criterion C is precisely that the deception persists in the absence of obvious external rewards. Voluntariness of production is shared by both feigned conditions and so cannot tell them apart; only the external incentive can.

THE PRESENTATION	SYMPTOM INTENTIONALLY PRODUCED?	EXTERNAL INCENTIVE
Genuine somatic symptom disorder	No, not intentionally produced	**Absent; the distress is real and the response excessive**
Factitious disorder (F68.10)	Yes, consciously feigned	**Absent; the motive is the sick role (primary gain)**
Malingering (Z76.5)	Yes, consciously feigned	**Present; a tangible reward or an avoided obligation (secondary gain)**

The voluntariness-by-incentive grid applied to the case; production separates the genuine disorder from the two feigned conditions, and the external incentive separates malingering from factitious disorder (New Oxford Textbook of Psychiatry; DSM-5-TR 2022).

TRAP **Confusing factitious disorder with malingering.** Both are consciously feigned, so they feel alike; the difference is the external incentive, present in malingering, absent in factitious disorder. Reading a compensation claimant as factitious, or a sick-role patient as a malingerer, inverts the whole grid.

GOOD TO REMEMBER

- **The discriminator (the criterion anchor):** ask production first, then motivation. Genuine somatic disorders are not intentionally produced; of the two feigned conditions, factitious disorder has no external incentive (the sick role, primary gain, Criterion C) and malingering has one (secondary gain, coded Z76.5, strongly suspected on the four DSM-5-TR pointers, not a disorder). The single external-incentive axis carries the differentiation, and the register stays medical and non-accusatory, documenting inconsistency rather than branding dishonesty.

26.3 An erectile-dysfunction management case

case: a man in his early fifties with type 2 diabetes and hypertension reports gradually worsening difficulty attaining and maintaining an erection across all contexts, including reduced early-morning erections, for the past several months, and is distressed by it. He asks for "the tablet".

The reasoning. The history sorts aetiology before any test: an insidious onset with erections deficient in every context, nocturnal and masturbatory included, points to organic, most likely vasculogenic, erectile dysfunction rather than a psychogenic pattern (Kaplan and Sadock CTP 2024). Two consequences follow. First, in a man with vascular risk factors the complaint is a

cardiovascular sentinel, the small penile arteries narrowing before the coronaries, so he needs a proper cardiovascular risk assessment, blood pressure, fasting glucose or HbA1c and lipids, and not a prescription alone. Second, measure a morning total testosterone and confirm any low result on a repeat before calling it hypogonadism. Grade severity with the five-item IIEF-5: the total runs from 5 to 25, read as no erectile dysfunction (22 to 25), mild (17 to 21), mild to moderate (12 to 16), moderate (8 to 11) and severe (5 to 7), out of a possible 25; the bands run out of a possible 25.

The management. First-line for a man without a contraindication is an oral PDE5 inhibitor plus lifestyle and risk-factor optimisation (EAU male sexual dysfunction; AUA 2018). All the oral agents are similarly effective, so choice turns on how he wants to use them: sildenafil (Manforce, Penegra) is the high-efficacy pick, taken on-demand about one hour before, starting at **50 mg**; tadalafil (Tadacip, Megalis) is the tolerability pick with the longest window, on-demand from **10 mg** or a once-daily **5 mg** that decouples dosing from sex. Before any prescription, screen specifically for nitrate use, because any organic nitrate, nitric oxide donor, nicorandil or recreational nitrite with any PDE5 inhibitor is an absolute contraindication (cyclic-GMP accumulation and profound hypotension); alpha-blockers are a caution only. If oral therapy fails or is contraindicated, second-line is intracavernosal alprostadil or a vacuum device, and third-line a penile prosthesis. Where an antidepressant or antipsychotic is contributing, that reversible cause is addressed as in the Mood disorders: pharmacotherapy notes and the Schizophrenia: management, antipsychotics and adverse effects notes.

ORAL PDE5 INHIBITOR	ON-DEMAND START (MG)	THE POINT TO HOLD
Sildenafil (Manforce, Penegra)	50	**High-efficacy pick; onset 30 to 60 min, window up to 12 h; a high-fat meal delays absorption**
Tadalafil (Tadacip, Megalis)	10 on-demand, or 5 once daily	**Longest window, up to 36 h; the only agent also licensed for erectile dysfunction with benign prostatic hyperplasia, at 5 mg once daily**
Vardenafil	10	**Orally disintegrating form available**
Avanafil	100	**Fastest onset; taken 15 to 30 min before**

The first-line oral PDE5 inhibitors, all similarly effective, with the verified EAU and AUA 2018 starting doses; units are carried in the header (EAU male sexual dysfunction; AUA 2018).

The trap to close. Because he has diabetes and low-ish energy, the tempting error is empirical, long-term testosterone. Measure it, but treat only biochemically confirmed hypogonadism; testosterone can rescue a genuinely hypogonadal PDE5-inhibitor non-responder, but it will not fix a eugonadal man's erectile dysfunction and only adds androgen risk.

GOOD TO REMEMBER

- **Erectile dysfunction (the diagnosis):** persistent inability to attain or maintain an erection sufficient for satisfactory performance; the defining discriminator is the organic, psychogenic or mixed classification, read first from preserved versus absent nocturnal and masturbatory erections, with vasculogenic disease a cardiovascular warning.
- **First-line erectile-dysfunction drug (guideline-anchored, EAU and AUA 2018):** an oral PDE5 inhibitor plus risk-factor optimisation; sildenafil starts at **50 mg** on-demand about one hour before, tadalafil at **10 mg** on-demand or **5 mg** once daily; any nitrate in any form is an absolute contraindication, and empirical long-term testosterone is never started in a man whose testosterone is normal.

26.4 A gender-incongruence affirmative-care case

case: a young adult, assigned male at birth, has experienced herself as female persistently since adolescence and comes seeking recognition, support and onward referral; her low mood and anxiety are driven largely by family rejection, misgendering and fear of discrimination, not by the gender identity itself.

The reasoning. The affirming frame is the whole answer. Gender incongruence, the marked and persistent mismatch between experienced gender and sex assigned at birth, is not a mental disorder; ICD-11 moved it out of the mental disorders chapter into "Conditions related to sexual health", and it carries no distress criterion at all (ICD-11). Gender dysphoria is the DSM-5-TR term for the clinically significant distress that only *some* people with that incongruence experience, and it is that distress, understood largely as gender minority stress, that is the target of care, never the identity. So the clinician affirms who she is and treats the distress, the comorbid depression and the effects of stigma.

The pathway. Management is a stance codified in the eighth version of the Standards of Care, WPATH SOC-8 (2022): individualised, multidisciplinary and informed-consent based, with a flexible staged transition running fully reversible (social) then partially reversible (hormonal) then irreversible (surgical) steps, and mental-health support offered where needed rather than as a universal gate. The psychiatrist's role is bounded and specific: assess readiness and capacity to give informed consent, diagnose and treat comorbid mental illness (stabilise it, do not use it to exclude her), give psychoeducation and psychosocial support, and refer. The psychiatrist does not initiate or titrate gender-affirming hormones, which are endocrinology-led (feminising therapy combines an oestrogen with an anti-androgen; Endocrine Society 2017).

RULE **Affirm the identity; treat only the distress.** Gender incongruence is not the pathology. The guideline-anchored target of care is the dysphoria, the comorbidity and the effects of stigma, and so-called conversion or reparative efforts are ineffective, harmful and outside the standard of care.

GOOD TO REMEMBER

- **Gender incongruence (the criterion anchor, ICD-11):** a marked, persistent mismatch between experienced gender and sex assigned at birth, at least two of the four indicators, present for at least several months, not assignable before puberty, and with NO distress criterion; it sits in "Conditions related to sexual health", so it is explicitly not a mental disorder. Gender dysphoria is the DSM-5-TR distress-gated term for the suffering only some experience.
- **Affirmative-care pathway (the guideline anchor, WPATH SOC-8 2022):** individualised, multidisciplinary, informed-consent care with a flexible social-then-hormonal-then-surgical transition; the psychiatrist assesses readiness and capacity, treats comorbidity, supports and refers, and does not initiate hormones (endocrinology-led).

INDIA

The clinical and legal stances now point the same way. In the NALSA judgment (National Legal Services Authority v Union of India, Supreme Court, 15 April 2014) the court recognised transgender persons as a third gender and affirmed the right to self-identified gender; the Transgender Persons (Protection of Rights) Act, 2019 then gave statutory recognition, prohibited discrimination in employment, education and healthcare, and set out welfare provisions. India also has its own long-standing third-gender tradition in the hijra community. The psychiatrist works within this frame, offering affirmative, non-judgemental care and appropriate referral, and never conversion approaches.

26.5 A suicide-risk-assessment-and-safety-planning case

case: a person is seen in acute distress after a recent crisis, a job loss and a relationship breakdown in the same fortnight, against a background of a current depressive episode and a past attempt in the history. This case is written under strict safe-messaging: no method is named anywhere, access to means is spoken of only at the category level, and the register stays compassionate and safeguarding throughout.

The reasoning. The task is a structured evaluation, a compassionate clinical interview that systematically covers the same domains every time, not a checklist score. Move gently along the continuum, from low mood to whether life feels worth living, to active thoughts, plan and intent, and, just as deliberately, ask what has kept the person going. Asking directly does not plant the idea. Then weigh the two halves of the balance. The static load is heavy here, a previous attempt with a current major depressive episode being together among the two strongest predictors of future suicide. The dynamic load is what has surged, hopelessness (the pre-eminent dynamic factor), a fresh interpersonal and financial crisis, agitation and isolation, with access to lethal means considered only at the category level. Against these sit the protective factors to seek out and strengthen, help-seeking, family support, concrete reasons for living and responsibilities to others. Hold chronic and acute risk as two separate axes; the person elevated on both warrants the most immediate response. Structure the interview with the Columbia Suicide Severity Rating Scale (C-SSRS), whose ideation subscale is an ordered ladder of five levels of increasing severity, and screen with PHQ-9 item nine; remember that SAD PERSONS is only a teaching aide, and that no instrument or clinician reliably predicts individual suicide, so a low-medium-high label must never be used to ration care.

TRAP **Treating a denied ideation as a cleared risk.** A bare verbal "no" does not neutralise a high risk-and-protective balance. When the structured evaluation shows heavy static and dynamic loading with thin protection, the denial is one data point, not an all-clear; the assessment governs the plan, not the last sentence spoken.

The management link. The assessment earns its keep only when it produces a plan. Build a collaborative Stanley-Brown Safety Planning Intervention *with* the person: recognise personal warning signs, use internal coping strategies, use social contacts and settings that provide distraction, identify people who can help, list professionals and crisis or helpline contacts, and make the environment safer by reducing access to lethal means, the last framed positively as putting time and distance between a person and a crisis, involving family where appropriate. Match the level of care, community follow-up, crisis team or admission, to assessed need, and arrange rapid follow-up, because the transition after any care contact is a high-risk window. Treating the driving disorder is itself anti-suicidal, and two agents carry specific evidence, lithium in mood disorders and clozapine in schizophrenia, developed in the Mood disorders: pharmacotherapy notes and the Schizophrenia: management, antipsychotics and adverse effects notes; the acute triage of the patient in crisis is developed in the emergency psychiatry chapter, and the population-level prevention deep dive in the Community psychiatry and public health notes.

WORKED EXAMPLE

Taking this person's eventual "I just want to go home" at face value and discharging would be the cardinal error, because the whole balance, not the last answer, is heavily loaded. The defensible course keeps them in active care, documents chronic and acute risk separately and states what has changed acutely, mobilises the protective factors, and produces a written collaborative safety plan with positively framed means-restriction counselling and a rapid follow-up appointment. The denial is noted, not trusted as an all-clear.

GOOD TO REMEMBER

- **Structured suicide risk assessment (the principle anchor):** a compassionate structured interview that weighs static against dynamic risk factors and protective factors, separates chronic from acute risk, structures with the C-SSRS ideation ladder (five levels) and screens with PHQ-9 item nine; no tool predicts individual suicide, so stratifying into low-medium-high to ration care is discouraged, and a denied ideation is never a cleared risk.
- **Safety planning and means restriction (the management step, NICE-aligned NG225 2022):** the first move after assessment is a collaborative Stanley-Brown safety plan plus positively framed means-restriction counselling, then a level of care matched to need with rapid follow-up; means restriction is the highest-yield lever, and drugs treat the driving disorder (lithium, clozapine) and supplement, never replace, the plan.

INDIA

India carries a large share of the world's suicide deaths, and suicide is among the leading causes of death in young Indian adults, a burden stated here without any reference to means and one that makes competent, compassionate assessment a public-health priority. The legal anchor is Section 115 of the Mental Healthcare Act 2017: a person who attempts suicide is presumed, unless proved otherwise, to be under severe stress, and shall not be tried or punished, effectively overriding Section 309 of the Indian Penal Code, and the state owes them care and rehabilitation to reduce recurrence. National helpline infrastructure such as Tele MANAS and the Indian Psychiatric Society position reinforce the shift from punishment to care.

25	50	30	5
IIEF-5 TOP SCORE (NO ED FROM 22 UP)	SILDENAFIL ON-DEMAND START (MG)	DAPOXETINE ON-DEMAND START (MG)	C-SSRS IDEATION-SEVERITY LEVELS

HOLD THIS

Read every vignette in two moves, the discrimination that names the frame and the guideline step that follows: somatic symptom disorder turns on the POSITIVE psychological criterion and is managed physician-centred; the produced-symptom pair splits only on the external incentive (present in malingering, absent in factitious disorder); erectile dysfunction is first-line an oral PDE5 inhibitor (sildenafil **50 mg** on-demand, tadalafil **10 mg** on-demand or **5 mg** once daily) with nitrates absolutely contraindicated and testosterone only for confirmed hypogonadism; gender incongruence is affirmed, not pathologised, along the WPATH SOC-8 pathway within the NALSA judgment and the Transgender Persons Act 2019; and the suicidal patient gets a structured assessment weighing risk against protection, never a predictive score, with a collaborative safety plan and positively framed means restriction, remembering that a denied ideation is not a cleared risk and that Section 115 of the Mental Healthcare Act 2017 decriminalised the attempt.

27 · Consolidation

The whole chapter now stands in front of you, and this closing topic is not new content but the machinery that turns reading into recall. The examination does not reward the candidate who has *read* the somatic, sexual, impulse and suicide block; it rewards the one who can, cold and under pressure, name the positive criterion that defines a somatic symptom disorder, split factitious from malingering on a single axis, place a sexual complaint on the response cycle and reach for the first-line drug, state that being transgender is not an illness, and run a compassionate structured suicide assessment. Those retrievals are what this topic drills. The single most robust finding in the science of learning is that **active recall** (pulling an answer out of an empty page) and **retrieval practice** (repeatedly testing yourself rather than re-reading) beat every passive method for durable memory, so the design here is deliberately answer-sparse: prompts first, and the answers held elsewhere in the chapter so you must fetch them.

Why it matters, and what this note owns. This note owns three things: the master **mnemonic** that ties the chapter together, paid off from where it was seeded at the somatic-symptom-disorder opener; a set of answer-free prompt lists for **active recall** across the somatic nosology and its positive criterion, the factitious-versus-malingering discriminator, the sexual response

cycle and the erectile-dysfunction first-line, the gender-incongruence depathologisation, and the suicide risk-assessment principles and safety planning; and a whole-chapter **synthesis map** you are meant to **redraw from memory**. It re-derives no criterion, dose or cut-off of its own; every figure quoted here is a pointer back to the topic that verified it. The deep antidepressant and lithium anti-suicidal pharmacology lives in the Mood disorders: pharmacotherapy notes, the clozapine anti-suicidal pharmacology in the Schizophrenia: management, antipsychotics and adverse effects notes, and the transcultural frame of Dhat in the Consultation-liaison, geriatric and transcultural psychiatry notes. The synthesis map that carries the whole block is drawn in the accompanying figure, framed cover-the-branches so it can be used as a retrieval test.

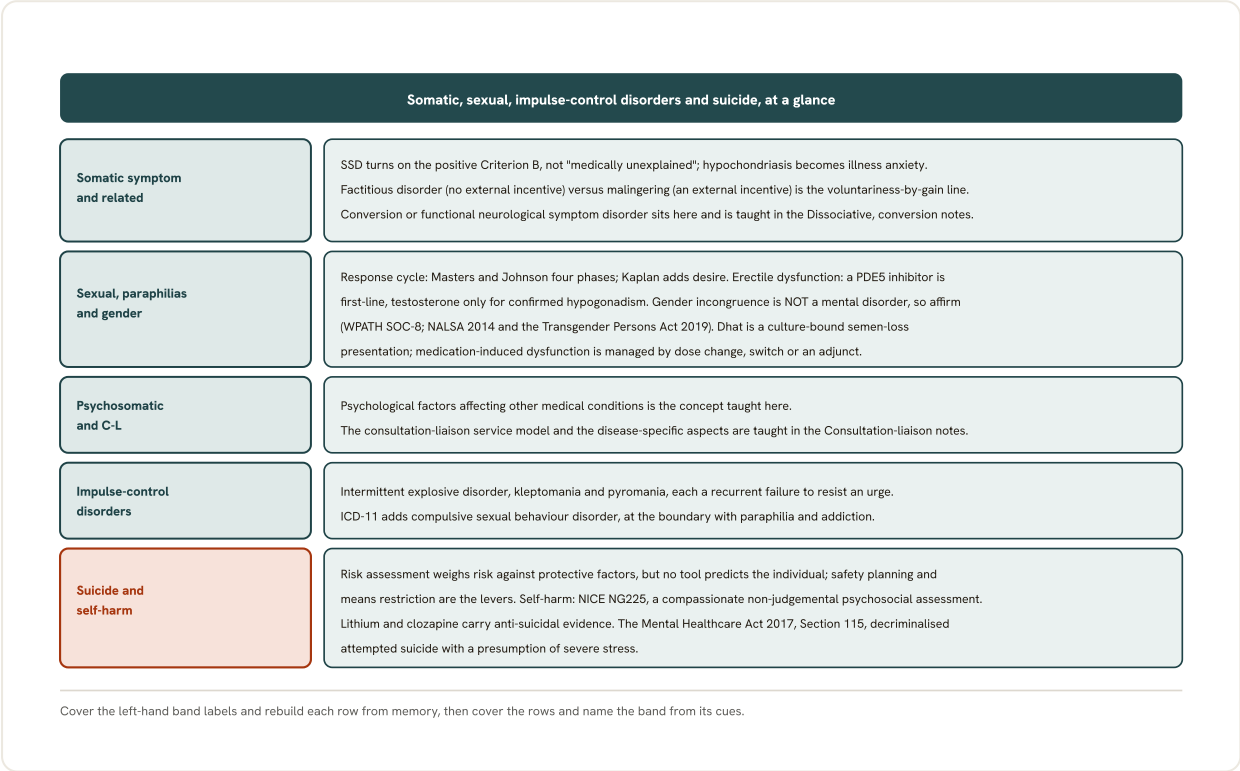


Fig 18.20 The chapter at a glance. Read across each band once, then use the map for retrieval: cover the left-hand labels and rebuild each row from its cues, then cover the rows and name the band. The somatic band turns on the positive Criterion B and the voluntariness-by-incentive line that separates factitious disorder from malingering. The sexual and gender band holds the response cycle, the phosphodiesterase-5 inhibitor as first-line for erectile dysfunction, the affirming frame for gender incongruence with its Indian legal basis, and Dhat. The psychosomatic and consultation-liaison band is the concept taught here with the service model cross-referenced. The impulse-control band gathers the disorders of urge. The suicide and self-harm band is the core: assessment that guides rather than predicts, safety planning and means restriction, the compassionate NICE stance to self-harm, the anti-suicidal evidence for lithium and clozapine, and the decriminalisation of attempted suicide under the Mental Healthcare Act.

27.1 The master mnemonic, paid off: SEED

Seeded at the opener, closed here. The chapter opened by seeding the master mnemonic **"SEED"** at somatic symptom disorder, and this is where it is reaped, because its four letters are the four rooms of a single house, arranged as the body moves from complaint to desire to urge to the protection of life. **S** is the *Somatic* room, where the body *complains*: somatic symptom disorder and the ICD-11 bodily distress disorder, with factitious disorder and malingering standing at its far door. **E** is *Eros*, where the body *desires* and identity is *affirmed*: the sexual dysfunctions and gender incongruence. **E** is the *Explosive urges*, where the urge *acts*: the impulse-

control disorders, each running the mounting-tension-then-relief arc. **D** is the *Defence of life*, the protective, compassionate stance the chapter closes on: suicide risk assessment, safety planning and prevention. If you can name the four rooms and walk their contents without looking, you hold the spine of the whole chapter.

MNEMONIC

SEED

The chapter master mnemonic, paid off. **S** = the *Somatic* room (the body complains): somatic symptom disorder defined by the positive psychological criterion, ICD-11 bodily distress disorder, and the feigned pair, factitious disorder and malingering, at the door. **E** = *Eros* (the body desires, identity is affirmed): the sexual dysfunctions mapped on the response cycle, and gender incongruence, which is not a mental illness. **E** = *Explosive urges* (the urge acts): the impulse-control disorders and their tension-then-relief arc. **D** = the *Defence of life*: compassionate, structured suicide risk assessment and collaborative safety planning. Four rooms, one house: S-E-E-D.

27.2 Active-recall prompt list: the somatic room, the positive criterion and the feigned pair

Cover the answers and pull each one. This is a **retrieval practice** list, not a summary. For each prompt below, say aloud (or write) the discriminator before you check it against the topic that verified it. The point is the effort of retrieval: the harder the pull, the stronger the trace.

- **The positive criterion.** Prompt: what now defines somatic symptom disorder, and what was abolished? (Answers in the somatic-symptom-disorder topic: Criterion B, the excessive *Thoughts, Anxiety and Behaviour* about the symptoms, is the defining **positive psychological criterion**; the old "medically unexplained" requirement is gone, so a medically explained symptom with an excessive response still qualifies, and severity is counted from Criterion B, not from the number of symptoms.)
- **The forward collapse.** Prompt: where did the DSM-IV somatoform family go? (Somatisation, undifferentiated and pain disorder folded into somatic symptom disorder; hypochondriasis split into somatic symptom disorder and illness anxiety disorder; conversion retained as functional neurological symptom disorder; body dysmorphic disorder migrated to the obsessive-compulsive spectrum. The positive signs of conversion are in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes, and body dysmorphic disorder in the Anxiety, OCD and trauma-related disorders notes.)
- **The ICD-11 parallel.** Prompt: the ICD-11 name and its logic? (Bodily distress disorder, code 6C20, distressing symptoms plus excessive attention, positively defined and not unexplained-based, present on most days for at least several months; ICD-11 sends its hypochondriasis to the obsessive-compulsive and related disorders.)
- **Factitious versus malingering.** Prompt: both are feigned, so what tells them apart? (Both are consciously produced, so voluntariness is shared and cannot separate them; the discriminator is the *external incentive*. Malingering has one, secondary gain, coded Z76.5 as a condition and not a mental disorder, strongly suspected on the four DSM-5-TR pointers; factitious disorder

has none, the motive being the sick role and primary gain, its severe wandering form being Munchausen syndrome. The genuine somatic disorders are not intentionally produced at all.)

RULE **Read production, then incentive.** The whole somatic room reduces to two questions asked in order: is the symptom intentionally produced, and if so, for an external incentive (malingering, secondary gain) or for the sick role (factitious disorder, primary gain); the genuine somatic disorders answer the first question with no.

GOOD TO REMEMBER

- **The somatic room (the criterion anchors):** somatic symptom disorder is defined by the positive Criterion B (excessive thoughts, feelings and behaviours), not by being medically unexplained; ICD-11 makes the same move as bodily distress disorder (6C20). The feigned pair separate only on the external incentive, present in malingering (Z76.5, not a disorder) and absent in factitious disorder (the sick role); a denied external motive does not turn a compensation claimant into a factitious patient.

27.3 Active-recall prompt list: the Eros room, the response cycle, the ED first-line and the depathologisation

Localise first, then treat, then affirm. This room holds a schematic model, one clean first-line drug position, and one reclassification. Retrieve each before checking it against its topic.

- **The response cycle.** Prompt: the three named models and the wiring? (Masters and Johnson gave four phases, excitement, plateau, orgasm and resolution, with a male-only refractory period; Kaplan's triphasic model added the desire phase to make desire, excitement and orgasm, and that phase map is how DSM-5-TR classifies the dysfunctions; Basson's circular model shows female desire can be responsive and follow arousal; the wiring is point and shoot, parasympathetic sacral outflow at **S2 to S4** for erection and sympathetic thoracolumbar outflow at **T11 to L2** for emission and ejaculation.)
- **The disrupted phase names the disorder.** Prompt: which phase gives which complaint? (A desire-phase failure gives hypoactive desire; an excitement-phase failure gives erectile dysfunction; an orgasm-phase failure gives anorgasmia or premature ejaculation. Localise to a phase and the differential is narrowed before a criterion is named.)
- **The erectile-dysfunction first-line.** Prompt: the first-line drug, the two doses, the one absolute contraindication, the testosterone rule? (An oral PDE5 inhibitor plus risk-factor optimisation; sildenafil starts at **50 mg** on-demand about one hour before, tadalafil at **10 mg** on-demand or **5 mg** once daily; any nitrate in any form is an absolute contraindication; test a morning testosterone and treat only confirmed hypogonadism, never long-term testosterone in a eugonadal man. The ladder is Pills, then Pokes and Pumps, then Prosthesis.)
- **Premature ejaculation.** Prompt: the only licensed first-line drug and its dosing rule? (On-demand dapoxetine, started at **30 mg**, taken one to three hours before, maximum 60 mg, not more than once every 24 hours; it should not routinely be combined with a PDE5 inhibitor because of syncope risk.)

- **The gender depathologisation.** Prompt: the headline reclassification, the DSM contrast, and the management stance? (ICD-11 renamed transsexualism as gender incongruence and moved it out of the mental disorders chapter to "Conditions related to sexual health," needing no distress criterion; DSM-5-TR keeps gender dysphoria, gated by Criterion B distress; management is not a drug but the affirmative-care pathway, individualised and informed-consent based, with the psychiatrist treating distress and comorbidity, never the identity.)

GOOD TO REMEMBER

- **Erectile dysfunction first-line (guideline-anchored, ISSM, BSSM, EAU, AUA 2018):** an oral PDE5 inhibitor plus risk-factor optimisation is first-line for every man without a contraindication; sildenafil (Manforce, Penegra) starts at 50 mg on-demand, tadalafil (Tadacip, Megalis) at 10 mg on-demand or 5 mg once daily; a nitrate is an absolute contraindication, and long-term testosterone is never started for a eugonadal man. Premature ejaculation is first-line on-demand dapoxetine (Duralast, Sustinex), started at 30 mg.
- **Gender incongruence (the criterion anchor and stance):** a marked, persistent mismatch between experienced gender and sex assigned at birth is *not* a mental disorder; ICD-11 relocated it out of the mental disorders chapter with no distress criterion, DSM-5-TR retains gender dysphoria gated by distress, and management is the WPATH SOC-8 individualised, informed-consent, gender-affirmative pathway. The discriminator to hold is that the target of care is the distress, the comorbidity and the stigma, never the person's gender.

27.4 Active-recall prompt list: the defence of life, risk assessment and safety planning

A weighing skill, held with a safeguarding tone. This is the room the chapter closes on, and it is examined as a skill, not a fact-list. Retrieve each principle before checking it against the suicide risk-assessment topic, and keep the register compassionate throughout: the assessment exists to guide care and safety, never to forecast an outcome or to allocate blame.

- **The structured evaluation.** Prompt: what is it, and what is it not? (A compassionate **structured evaluation** that weighs static and dynamic risk factors against protective factors and the current mental state, and separates chronic from acute risk; it is not a checklist score or a numerical prediction. Asking directly and calmly about suicidal thoughts is a core skill and does not plant the idea.)
- **The three named aides.** Prompt: the gold standard, the teaching aide, and the single screening item? (The C-SSRS is the gold-standard clinician-administered interview, its ideation subscale an ordered ladder of five levels; SAD PERSONS is only a teaching aide scored out of a possible ten, explicitly not validated to predict individual risk or to ration care; PHQ-9 item nine is a single screening item that, if endorsed, mandates a full structured assessment.)
- **The limits of prediction.** Prompt: the governing principle? (No tool or clinician reliably predicts individual suicide, so risk-stratification scores must not be used to predict or to ration care; the field favours a prevention-oriented formulation of four judgements, risk status, risk state, resources and foreseeable changes, over a low-medium-high label.)
- **Safety planning and means restriction.** Prompt: the guideline first move after assessment? (A collaborative Stanley-Brown Safety Planning Intervention built with the person, plus

means-restriction counselling framed positively as putting time and distance between a person and a crisis, then a level of care matched to need with rapid follow-up. Reducing access to lethal means, named only at the category level, is the single most robustly evidenced lever, and where a driving disorder is present its treatment is itself anti-suicidal, lithium in mood disorders and clozapine in schizophrenia.)

TRAP **Treating a denied ideation as a cleared risk.** A verbal "no" does not neutralise a high risk-and-protective balance; when the structured evaluation shows heavy static and dynamic loading with thin protection, the denial is one data point among many, and the assessment, not the last sentence spoken, governs the safety plan.

GOOD TO REMEMBER

- **Suicide risk assessment and safety planning (guideline-anchored, NICE NG225 2022, WHO LIVE LIFE 2021):** weigh static and dynamic risk factors against protective factors and separate chronic from acute risk; use the C-SSRS ideation ladder to structure and PHQ-9 item nine to screen, and remember no instrument predicts individual suicide, so stratifying to ration care is discouraged. The first move after assessment is a collaborative Stanley-Brown safety plan plus positively framed means restriction, the highest-yield lever; drugs (lithium, clozapine) treat the driving disorder and supplement, never replace, the plan.

INDIA

The Indian thread runs through every room and is worth carrying as one line at consolidation. In the Somatic room, distress is very commonly first brought to the clinician as bodily symptoms, so the culture-bound Dhat presentation must be read through a cultural formulation rather than pathologised on its surface, its transcultural frame sitting in the Consultation-liaison, geriatric and transcultural psychiatry notes. In the Eros room, the generics are familiar Indian brands, sildenafil (Manforce, Penegra), tadalafil (Tadacip, Megalis) and dapoxetine (Duralast, Sustinex), and gender-affirmative care is reinforced in law by the 2014 NALSA judgment, which recognised a third gender and the right to self-identified gender, and the Transgender Persons (Protection of Rights) Act, 2019. In the Defence-of-life room, India carries a large share of the world's suicide deaths, a burden stated here without any reference to means, and Section 115 of the Mental Healthcare Act 2017 decriminalised the attempt through a presumption of severe stress and a duty of care, superseding Section 309 of the Indian Penal Code; the Indian Psychiatric Society endorses the shift from punishment to care.

27.5 The whole-chapter synthesis map, framed cover-the-branches

Build the house, then redraw it blind. The strongest single revision act for this block is to **redraw from memory** a **synthesis map** that hangs every entity off its SEED room. The map has four rooms: the *Somatic* (the body complains), *Eros* (the body desires and identity is affirmed), the *Explosive urges* (the urge acts), and the *Defence of life* (the life protected). From each room hang its disorders, and from each disorder hang the one anchor to pull cold, its criterion, its discriminator or its first-line. The accompanying figure draws this map; use it as a retrieval test by covering all the branches and regenerating them, then uncovering to score yourself, exactly the cover-the-branches method that makes **retrieval practice** work.

SEED ROOM	WHAT HANGS FROM IT	THE ONE ANCHOR TO PULL COLD
S · Somatic (the body complains)	Somatic symptom disorder, illness anxiety, bodily distress disorder, conversion; factitious disorder and malingering at the door	**The positive psychological criterion (Criterion B), then production-before-incentive for the feigned pair**
E · Eros (the body desires, identity affirmed)	The response-cycle phases and their dysfunctions, erectile dysfunction, premature ejaculation, gender incongruence	**The disrupted phase names the disorder; ED first-line is a PDE5 inhibitor; gender incongruence is not a mental illness, so affirm**
E · Explosive urges (the urge acts)	The impulse-control disorders, each running the tension-then-relief arc	**Mounting tension relieved by the act, the ego-syntonic urge distinguishing them**
D · Defence of life (the life protected)	Suicide risk assessment, safety planning, prevention	**Weigh the whole balance not the last sentence; means restriction framed positively; the attempt is decriminalised**

The four-room SEED synthesis map, framed cover-the-branches; each room's single anchor is the fact to regenerate before uncovering the row (verified against the individual chapter topics, drawn in the accompanying figure).

How to use it. First pass: cover everything but the four room-names and list the disorders under each. Second pass: for each disorder, cover the anchor and pull it. Third pass: recite the one first-line or discriminator per room. A branch you cannot regenerate is a branch to re-read in its own topic; a branch you can is one you can leave. Repeated over spaced sittings, the map converts the chapter from something you recognise into something you can produce.

5	15	50
C-SSRS IDEATION-SEVERITY LEVELS	PHQ-15 HIGH-SEVERITY CUT-OFF (0 TO 30 SCALE)	SILDENAFIL ON-DEMAND START DOSE (MG)

PEARL

The whole chapter collapses to four rooms and four anchors. The *Somatic* room turns on the positive criterion and the production-before-incentive grid; *Eros* turns on the response-cycle phase and the clean PDE5-inhibitor first-line, with gender incongruence affirmed rather than treated; the *Explosive urges* turn on the tension-then-relief arc; and the *Defence of life* turns on the weighed balance, the safety plan and the positively framed means restriction. Redraw the four rooms, name their anchors, and you own the block.

HOLD THIS

Redraw the four-room SEED synthesis map from memory: Somatic (defined by the positive Criterion B, not by being medically unexplained, with factitious and malingering split on the external incentive), Eros (the disrupted phase names the sexual disorder, erectile dysfunction is first-line a PDE5 inhibitor, and gender incongruence is not a mental illness so it is affirmed), Explosive urges (the mounting-tension-then-relief arc of the impulse-control disorders), and the Defence of life (a compassionate structured assessment that weighs the balance rather than trusting a denial, driving a collaborative safety plan and positively framed means restriction, with the attempt decriminalised by Section 115 of the Mental Healthcare Act 2017).

Previously asked

This is a broad territory that is examined at two levels, the syndrome (its clinical features, its differential diagnosis and its course) and the management, with one band, suicide and self-harm, carrying much of the essay weight. The reliable pattern is that the somatic-symptom and conversion disorders recur as full essays, that suicide is the dominant management essay and is repeatedly asked with an Indian and a medico-legal slant, and that the sexual dysfunctions, Dhat, the paraphilias, and the consultation-liaison and psychosomatic topics come as standalone notes. The impulse-control disorders are drawn together in an enumerate-and-describe essay. Every long essay ends in a management plan, so the first-line and the reason for it must be exam-ready, and the suicide answers must be written with the safe, structured, compassionate stance the block rewards. The genuine questions on record are grouped by band below.

HOW THIS TERRITORY IS ACTUALLY TESTED

Q **The somatic-symptom and conversion disorders, as essays.** "Describe the clinical features, differential diagnosis and management of Somatoform Disorder" has come as a 25-mark essay across more than one sitting, alongside "Discuss the etiology, clinical features and management of Conversion Disorder", "Clinical features and differential diagnosis of Conversion Disorder" and "Differential diagnosis of somatoform pain disorder and its prognosis"; "Pseudoseizures" and "Malingering" recur as 10-mark notes. Prepare the somatoform-to-somatic-symptom-disorder nosology shift and the positive psychological criterion, the somatic-versus-factitious-versus-malingering discrimination, and the physician-centred management of medically unexplained symptoms. essay and short note, recurring

Q **The suicide and self-harm band, the dominant essay theme.** "Enumerate various risk factors for suicide and describe the outline of management of attempted suicide", "Describe the management of the suicidal patient", "Discuss suicide and mental disorders" and "Discuss suicide with special reference to the Indian setting in detail" have all come as 25-mark essays, and "Differential diagnosis and synonym for deliberate self-harm" and the medico-legal "critical appraisal regarding attempted suicide as a crime" as 10-mark notes. Prepare the structured risk assessment and the limits of individual-risk prediction, safety planning and means restriction, the Mental Healthcare Act 2017 decriminalisation of attempted suicide under Section 115, and the anti-suicidal evidence for lithium and clozapine, all written with strict safe-messaging. essay and short note, recurring

Q **The sexual dysfunctions and paraphilias, as notes.** "Premature ejaculation" recurs as a 10-mark note across several sittings, and "Erectile dysfunction" and "Paraphilias" as 10-mark notes. Prepare the normal sexual response cycle, the phosphodiesterase-5-inhibitor-first management of erectile dysfunction, the

on-demand dapoxetine for premature ejaculation, and the consent, distress and harm framing of the paraphilic disorders. short note, recurring

Q **Dhat and the culture-bound presentations, as notes.** "Enumerate the culture-bound syndromes and describe Dhat syndrome in detail" and "Dhat syndrome" recur as 10-mark notes. Prepare Dhat as an Indian culture-bound sexual presentation, the semen-loss attribution, the cultural formulation, and the non-confrontational psychoeducational management. short note, recurring

Q **Consultation-liaison and psychosomatic medicine, as notes.** "Consultation liaison psychiatry" and "The role of the psychiatrist in psychosomatic medicine" have come as 10-mark notes. Prepare the psychosomatic concept and the biopsychosocial model here; the consultation-liaison service model and the disease-specific aspects are developed in the Consultation-liaison, geriatric and transcultural psychiatry notes. short note, recurring

Q **The impulse-control disorders, as an enumerate-and-describe essay.** "Enumerate the various impulse-control disorders and describe the etiology, clinical features and management of trichotillomania" gathers the group into one answer. Prepare intermittent explosive disorder, kleptomania, pyromania and the ICD-11 compulsive sexual behaviour disorder as a compact group, each a recurrent failure to resist an urge.

essay, enumerate

Prepare this material to be assessed and managed, not just recited: the somatic-symptom nosology and the factitious-versus-malingering discrimination, the erectile-dysfunction algorithm and the verified doses, the gender-incongruence affirming frame with its Indian legal basis, and the structured, safe suicide risk assessment and safety planning in these notes are built to the way the block is examined. The positive functional-neurological signs and the full management of conversion or functional neurological symptom disorder are developed in the Dissociative, conversion and anxiolytic/hypnotic pharmacology notes; the deep antidepressant and antipsychotic sexual-dysfunction pharmacology and the lithium and clozapine pharmacology in the Mood disorders: pharmacotherapy notes and the Schizophrenia: management, antipsychotics and adverse effects notes; the consultation-liaison service model and the disease-specific aspects in the Consultation-liaison, geriatric and transcultural psychiatry notes; and the population and public-health suicide prevention in the Community psychiatry and public health notes.

Quick review

SOMATIC SYMPTOM AND RELATED DISORDERS: THE NOSOLOGY, THE DISCRIMINATION, THE MANAGEMENT	
THE NOSOLOGY SHIFT	ICD-10 somatoform disorders collapse into DSM-5 **somatic symptom disorder**, which turns on the **positive psychological Criterion B** (excessive thoughts, feelings and behaviours about the symptoms), NOT on the symptom being "medically unexplained"; a medically explained symptom can qualify. Hypochondriasis becomes **illness anxiety disorder**. ICD-11 uses one graded **bodily distress disorder**.
THE DISCRIMINATION	Somatic symptom disorder and illness anxiety are **genuine, no external incentive**. Conversion or FND is not consciously feigned and is recognised by **positive signs** (taught in the Dissociative notes). **Factitious** = feigned, **no** external incentive (internal sick role; Munchausen, and by proxy). **Malingering** = feigned, **external** incentive; not a disorder. Secondary gain alone is not malingering.
THE SCALES	**PHQ-15**: 15 items 0 to 2, total out of a possible 30; bands 0-4, 5-9, 10-14, 15-30. **SSD-12**: 12 items 0 to 4, total out of a possible 48; cut-off **23 and above**.
MANAGEMENT (IPS 2020, WHO MHGAP)	**Physician-centred care**: one coordinating clinician, validate distress, restrict unnecessary testing, treat comorbid depression or anxiety, shift focus to functioning; reattribution; **CBT** first-line. Do NOT prescribe an antidepressant or anxiolytic for medically unexplained symptoms without specialist advice (mhGAP).
SEXUAL DYSFUNCTIONS, PARAPHILIAS AND GENDER	
RESPONSE CYCLE	Masters and Johnson four phases (excitement, plateau, orgasm, resolution); Kaplan adds **desire** (triphasic); Basson's circular model for responsive female desire.
ERECTILE DYSFUNCTION (ISSM, BSSM)	Screen cardiometabolic risk (an early vascular marker); confirm with the IIEF-5. **PDE5 inhibitor first-line**: sildenafil 25/50/100, tadalafil on-demand 10 or 20 and once-daily 2.5 or 5, vardenafil, avanafil. **Absolute contraindication with nitrates**. Test testosterone, replace only confirmed hypogonadism; no empirical testosterone in a eugonadal man. Second-line alprostadil or vacuum device; third-line prosthesis. IIEF-5 out of a possible 25 (22-25 none to 5-7 severe).
PREMATURE EJACULATION, HSDD	**Dapoxetine** on-demand 30 to 60 mg, 1 to 3 hours before activity, for premature ejaculation. **Flibanserin** 100 mg nightly for premenopausal HSDD (alcohol and hypotension cautions). Female dysfunctions: biopsychosocial and sex therapy first; local oestrogen for GSM dyspareunia; pelvic-floor physiotherapy and graded dilators for GPPPD.

SEXUAL DYSFUNCTIONS, PARAPHILIAS AND GENDER	
GENDER INCONGRUENCE	ICD-11 **depathologises** it: gender incongruence is a sexual-health condition, NOT a mental disorder (as homosexuality was earlier removed). Affirm; WPATH SOC-8 individualised informed-consent pathway. India: **NALSA 2014** and the **Transgender Persons Act 2019**. Trap: pathologising the identity.
DHAT; MEDICATION-INDUCED	**Dhat**: an Indian culture-bound presentation, symptoms attributed to semen loss; cultural formulation and psychoeducation, treat comorbid depression or anxiety. Medication-induced dysfunction: watchful waiting, dose reduction, switch (bupropion, mirtazapine, vortioxetine), or an adjunct; antipsychotic **hyperprolactinaemia** (worst with risperidone, least with aripiprazole).
PARAPHILIC DISORDERS	A paraphilia is a **disorder** only with distress or impairment, or harm or a non-consenting person. Types from exhibitionistic and voyeuristic to paedophilic disorder; psychological relapse-prevention, SSRI, and antiandrogen or GnRH-analogue in high-risk cases.
PSYCHOSOMATIC MEDICINE, CONSULTATION-LIAISON AND THE IMPULSE-CONTROL DISORDERS	
PSYCHOSOMATIC CONCEPT	Psychological factors affecting other medical conditions; the biopsychosocial model; stress-illness pathways (HPA, autonomic, immune). Taught compactly here.
CONSULTATION-LIAISON (CROSS-REF)	The C-L service model and the disease-specific aspects (psycho-oncology, HIV, endocrine, cardiac, transplant, surgical and ICU) are taught in the Consultation-liaison, geriatric and transcultural psychiatry notes.
IMPULSE-CONTROL DISORDERS	**Intermittent explosive disorder** (impulsive aggression out of proportion), **kleptomania** (stealing objects not needed), **pyromania** (fire-setting with fascination), and the ICD-11 **compulsive sexual behaviour disorder** (at the boundary with paraphilia and addiction). Each a recurrent failure to resist an urge.
SUICIDE AND SELF-HARM (THE HIGH-STAKES CORE)	
RISK ASSESSMENT	Weigh **static** factors (a previous attempt the strongest; mental illness; chronic illness; family history) against **dynamic** ones (hopelessness the leading one; ideation with plan and intent; a recent crisis; agitation; access to means at the category level) and the **protective** factors. Separate **chronic** from **acute** risk. The C-SSRS structures an ideation ladder plus a behaviour subscale.
LIMITS OF PREDICTION	The governing principle: **no tool predicts an individual suicide.** Risk-stratification scores must NOT decide who gets care; use a prevention-oriented formulation (risk status, risk state, resources, foreseeable changes). Assessment guides care, it does not forecast.

SUICIDE AND SELF-HARM (THE HIGH-STAKES CORE)	
MANAGEMENT AND SAFETY PLANNING	A compassionate, non-judgemental assessment (NICE); a **collaborative safety plan** (warning signs, coping, contacts, crisis lines, means-restriction counselling framed positively); the level of care (LOCUS); treat the disorder; active follow-up in the high-risk post-discharge window. A denied ideation is not a cleared risk.
DELIBERATE SELF-HARM (NICE NG225)	Self-harm is self-poisoning or self-injury **irrespective of intent**; NSSI is the intent-free subset. Every episode earns a full needs-based psychosocial assessment; **no risk-stratification tool** to predict or to ration care; apparent medical triviality is no reassurance; any self-harm raises future suicide risk.
PREVENTION AND ANTI-SUICIDAL DRUGS	**WHO LIVE LIFE**: limit access to means (highest-yield), responsible media, adolescent life skills, early identification. **Lithium** reduces suicide in mood disorders (Cipriani 2013, 48 RCTs); **clozapine** reduces suicidal behaviour in schizophrenia (InterSePT, Meltzer 2003). India: **Section 115 of the Mental Healthcare Act 2017** presumes severe stress and decriminalises an attempt.
THE GUIDELINE SPINE, THE INDIA CONTEXT AND THE TRAPS	
THE GUIDELINE ORDER	Guidelines-first on the where-to-treat, target-by-phase, modes-of-treatment spine: **NICE** leads the self-harm and suicide pathway, with **WHO LIVE LIFE** for prevention; **ISSM and BSSM** for the sexual dysfunctions; **WPATH SOC-8** for gender; the IPS somatoform guideline and WHO mhGAP for the somatic band.
THE INDIA CONTEXT	The Mental Healthcare Act 2017 **Section 115** (attempted suicide presumed under severe stress, not punished); the National Suicide Prevention Strategy 2022; **Dhat** as a culture-bound presentation; gender-affirmative care via **NALSA 2014** and the **Transgender Persons Act 2019**.
THE TRAPS	Calling somatic symptom disorder "medically unexplained"; confusing factitious (no incentive) with malingering (external incentive); empirical testosterone for a eugonadal man with ED; pathologising gender incongruence; reading a Dhat presentation without the cultural formulation; and the cardinal one, treating a denied ideation as a cleared risk, or a stratification score as a licence to discharge.

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The somatic-symptom, sexual, impulse-control and suicide content is grounded in the standard psychiatry and psychopharmacology sources (the source hierarchy below), with Kaplan and Sadock and the Maudsley Prescribing Guidelines as the depth bar for the phenomenology, the neurobiology, the scale cut-offs and the doses, the New Oxford Textbook and the Companion for

the nosology, and Clinical Methods in Psychiatry for the Indian context. The management is guideline-first: NICE leads for the self-harm and suicide pathway, with WHO LIVE LIFE for prevention, ISSM and BSSM for the sexual dysfunctions, WPATH Standards of Care version 8 for gender-affirmative care, and the Indian Psychiatric Society somatoform guideline and WHO mhGAP for the somatic band. The Indian legal provisions (the Mental Healthcare Act 2017 Section 115, the NALSA judgment 2014 and the Transgender Persons (Protection of Rights) Act 2019) were checked against their primary texts. Every scale cut-off, dose, criterion and legal provision was checked against these sources; anything that could not be confirmed was omitted and flagged rather than guessed. Each journal identifier below was verified against PubMed this build and matched on title, first author and year; books, guidelines and statutes are cited by author or body, title and year.

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PART XII

XII

Psychotherapies, Clinical Assessment, MSE and Nosology

How psychiatry treats and how it assesses: the psychotherapies, the clinical interview, the mental state and nosology.

01 Psychotherapies: general and specific

02 Psychiatric assessment and rating scales

03 Nosology and cross-cutting clinical issues

04 Apply and consolidate

PAPER II

Psychotherapies, clinical assessment, MSE and nosology

Three sections . one complete notes document

This material gathers the psychotherapies, the clinical assessment and the nosology into one document, taught as skills rather than syndromes. The first band is **the psychotherapies**: the classification of the therapies and the common factors that carry much of the outcome, then each modality with its model, its core techniques, its evidence and its lead indication, from supportive psychotherapy, cognitive behaviour therapy and behaviour therapy through psychoanalysis and the ego defences, interpersonal, group and family therapy, the third-wave therapies and motivational interviewing, to the Indian and culturally-adapted context and the selection of the right therapy for the presentation. The second band is **clinical assessment and rating scales**: the psychiatric interview and the mental state examination in full, the cognitive examination with the MMSE and the MoCA, the biopsychosocial formulation, the rating scales as a catalogue, and reliability and validity. The third band is **nosology and cross-cutting clinical issues**: the principles of classification, the ICD-11 and DSM-5 and the changes between them, the categorical-versus-dimensional debate, comorbidity, the cultural concepts of distress, the forensic essentials, the Mental Healthcare Act 2017 and capacity, consent and confidentiality. The examinable skill is to choose the right therapy, examine and formulate a patient, pick the right scale, and place a presentation in the current classification. The disorder-specific therapy protocols and the disorder-specific scales are taught in their disorder chapters and cross-referenced here; a consolidated appendix reproduces or typesets the rating scales of the whole series.

HOW TO USE THESE NOTES

Read the three bands as one continuous account of how a psychiatrist treats with words, examines a mind, and names what is wrong. The **psychotherapies** band is organised by the psychotherapy-family tree: the schools branching to the modalities. It opens with the classification of the therapies and the common, non-specific factors and the therapeutic alliance, then teaches each modality with its model, its core techniques, its evidence and its one lead indication, and closes by choosing the right therapy for the presentation. The widely-practised therapies are taught in full; the niche modalities are kept compact. The **clinical assessment and rating scales** band is organised by the assessment framework: the psychiatric interview and history, then the **mental state examination** in full, domain by domain, as the key examinable skill, then the cognitive examination with the MMSE and the MoCA, the biopsychosocial and 4-Ps formulation, the rating scales as a catalogue, and reliability and validity. The **nosology and cross-cutting** band teaches the principles of classification and the diagnostic process, the ICD-11 taught forward with the DSM-5-TR cross-mapped and the changes between the editions flagged, the categorical-versus-dimensional debate, comorbidity, the cultural concepts of distress, the forensic essentials, the Mental Healthcare Act 2017 and capacity, consent and confidentiality. Figures declare one axis and code it in colour: **petrol** marks structure and the neutral case, **coral** marks the trap, and **marigold** highlights the number to hold. The rating scales are reproduced as the actual instruments where the licence permits and typeset from their structure where it does not, gathered in a consolidated appendix at the back, with every cut-off verified; the cognitive instruments are typeset because they are permission-required. Several boundaries are stated up front: the deep psychometric theory and descriptive psychopathology are taught in the Psychometry, Assessment and Descriptive Psychopathology notes and cross-referenced here; the disorder-specific therapy protocols and the disorder-specific rating scales live in their disorder chapters; and the fuller mental-health legislation and forensic procedure live in the legislation and forensic notes. The modality models, the clinical MSE and assessment skill, the general cognitive instruments and the nosology are owned and fully taught here. This is doctor-facing revision, so the full technical vocabulary is used, the India context is genuine and verified (the Indian Psychiatric Society guidelines, culturally-adapted therapy, yoga and meditation-based interventions, the Mental Healthcare Act 2017), and every MSE component, therapy indication, scale cut-off, eponym count and nosology fact is verified against a source or omitted and flagged.

Psychotherapies: general and specific

1 · Classification of the psychotherapies and the common factors

This is the orienting topic for the whole psychotherapies band, and it earns its place because the examiner rarely asks "describe cognitive behaviour therapy" cold; the marks are in the *map*, being able to place any named therapy on its axes, and in the counter-intuitive fact that most of what heals a patient is not the branded technique at all. Two ideas do the heavy lifting. The first is the **classification of psychotherapies**, the small set of axes (depth, school, duration and format) onto which the twenty-odd named modalities of this chapter are sorted. The second is the **common factors** literature, the finding that the ingredients shared by *all* bona fide therapies,

above all the relationship, carry a larger share of the outcome than the specific procedures that distinguish one school from another.

How to use this page. Fix the definition first, then build the four-axis frame and the **schools of psychotherapy**, learning the master mnemonic seeded here because it is paid off at consolidation and anchors the psychotherapy-family tree for the entire chapter. Then internalise the **non-specific factors** and the **therapeutic alliance**, the **transtheoretical model** with its **stages of change**, and finally the **evidence hierarchy** that ranks how confident a guideline may be. The specific modalities that follow (psychodynamic, behavioural, cognitive, humanistic, systemic and the third-wave therapies) each get their own model, technique, evidence and lead indication; here we teach only the scaffold that holds them.

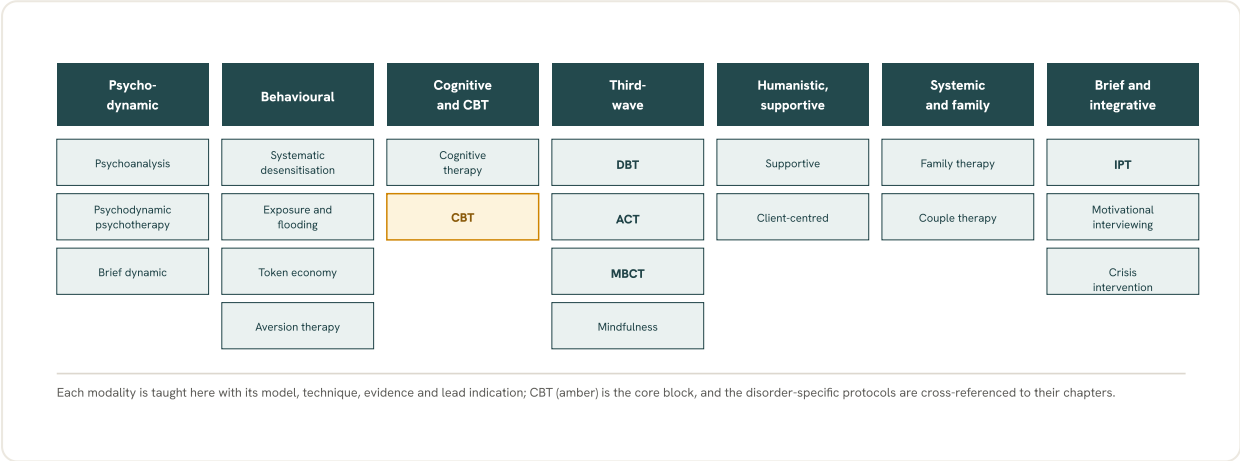


Fig 19.1 The schools of psychotherapy and their modalities. The therapies group into families by their theory of change: the psychodynamic therapies working with the unconscious and the transference; the behavioural therapies applying learning theory through exposure and reinforcement; the cognitive and cognitive-behavioural therapies working with thought and behaviour together, with CBT the most-evidenced modality of all; the third-wave acceptance-and-mindfulness therapies; the humanistic and supportive therapies working through the relationship itself; the systemic and family therapies treating the system rather than the individual; and the brief, interpersonal and integrative therapies. Each is taught here with its model, its core technique, its evidence and its one lead indication.

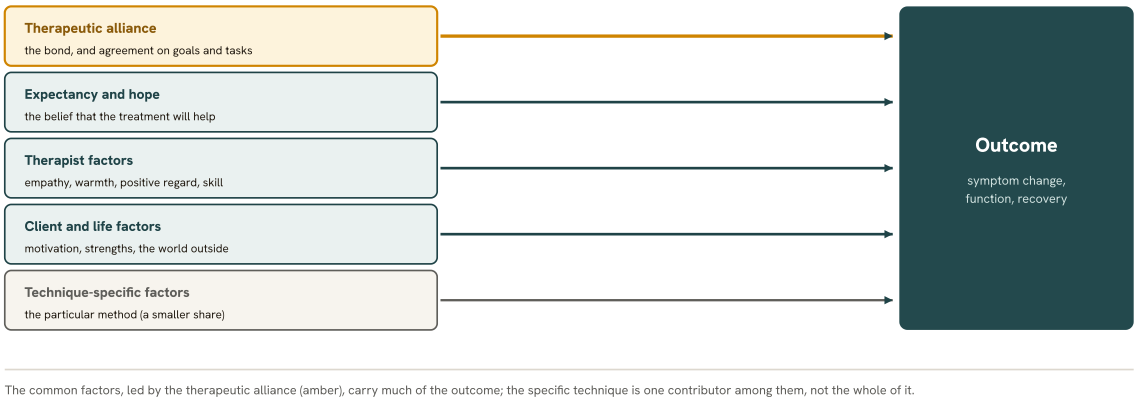


Fig 19.2 The common factors and the therapeutic alliance. Across the psychotherapies, a large share of the outcome is carried not by the specific technique but by factors common to all of them: above all the therapeutic alliance, the bond between patient and therapist together with their agreement on the goals and the tasks of the work, and alongside it the patient's expectancy and hope, the therapist's empathy and warmth, and the patient's own motivation and life circumstances. The particular method contributes too, but it is one factor among several. This is why the quality of the relationship is attended to first in every modality, and why a shared, credible rationale matters as much as the technique itself.

1.1 What psychotherapy is, and is not

A treatment by psychological means, not merely a kind conversation. The durable definition is Wolberg's: psychotherapy is the treatment, by psychological means, of problems of an emotional nature, in which a trained person deliberately establishes a professional relationship with the patient with the object of removing, modifying or retarding existing symptoms, of mediating disturbed patterns of behaviour, and of promoting positive personality growth and development (Wolberg, Technique of Psychotherapy). Three clauses in that sentence are examinable in their own right. **By psychological means** separates psychotherapy from pharmacological and physical treatments: the agent of change is a psychological process (learning, insight, emotional processing, a corrective relationship), not a molecule. **A trained person and a professional relationship** separate it from the genuine but unstructured support of friends, clergy or family: it is deliberate, contracted and bounded. **The stated objects**, from symptom removal at the modest end to personality growth at the ambitious end, foreshadow the depth axis of the classification below.

RULE **The medium is psychological, the relationship is professional and deliberate.** If the agent of change is a drug or a device, or the helper is untrained and the relationship social rather than contracted, it is not psychotherapy, however therapeutic it feels.

1.2 The classification of psychotherapies: four axes, not one

Any therapy is located, not labelled. There is no single correct taxonomy; a given therapy is placed simultaneously on four independent axes, and a clean exam answer names the axis before the category (Kaplan and Sadock CTP 2024; Wolberg). The **depth (or goal) axis** is Wolberg's classical tripartition and the one most often examined: supportive therapy bolsters existing defences and coping without probing, re-educative therapy targets conscious attitudes and

behaviour to build new adaptive patterns, and reconstructive therapy works with unconscious conflict to remodel the personality structure itself. The **school (or theory) axis** sorts by the model of the mind that drives the technique, and is developed as the psychotherapy-family tree below. The **duration axis** runs from brief, time-limited work (often fewer than about twenty-five sessions, with a focal contract) to long-term or open-ended therapy. The **format axis** is defined by who is in the room: individual, group, couple or family. A single named therapy carries a coordinate on each: dialectical behaviour therapy, for instance, is re-educative in depth, cognitive-behavioural and third-wave in school, long-term in duration, and combines individual with group formats.

AXIS	CATEGORIES	THE EXAM HANDLE
Depth / goal (Wolberg)	Supportive; re-educative; reconstructive	**Supportive props up defences; reconstructive remodels the personality via the unconscious**
School / theory	Psychodynamic; behavioural; cognitive and cognitive-behavioural; humanistic and experiential; systemic and family; third-wave	**The model of the mind dictates the technique (the family tree)**
Duration	Brief and time-limited; long-term and open-ended	**Brief work carries a focal contract; most guideline therapies are time-limited**
Format	Individual; group; couple; family	**Defined by who is in the room, not by the theory used**

The four independent axes onto which every named psychotherapy is located; a therapy carries one coordinate on each (Kaplan and Sadock CTP 2024; Wolberg). The psychotherapy-family tree in the accompanying figure expands the school axis.

TRAP **Treating "supportive" as a school.** Supportive is a position on the depth axis, not a theoretical school; a supportive stance can be delivered from a psychodynamic, cognitive or humanistic base. Naming the axis first stops this error.

1.3 The schools of psychotherapy and the "three forces"

Six families, and the master mnemonic for the chapter. The school axis is the psychotherapy-family tree, and the six families it branches into organise the specific-modality topics that follow (Kaplan and Sadock CTP 2024; New Oxford Textbook). A useful historical overlay is the "three forces" of psychology: the **first force** is the psychoanalytic and psychodynamic tradition (Freud and successors, working with the unconscious); the **second force** is behaviourism (learning theory, exposure and contingency); and the **third force** is the humanistic and experiential movement (Rogers and the existentialists, working with the here-and-now, meaning and self-actualisation). The cognitive and cognitive-behavioural school then bridges the second force into the modern mainstream, the systemic and family school shifts the unit of treatment from the person to the relationship, and the third-wave therapies (dialectical behaviour therapy, acceptance and commitment therapy, mindfulness-based cognitive therapy) add acceptance,

mindfulness and dialectics to the cognitive-behavioural core. The accompanying figure draws the tree from these six trunks to their named modalities.

MNEMONIC

PLEASE BRING CARE, HOPE, SUPPORT, TRUST

The chapter's master mnemonic for the six **schools of psychotherapy**, read in order of the family tree: **P**sychodynamic, **B**ehavioural, **C**ognitive (and cognitive-behavioural), **H**umanistic (and experiential), **S**ystemic (and family), **T**hird-wave. The phrase is chosen so its meaning, care, hope, support and trust, is itself the payload of the common-factors half of this topic; the modality-specific mnemonics later in the chapter hang off these six trunks.

1.4 The common (non-specific) factors and their share of the outcome

What the therapies share matters more than what divides them. The **common factors** are the ingredients present in every bona fide therapy regardless of school, and the central empirical claim of the field is that these **non-specific factors** account for a larger portion of the improvement than the specific techniques do (Wampold, 2001; Tasman). Jerome Frank's classic analysis distilled the shared features to four: an emotionally charged, confiding relationship with a helping person; a healing setting; a credible rationale or conceptual scheme that explains the distress; and a ritual or procedure, believed by both parties, that requires the patient's active participation (Frank and Frank, Persuasion and Healing). Meta-analytic estimates converge on the same message: the therapeutic relationship and the other common factors carry roughly one-third to one-half of the therapeutic gain, far exceeding the modest and often statistically fragile increment attributable to any one school's signature technique (Tasman; Wampold). This is not an argument that technique is worthless; it is an argument that a credible technique delivered inside a strong relationship, by a therapist the patient trusts, is doing most of its work through channels every therapy shares. The accompanying figure sets the alliance at the centre of these shared ingredients.

RULE **Common factors outweigh specific factors.** Across bona fide therapies, the alliance and the other non-specific factors account for a larger share of outcome than the branded technique; the technique still matters, but chiefly as a credible vehicle for the shared ingredients.

FRANK'S FOUR COMMON INGREDIENTS OF EVERY PSYCHOTHERAPY

An emotionally charged, **confiding relationship** with a helper; a **healing setting**; a plausible **rationale or myth** that names the problem; and a **ritual or procedure** both believe in and that demands the patient's active participation. Any effective therapy, from psychoanalysis to a village healer's rite, can be read off these four (Frank and Frank).

1.5 The therapeutic alliance: the bond, the goals and the tasks

The single best-evidenced common factor. Of all the non-specific factors, the **therapeutic alliance** is the most robust and most replicated predictor of outcome, and it is the one to be able to define precisely (Horvath and Luborsky; Tasman). Bordin's tripartite model is the standard

answer: the alliance is the sum of three components, the **bond** (the affective attachment of trust, respect and warmth between patient and therapist), agreement on the **goals** of therapy (a shared view of what the work is for), and agreement on the **tasks** (a shared view of how the work will be done and each party's role in it). The clinically useful part of Bordin's model is that it is pan-theoretical and it is negotiated: a rupture in any of the three, a break in the bond, a drift in goals, or disagreement about a task such as a homework assignment or an exposure exercise, damages outcome and must be repaired explicitly rather than pushed through. The alliance is measurable (for example on the Working Alliance Inventory) and, importantly, an early alliance predicts later improvement more than early improvement predicts the alliance, which is part of why it is read as an active ingredient rather than a by-product of getting better.

BORDIN'S THREE COMPONENTS OF THE ALLIANCE

Bond, the affective tie of trust and mutual respect; **goals**, agreement on the aims of the work; **tasks**, agreement on the methods and each person's role. Hold "bond, goals, tasks" as a single unit; a viva favourite is to ask for the components by name and for what happens when one ruptures (repair, do not override).

1.6 Expectancy, therapist and client factors

The rest of the shared machinery. Beyond the alliance sit three further common factors, and a complete answer names all four groups. **Expectancy and hope** (the remoralisation Frank called the antidote to demoralisation) is the patient's belief that the treatment can help, the psychotherapy cousin of the placebo response and a genuine active ingredient rather than an artefact to be subtracted away. **Therapist factors** are the reliable finding that some therapists get consistently better results than others across techniques, mediated by empathy, warmth, positive regard and the capacity to form and repair alliances; the person of the therapist is itself a variable. **Client and extratherapeutic factors**, the patient's motivation, ego strength, social support and the ordinary life events that unfold outside the room, carry a large part of the change and are the reason the same therapy helps one patient far more than another. In Lambert's widely-cited apportionment of the outcome, client and extratherapeutic factors take the largest slice, the therapeutic relationship the next, with expectancy and specific technique smaller and roughly comparable; the exact percentages are contested, but the rank order (client, then relationship, then expectancy and technique) is the durable teaching point.

TRAP **Equating "non-specific" with "inert".** Non-specific factors are shared, not weak; expectancy, alliance and therapist effects are active ingredients with large effects. Calling them "just placebo" and discounting them is the error the common-factors literature exists to correct.

1.7 The transtheoretical model and the five stages of change

A stage map of readiness that cuts across every school. The **transtheoretical model** of Prochaska and DiClemente describes behaviour change as a movement through a sequence of **stages of change**, and its clinical value is that it tells the therapist to match the intervention to the patient's readiness rather than pushing action on someone not yet ready to act (Prochaska and DiClemente; Kaplan and Sadock CTP 2024). The five core stages are **precontemplation** (no

intention to change, often unaware of the problem or attending under pressure), **contemplation** (aware a problem exists and weighing change but not yet committed), **preparation** (intending to act soon, often taking small first steps), **action** (overt behaviour change is underway), and **maintenance** (consolidating gains and preventing relapse). Change is a spiral, not a straight line: **relapse** returns the person to an earlier stage, from which they recycle through the sequence rather than starting from zero, and most people cycle several times before durable change. Some versions add a final **termination** stage where the change is complete and relapse no longer threatens. The model underpins motivational interviewing, whose stage-matched, ambivalence-resolving style is developed for substance use in the Substance use disorders notes.

STAGE	THE PATIENT'S POSITION
Precontemplation	**No intention to change; often unaware, or attending under external pressure**
Contemplation	**Aware of the problem, ambivalent, not yet committed to act**
Preparation	**Intends to act soon; taking small preparatory steps**
Action	**Overt behaviour change actively underway**
Maintenance	**Consolidating gains and guarding against relapse**

The five stages of the transtheoretical model; relapse returns the patient to an earlier stage and they recycle through the sequence (Prochaska and DiClemente).

TRAP **Prescribing action to a precontemplator.** Handing an action-stage plan to a patient who does not yet accept there is a problem breeds resistance; the model's whole point is to meet the patient at the stage they are in and move them one step, not to leap to action.

1.8 The evidence hierarchy, empirically-supported treatments and the dodo-bird debate

How confident may a guideline be. The **evidence hierarchy** ranks the strength of the evidence behind a recommendation, from the weakest (case reports, uncontrolled series and expert opinion) up through non-randomised and randomised controlled trials to the strongest (systematic reviews and meta-analyses of trials), with clinical practice guidelines such as those of NICE and the Indian Psychiatric Society sitting on top as the applied synthesis (Kaplan and Sadock CTP 2024). Out of this tradition grew the idea of empirically-supported treatments, therapies that have demonstrated efficacy for a specific disorder in properly controlled trials, typically manualised and replicated (the American Psychological Association Division 12 criteria); this is the logic behind every "first-line psychotherapy for X" claim in the modality topics that follow, and it is why cognitive behaviour therapy, the most-trialled therapy, is recommended across the widest range of disorders. Against this specificity sits the dodo-bird verdict, named by Rosenzweig in 1936 from the dodo's ruling in Alice in Wonderland that "everybody has won and all must have prizes": the claim, supported by the common-factors reading of the outcome data, that all bona fide psychotherapies produce broadly equivalent results. The verdict is genuinely contested rather than settled: some meta-analyses find a specific

therapy superior for a specific condition (Kaplan and Sadock note a meta-analysis in which cognitive behaviour therapy outperformed other bona fide treatments), so state it as a live debate, not a fact, and let the disorder-specific evidence in each modality topic adjudicate.

RULE **State the dodo-bird verdict as a debate.** "All therapies are equivalent" is a contested hypothesis, not an established finding; the guideline evidence still names specific first-line therapies for specific disorders, and the safe exam line acknowledges both the strong common factors and the residual specific effects.

3	6	5	11
WOLBERG DEPTH LEVELS (SUPPORTIVE, RE-EDUCATIVE, RECONSTRUCTIVE)	SCHOOLS IN THE PSYCHOTHERAPY-FAMILY TREE	STAGES OF CHANGE (TRANSTHEORETICAL MODEL)	YALOM'S THERAPEUTIC FACTORS (DEVELOPED UNDER GROUP THERAPY)

INDIA

The classification and the common factors are examined from the Indian syllabus directly. The Indian Psychiatric Society has published a dedicated clinical practice guideline on the psychotherapies (Agarwal, Nischal, Praharaj, Menon and Kar; Indian Journal of Psychiatry 2020), and it embeds psychotherapy recommendations across its disorder-specific guidelines, so "which psychotherapy, and on what evidence" is a live examinable question here, not a Western import. The common-factors frame also carries a genuine Indian point: because the alliance, a credible rationale and the mobilisation of hope are what travel across cultures, the guideline emphasis on culturally-congruent, often family-inclusive delivery, and the developing evidence base for culturally-adapted cognitive behaviour therapy, is not a dilution of technique but an attempt to strengthen exactly these shared ingredients. Yoga and meditation-based interventions sit at the adjunct level of the evidence, not as stand-alone first-line treatments.

GOOD TO REMEMBER

- **The classification of psychotherapies (the principle):** four independent axes, depth (Wolberg's supportive, re-educative and reconstructive), school (the six families of the psychotherapy-family tree), duration (brief and time-limited versus long-term) and format (individual, group, couple, family). Locate a therapy on each axis; the one discriminator to hold is that supportive is a depth level, not a school.
- **The common factors (the principle):** the non-specific ingredients shared by all bona fide therapies, chiefly the therapeutic alliance (Bordin's bond, goals and tasks), expectancy and hope, therapist factors and client and extratherapeutic factors, account for a larger share of outcome than the specific technique (Wampold; roughly one-third to one-half for the relationship and common factors). The one exam fact is that non-specific does not mean inert.

HOLD THIS

Every psychotherapy is located on four axes (depth, school, duration, format), the six schools branch from the psychotherapy-family tree (PLEASE BRING CARE, HOPE, SUPPORT, TRUST), and the common (non-specific) factors, above all the therapeutic alliance of bond, goals and tasks (Bordin), carry more of the outcome than any branded technique (Wampold), which is why the dodo-bird verdict of broad equivalence is debated rather than dismissed.

2 · Supportive psychotherapy

This opens the psychotherapies chapter with the therapy you will actually practise most, on the ward round, in the emergency room, in the follow-up clinic and beside the medically ill: **supportive psychotherapy**. It is the commonest psychological treatment in real-world psychiatry and the default relational stance of all good general care, yet it is the one candidates most often under-prepare, because it looks like "just talking". It is not. It is a definable modality with an explicit stance, a named set of techniques and a defined aim, and the examiner tests exactly those three: the **ego-supportive** rather than ego-exploratory stance, the technique list, and the fact that its goal is to *maintain or restore* functioning, never to remodel the personality.

How to use this page. Fix the one defining contrast first, that supportive work bolsters defences and coping while expressive, insight-oriented work uncovers and interprets them; then learn the aim, then the technique list (the marks live here), then the two poles of indication (very low ego strength at one end, an acutely overwhelmed but ordinarily healthy person at the other). Ground every evidence claim carefully: supportive psychotherapy is broadly useful and performs surprisingly well as a comparator, but it is a guideline first-line stand-alone treatment in only a few specific, manualised roles, so do not overstate it.

2.1 The ego-supportive stance: bolstering defences, not uncovering them

Support the ego rather than explore it. The defining feature of supportive psychotherapy is that it is **ego-supportive**, not ego-exploratory (Kaplan and Sadock CTP 2024; Tasman). Expressive or insight-oriented therapies deliberately loosen defences and interpret unconscious conflict and transference to produce insight and structural change; supportive therapy does the opposite, working to *shore up* the patient's existing defences, self-esteem, reality testing and coping so they can withstand illness, deficit and life stress without decompensating. The two sit on a single expressive-supportive continuum: every real therapy blends the two, and the clinician slides toward the supportive pole exactly as the patient's ego strength falls. It is deliberately non-interpretive and stays in the here and now, addressing present interpersonal and environmental challenges rather than reconstructing the past. Its lineage is old, traceable to the eighteenth-century moral treatment of Pinel, which first held that a consistent, humane, containing relationship is itself therapeutic.

RULE **Ego-supportive, not ego-exploratory.** Supportive psychotherapy strengthens defences, coping and reality testing; expressive, insight-oriented therapy uncovers and interprets them. When ego strength is low, you move toward the supportive pole.

2.2 The aim: maintain or restore functioning, not structural change

Best possible functioning given the illness and the circumstances. The goal is explicit and examinable: to restore or maintain the patient's best possible level of functioning, given the constraints of the illness and the situation, and to prevent decompensation and regression (Tasman). It is a modest, honest aim. The therapist works to maintain the current level of psychological functioning, restore premorbid adaptation where that is possible, enhance coping mechanisms, strengthen adaptive defence mechanisms (leaving alone only those that are frankly

maladaptive) and support reality testing. What it does *not* set out to do is produce structural personality change or deep insight; symptom relief and better adaptation, not remodelling of the personality, are the currency of success. This distinction was tested directly by the Menninger Psychotherapy Research Project, a longitudinal study spanning twenty-three years (Kaplan and Sadock CTP 2024; Gabbard puts Wallerstein's follow-up of the 42 patients at thirty years) that compared classical psychoanalysis, psychoanalytic psychotherapy and a supportive arm; it found no significant differences among them, that supportive elements accounted for much of the change seen in all three, and that improvement did not occur in proportion to insight. The verdict quietly rehabilitated supportive work as a bona fide therapy rather than a second-best.

2.3 The core techniques

A named toolkit, all delivered inside a warm alliance. The techniques of supportive psychotherapy are concrete and must be reproducible on demand; they are limited only by the clinician's creativity, but the classic core is the following (Kaplan and Sadock CTP 2024; Wolberg). Note that each is a deliberate move, not an accident of kindness, and all are most effective when carried inside a positive therapeutic alliance.

Reassurance

Correcting distorted, catastrophic fears with realistic, credible information; genuine only when grounded in the facts of the case, never empty comfort.

Ventilation and catharsis

Allowing the patient to pour out pent-up feelings in a safe, accepting space, which relieves tension and, of itself, is often experienced as help.

Explanation and guidance

Explaining symptoms and situations so they feel comprehensible and less alien, then offering direct guidance and advice on concrete real-life problems.

Encouragement and praise

Instilling hope and recognising effort and small gains, which lifts self-esteem; over time the patient may introject the therapist's acceptance ("lending ego").

Advice and environmental manipulation

Actively changing external stressors, through significant others, employers or helping agencies, so the load on a fragile ego is reduced.

Ego-strengthening

Reinforcing adaptive defences and building coping and self-soothing skills, so the patient can regulate distress without acting out.

The therapeutic relationship

The consistent, predictable, caring relationship is itself the treatment, the vessel that carries every other technique.

MNEMONIC

GRACE

Hold the technique set as **GRACE**, carried by the relationship. **G**uidance and explanation; **R**eassurance; **A**dvice and environmental manipulation; **C**atharsis, that is ventilation of feelings; **E**ncouragement, praise and ego-strengthening. All five are delivered *through* the therapeutic relationship, which is why the alliance is listed as a technique in its own right, not just a backdrop.

GOOD TO REMEMBER

- **The technique set (GRACE):** guidance and explanation, reassurance, advice and environmental manipulation, catharsis (ventilation), and encouragement, praise and ego-strengthening, all delivered inside the therapeutic relationship. The single point to hold is that reassurance is credible only when grounded in the facts, and that the relationship is itself a technique, not merely the setting.

2.4 The relationship and the corrective emotional experience

A positive transference, deliberately maintained, is the cornerstone. Where expressive therapy analyses the transference, supportive therapy manages it: the therapist works to maintain a *positive* transference and, when the alliance is strained, repairs the rupture by actively providing comfort and reassurance rather than by interpreting it (Kaplan and Sadock CTP 2024). The healing mechanism was named by Franz Alexander as the corrective emotional experience: the patient re-lives difficult feelings within an accepting, nurturant relationship and emerges changed by that experience of being contained, without needing insight to have caused it. The therapist's style is therefore conversational and warm, not a blank screen; the long anxiety-provoking silences of analytic work are avoided. Confrontation, in the technical sense of gently holding a mirror to a self-defeating pattern, is available but only where the alliance is strong enough to carry it, and it is delivered in an accepting, never a stern, manner.

PEARL

The alliance is not just a nicety here, it is the active ingredient. The therapeutic alliance is the factor most consistently correlated with good outcome across every therapy, patient type and country, and in supportive work it is deliberately cultivated and protected. This is why supportive psychotherapy delivered by non-specialists, including nurses and family physicians, still works: the powerful common factor, a trusted relationship, is precisely what it maximises.

2.5 Supportive versus expressive, insight-oriented therapy

The same continuum, opposite ends. The cleanest way to hold supportive therapy is against its expressive, insight-oriented counterpart, remembering that real treatments mix the two and shift with the patient's capacity. The contrast is drawn below.

DIMENSION	SUPPORTIVE (EGO-SUPPORTIVE)	EXPRESSIVE, INSIGHT-ORIENTED (EGO-EXPLORATORY)
Aim	Maintain or restore best possible functioning	**Insight and structural personality change**
Stance to defences	Strengthen and support adaptive defences	**Loosen and interpret defences**
Transference	Kept positive, managed, repaired	**Analysed and interpreted, allowed to regress**
Interpretation	Minimal, non-interpretive	**Central, the main lever of change**
Time frame	Here and now, present problems	**Past and unconscious roots of the present**
Suited to	Lower ego strength; acute crisis	**Higher ego strength, psychological mindedness**

The supportive versus expressive contrast along one expressive-supportive continuum; the clinician slides toward the supportive pole as ego strength falls (Tasman; Kaplan and Sadock CTP 2024).

TRAP **Treating "supportive" as doing nothing, or as inferior therapy.** Supportive psychotherapy is a defined modality with explicit techniques and aims, not the absence of technique; the old jibe that "if it is supportive it cannot be psychotherapy" was overturned by the Menninger findings.

2.6 Indications for supportive psychotherapy

Two poles, both defined by a temporarily or chronically overwhelmed ego. The **indications for supportive** psychotherapy fall at two ends of a range (Tasman). At one pole sit patients with *low ego strength*, whose difficulties are better understood as chronic deficits than as neurotic conflict to be interpreted: severe and chronic mental illness such as schizophrenia and bipolar disorder, marked personality pathology with poor impulse control, cognitive deficit, poor psychological mindedness, low frustration tolerance and thin social support; interpreting such a patient would overwhelm rather than help. At the other pole sit ordinarily well-functioning people who have been acutely swamped by an external blow, that is an acute crisis, grief or bereavement, natural disaster, physical illness, or physical or sexual assault, where the ego is temporarily overloaded and needs holding until it recovers. Physical illness is a distinct and important indication, both because the medically ill are frequently distressed and because the psychiatrist meets them in consultation-liaison and general-hospital work. Underlying all of it is the broadest indication of all: supportive technique is the default relational stance of every good general psychiatric contact.

INDICATION	WHY SUPPORTIVE FITS	THE DISCRIMINATOR
Acute crisis and grief	Ego temporarily overwhelmed; needs holding to recovery	**Previously healthy person, external precipitant**
Chronic, severe mental illness	Bolsters coping and reality testing, prevents relapse	**Deficit-based, not conflict-based; interpretation would destabilise**
Low ego strength or personality pathology	Strengthens defences the patient cannot yet do without	**Poor impulse control, low frustration tolerance, thin support**
Physical illness	Sustains the person through the burden of the illness	**Distress and coping, not a primary psychiatric disorder**
General psychiatric care	The universal relational stance of good practice	**Applies to almost every patient as a baseline**

The two-pole indication map: chronically low ego strength at one end, acute overwhelming of a healthy ego at the other (Tasman; Kaplan and Sadock CTP 2024).

WORKED EXAMPLE

A previously well woman is referred a fortnight after her husband's sudden death: tearful, sleepless, unable to face the house, but with intact reality testing and no psychiatric history. The move here is not to interpret or to reach for a drug, but supportive: build the alliance, allow ventilation of grief, offer reassurance that her reactions are a normal response to loss (explanation), mobilise family and practical help (environmental manipulation) and encourage a graded return to routine. Held over a handful of sessions across the coming weeks, most such patients recover without ever needing an exploratory therapy.

2.7 The evidence base and the few guideline-anchored roles

Broadly useful, but a guideline first-line only in specific, manualised roles. The evidence picture is honest and examinable: supportive psychotherapy has a thin specific-efficacy trial base and has most often been studied as the comparator or "treatment as usual" arm, yet it repeatedly performs as well as the specialised therapy it was meant to lose to, precisely because it delivers the powerful common factors (alliance, empathy, positive regard). Its confirmed guideline roles are mostly adjunctive or context-dependent, with one manualised exception. Specialist supportive clinical management (SSCM), a manualised supportive approach, is one of three first-line options for adults with anorexia nervosa (NICE 2017, grade A). Supportive psychotherapy is an add-on once acute symptoms settle in schizophrenia (IPS_CPG 2017, grade B), and a substitute where CBT is not feasible in inhalant use disorder (IPS_CPG 2018). Non-directive supportive therapy is an option for mild-to-moderate depression in patients who decline pharmacotherapy and cannot access first-line psychotherapies (VA_DOD 2022). The one caution to memorise runs the other way: NICE explicitly advises *against* routinely offering supportive therapy for social anxiety disorder (NICE 2013), where structured CBT is the gold standard. The interpersonal and cognitive therapies that outrank it in mood and anxiety disorders are covered in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes; the structured therapies that take precedence in personality disorder are covered in the Personality disorders notes.

23	1984	3
YEARS SPANNED BY THE MENNINGER PSYCHOTHERAPY STUDY (CTP 2024)	WERMAN PUBLISHES THE FIRST SUPPORTIVE-THERAPY TEXTBOOK	FIRST-LINE OPTIONS FOR ADULT ANOREXIA; SSCM IS ONE (NICE 2017)

INDIA

Supportive and brief, motivation-based approaches are the mainstay the Indian Psychiatric Society endorses for older adults with alcohol use, delivered in a deliberately non-judgmental and non-confrontational style (IPS_CPG 2018), a good fit for the family-embedded, help-seeking-averse presentations common in Indian practice. The IPS has also published a dedicated Clinical Practice Guideline on psychotherapies (Agarwal, Nischal, Praharaj, Menon, Kar; Indian J Psychiatry 2020), within which supportive and brief techniques are treated as the accessible, generalist-deliverable backbone of psychosocial care rather than as a specialist product. The motivational-interviewing style that carries this work in the addictions is developed in the Substance use disorders notes.

GOOD TO REMEMBER

- **Supportive psychotherapy (the modality):** an ego-supportive, non-interpretive therapy that maintains or restores the best possible functioning by strengthening defences and coping, never aiming at structural personality change. Its lead guideline first-line role is specialist supportive clinical management (SSCM), one of three first-line treatments for adults with anorexia nervosa (NICE 2017, grade A); elsewhere it is adjunctive or the accessible default. The one technique to name is reassurance, delivered credibly inside a deliberately maintained positive therapeutic alliance.

HOLD THIS

Supportive psychotherapy is EGO-SUPPORTIVE, not ego-exploratory: it bolsters defences, coping and reality testing to maintain or restore the best possible functioning, and it never sets out to produce structural personality change; its techniques are guidance, reassurance, ventilation, advice and environmental manipulation, encouragement and ego-strengthening, all carried by a deliberately positive alliance (Alexander's corrective emotional experience), and its indications run from chronically low ego strength (severe chronic illness, marked personality pathology) to an acutely overwhelmed but ordinarily healthy ego (crisis, grief, physical illness), with SSCM for adult anorexia nervosa (NICE 2017, grade A) as its clearest guideline first-line role.

3 · Cognitive behaviour therapy

Cognitive behaviour therapy (CBT) is the single most examined psychotherapy in this paper, and for good reason: it is the reference-standard, best-evidenced psychological treatment, recommended first-line across the widest range of disorders, and its machinery, a small set of ideas about how thought, emotion and behaviour interlock, is elegant enough to test in a one-line viva and deep enough to fill a long essay. Derived by Aaron Beck from his work on depression in the nineteen-sixties, and drawing the behavioural half of its name from the learning-theory tradition, CBT is *structured, time-limited, present-focused, problem-oriented and collaborative*. Fix those five adjectives first; every technique below is a way of enacting them.

How to use this page. Learn the **cognitive model** as a causal chain, then the three levels of cognition that sit along it, then Beck's cognitive triad and the catalogue of cognitive distortions

that populate depressive thinking. Only then move to the doing of therapy, the cognitive and behavioural techniques, the shape of a single session and the arc of the whole course. Close on the evidence, because the examinable payoff of CBT is not a clever technique but the sentence "first-line, strongest evidence, widest range". The cardinal error the page is built to prevent is treating CBT as vague, insight-seeking talk; it is the opposite, a manualised, agenda-driven, homework-carrying method.

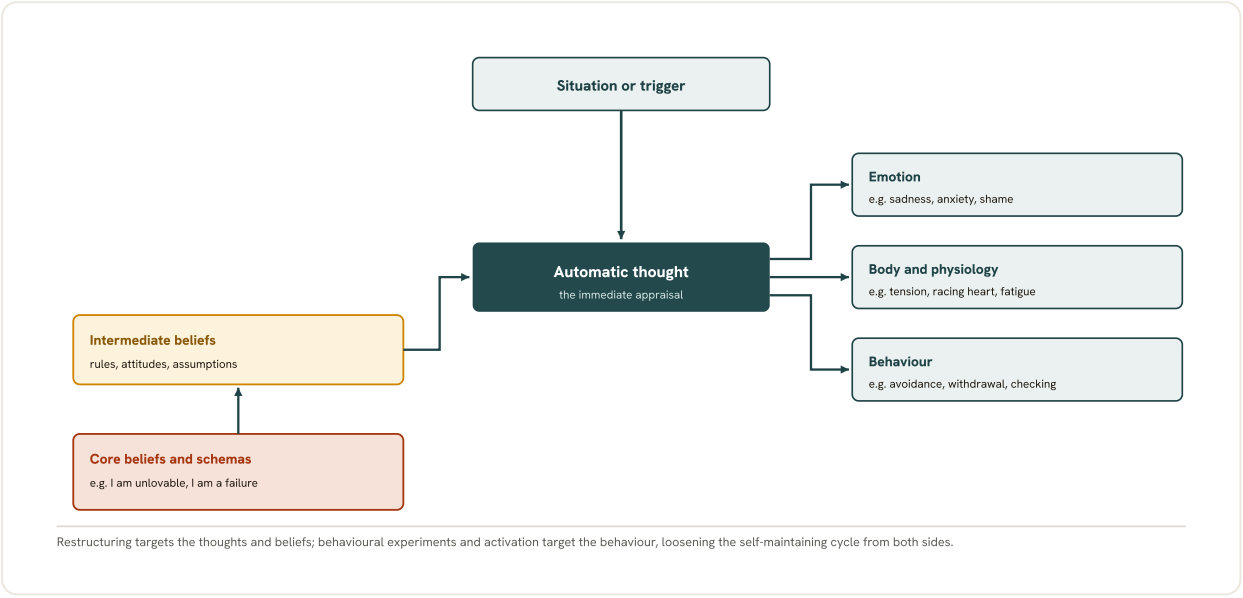


Fig 19.3 The cognitive model of CBT. A situation does not cause the feeling directly; it is the automatic thought, the immediate and often unnoticed appraisal, that drives the emotional, bodily and behavioural response. Those automatic thoughts are shaped by deeper layers: the intermediate beliefs (the rules, attitudes and assumptions a person lives by) and, beneath them, the core beliefs or schemas about the self, others and the world. The response in turn tends to confirm the belief, closing a self-maintaining cycle. Therapy enters at two points: cognitive restructuring tests and revises the thoughts and beliefs, while behavioural experiments and activation change the behaviour, each loosening the cycle from its own side.

3.1 The cognitive model: the situation is not the feeling

A situation triggers a thought, and the thought, not the situation, drives the response. The cognitive model is the foundational proposition of CBT: it is not events themselves but our *interpretation* of events that determines how we feel and act (Beck; Kaplan and Sadock CTP 2024). A situation activates an immediate, involuntary appraisal, the automatic thought, and that appraisal then drives three responses that run in parallel, an *emotional* response (the felt mood), a *physiological* response (bodily arousal) and a *behavioural* response (what the person does or avoids). Because two people meeting the same event can feel and behave utterly differently, the difference must lie in the interpretation, and that is precisely the lever CBT reaches for. The chain is also a vicious cycle: the behavioural response, characteristically avoidance or withdrawal, feeds back to confirm the original thought, so the loop tightens unless it is interrupted. The accompanying figure lays out this chain, situation to automatic thought to the emotional, physiological and behavioural response, with the maintaining feedback arrow closing the loop.

RULE **Interpretation, not the event, is the target.** CBT works because the automatic thought sits causally between the situation and the response; change the appraisal and you change the emotion, physiology and behaviour that follow it.

3.2 The three levels of cognition

Surface thoughts, the rules beneath them, and the bedrock beliefs at the base. Cognition in CBT is stratified into three depths, and knowing which level a therapist is working at is a favourite discrimination question (Beck, CBT Basics and Beyond). At the surface are automatic thoughts, the fleeting, involuntary, situation-specific appraisals that stream through the mind and are the most accessible layer, the one the patient learns to catch first. Beneath them lie **intermediate beliefs**, the relatively enduring rules, attitudes and conditional assumptions ("If I am not perfect, I have failed") through which experience is filtered. At the base sit the core beliefs, the deepest, most global and absolute ideas a person holds about the self, others and the world; when these organise experience as stable cognitive structures they are called schema. Beck grouped depressive core beliefs about the self into three families, the helpless, the unlovable and the worthless. Therapy usually begins at the accessible surface, with automatic thoughts, and works downward only as trust and skill accumulate, because the deeper the belief, the more central and the more defended it is.

TRAP **Confusing an automatic thought with a core belief.** An automatic thought is surface, fleeting and tied to one situation ("I got that wrong"); a core belief is deep, global and absolute ("I am worthless"). Early CBT targets the former; schema-level work targets the latter.

3.3 Beck's cognitive triad

Three negative views that together generate depression. The cognitive triad is Beck's account of the content of depressive cognition, and it has exactly three components (Beck 1967; Kaplan and Sadock CTP 2024): a negative view of the *self* (defective, inadequate, unworthy), a negative view of the *world* and current experience (demanding, defeating, unfair), and a negative view of the *future* (hopeless, certain to continue). Each corner feeds the others, and together they bias information processing so that neutral or positive events are discounted while negative ones are magnified. The triad is the reason depression feels globally, not locally, bleak, and it is why the therapeutic task is to reverse all three negative views rather than argue a single point. Attribute the count precisely: **3** views, self, world and future, no more and no fewer.

PEARL

Hold the triad as **Me, My world, My future**, all seen through a dark lens. Self, world, future, three corners; the hopeless view of the future is the corner most tightly linked to suicidal thinking and so the one to probe hardest in a depressed patient.

3.4 The catalogue of cognitive distortions

Systematic errors of logic that keep the negative beliefs in business. Cognitive distortions are the habitual, biased styles of reasoning through which automatic thoughts are generated and the cognitive triad is maintained (Beck; Burns). They are the workhorse of the thought record, because naming the distortion in a thought is the first step to loosening it. Ten recur often enough to be worth holding verbatim.

All-or-nothing thinking

Also called black-and-white or dichotomous thinking; a situation is seen in only two categories rather than on a continuum ("If I am not a total success, I am a failure").

Catastrophising

Also called fortune-telling; predicting the future negatively without considering more likely outcomes ("I will be so upset I will not be able to function").

Overgeneralisation

Drawing a sweeping negative conclusion that goes far beyond the current situation ("Because I felt awkward once, I cannot make friends").

Mind-reading

Believing you know what others are thinking, failing to consider more plausible possibilities ("He thinks I am incompetent").

Personalisation

Believing others behave negatively because of you, without weighing more likely explanations for their behaviour.

Emotional reasoning

Taking a feeling as proof of fact, discounting evidence to the contrary ("I feel like a failure, therefore I am one").

Should-statements

Also called imperatives; a fixed idea of how you or others ought to behave, with overestimation of how bad it is when the expectation is not met.

Magnification / minimisation

Unreasonably magnifying the negative and minimising the positive when evaluating yourself, another or a situation.

Mental filter

Also called selective abstraction; dwelling on a single negative detail so that the whole picture is darkened by it.

Labelling

Attaching a fixed, global label to yourself or others ("I am a loser") rather than describing the specific behaviour.

MNEMONIC

CBT is deceptively simple

Group the ten as the errors of the pessimist: he sees in two colours (all-or-nothing), foretells disaster (catastrophising), stretches one bad moment to all of life (overgeneralisation), presumes what others think (mind-reading), takes the blame (personalisation), trusts the feeling over the facts (emotional reasoning), tyrannises himself with shoulds (imperatives), inflates the bad and shrinks the good (magnification and minimisation), reads only the dark detail (mental filter) and names himself by his worst act (labelling).

3.5 Cognitive restructuring and the thought record

The core cognitive technique, worked on paper. Cognitive restructuring is the process of identifying, evaluating and modifying maladaptive automatic thoughts, and its principal instrument is the thought record (also called the dysfunctional thought record or automatic thought record). A patient learns to log, across columns, the *situation*, the *emotion* and its intensity, the *automatic thoughts* that arose, the *evidence for and against* each thought, the specific *distortion* at work, a more balanced *adaptive response*, and finally a *re-rating* of the emotion. The point is not positive thinking but *accurate* thinking: the patient becomes a scientist gathering evidence about a hypothesis rather than a defendant asked to think happy thoughts. Restructuring is what most people picture when they picture CBT, and it is examinable both as a named technique and as a worked sequence.

WORKED EXAMPLE

A woman whose email to a colleague goes unanswered feels a sharp drop in mood. Her automatic thought is "She is ignoring me because I annoyed her" (mind-reading and personalisation). On the thought record she lists the evidence: the colleague is on leave, has replied late before, and said nothing critical at their last meeting. Her adaptive response, "She is probably away or busy, and I have no evidence she is angry", drops the intensity of her distress from high to mild. Nothing about the situation changed; only the appraisal did.

3.6 Socratic questioning, guided discovery and collaborative empiricism

The therapist asks rather than tells, and patient and therapist test beliefs together. CBT is not delivered by lecturing the patient out of their beliefs; it is delivered by Socratic questioning, a series of graded, curious questions ("What is the evidence? What is an alternative view? What would you tell a friend who thought this?") that lead the patient to examine a thought for themselves. The wider stance this serves is *guided discovery*: the therapist guides, but the patient discovers, so that conclusions are owned rather than imposed. Both sit inside the defining relational posture of the whole therapy, collaborative empiricism, in which therapist and patient work as a team of co-investigators, treating each belief as a hypothesis to be tested against evidence rather than a truth to be accepted or a falsehood to be corrected (J. S. Beck; Tasman). This collaborative, empirical stance is what distinguishes a CBT exchange from supportive reassurance on one side and from confrontation on the other.

3.7 The behavioural techniques

Change behaviour to change belief, and to change mood directly. The behavioural half of the therapy supplies several techniques, and their examinable distinctions matter. Behavioural experiments are planned, real-world tests of a specific belief: the patient makes a prediction ("If I speak up, I will be humiliated"), designs an experiment to test it, runs it, and compares the outcome with the prediction, so belief change is driven by lived evidence rather than by discussion alone. This is distinct from exposure, whose aim is the extinction of anxiety rather than the disproof of a cognition. Behavioural activation re-engages a withdrawn, depressed patient with rewarding and mastery-giving activity, breaking the withdrawal-low mood-further withdrawal loop, and it has strong stand-alone evidence in depression. *Activity scheduling*, the

planning of the week hour by hour with activities rated for pleasure and mastery, is the practical tool that delivers behavioural activation. *Graded exposure*, the stepwise confrontation of feared situations along a hierarchy, is the behavioural engine for the anxiety disorders. The graded-exposure and response-prevention protocols, and the trauma-focused work, are developed where they belong, in the Anxiety, OCD and trauma-related disorders notes.

DO NOT CONFUSE THESE

A **behavioural experiment** tests a *belief* and its yardstick is whether the prediction came true; **graded exposure** reduces *anxiety* and its yardstick is habituation along a hierarchy. Both involve approaching what is avoided, but one is a cognitive test and the other is an anxiety-extinction procedure. **Behavioural activation** is different again: it targets the *withdrawal* of depression, not anxiety, and is delivered through activity scheduling.

3.8 The structure of a session, and of the course

Every session follows the same shape, and the whole therapy is time-limited. The **session structure** is not incidental; adhering to a standard format is a defining feature that makes the therapy efficient and teachable (Beck, CBT Basics and Beyond). A typical session opens with a brief *mood check*, moves to collaboratively *setting the agenda*, *bridges from the previous session by reviewing the homework*, then does *the work* on the agenda items, sets *new homework* (the action plan) that flows from that work, and closes by eliciting *feedback* and a summary. Homework is not an optional extra: it is where the therapy is generalised into life, and completion of it predicts outcome. The course as a whole is short and structured; a standard acute course for depression runs to about **12** to 20 sessions over a four to five month period (Kaplan and Sadock CTP 2024), most sessions lasting roughly **45** to 50 minutes, with the first evaluation session usually longer. The aim throughout is to make the patient their own therapist, so that gains outlast the therapy.

MNEMONIC

M-A-B-W-H-F

The order of a CBT session: **M**ood check, **A**genda set, **B**ridge from the last session (review homework), **W**ork the agenda, new **H**omework assigned, **F**eedback elicited. Same shape every time, which is exactly why the therapy is called structured.

3	12-20	45-50
VIEWS IN BECK'S COGNITIVE TRIAD (SELF, WORLD, FUTURE)	SESSIONS IN A STANDARD ACUTE COURSE FOR DEPRESSION	MINUTES, STANDARD SESSION LENGTH

3.9 The evidence base and the lead indications

The most-evidenced psychotherapy, and first-line across the widest range. If one sentence about CBT must be exam-ready, it is this: CBT is the reference-standard evidence-based psychotherapy, with strong meta-analytic support and the broadest first-line reach of any psychological treatment (Beck; the guideline evidence). It is a first-line psychological treatment for major depressive disorder (IPS_CPG 2017 grade A; CANMAT 2016; NICE 2022; WHO mhGAP 2023) and for the anxiety disorders across the board, generalised anxiety disorder

(IPS_CPG 2020; NICE 2011), panic disorder (NICE 2011 grade A; CANMAT 2014) and social anxiety disorder, where it is the gold standard (NICE 2013; CANMAT 2014). It is the psychological treatment of choice for obsessive-compulsive disorder when delivered with exposure and response prevention (IPS_CPG 2025 Level 1; NICE 2005), for post-traumatic stress disorder as trauma-focused CBT (NICE 2018 grade A), and for chronic insomnia as CBT for insomnia, CBT-I (BAP 2019 grade A; NICE 2023). Beyond these it is a recommended *adjunct*, not a monotherapy, for psychosis (NICE 2014; IPS_CPG 2017 B) and bipolar disorder (IPS_CPG 2017 A), and it supports relapse prevention in alcohol use disorder (IPS_CPG 2014 A). The interpersonal-therapy and CBT evidence in depression, together with the depression rating scales, is carried in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes.

3.10 The disorder-specific CBT protocols

One method, many manualised protocols; name them, do not re-teach them. The strength of CBT is that its core method is tailored into disorder-specific packages, each with its own evidence and its own home chapter. *Exposure and response prevention* (ERP) is the specific behavioural CBT protocol for obsessive-compulsive disorder, in which the patient is exposed to the obsessional trigger while the compulsive response is prevented; it, and *trauma-focused CBT* for post-traumatic stress disorder, are developed in the Anxiety, OCD and trauma-related disorders notes. *CBT-I*, cognitive behaviour therapy for insomnia, combines stimulus control, sleep restriction, sleep hygiene and cognitive work on sleep-related beliefs, and is the first-line treatment for chronic insomnia ahead of hypnotics. CBT for psychosis targets distressing delusional and hallucinatory beliefs without disputing them head-on. The examinable move is to recognise each as a branded CBT protocol resting on the one cognitive model above, and to place it in its disorder rather than to describe it as a separate therapy.

GOOD TO REMEMBER

- **ERP, trauma-focused CBT and CBT-I (the branded protocols):** ERP is CBT for OCD (exposure plus prevention of the compulsion); trauma-focused CBT is CBT for PTSD; CBT-I is CBT for chronic insomnia (stimulus control, sleep restriction, cognitive work). All three are the one cognitive model tailored to a disorder, not new therapies; learn them in their own chapters.

3.11 CBT in the Indian setting

Guideline-endorsed and culturally adaptable, with realistic caveats. The Indian Psychiatric Society places CBT first-line across depression, generalised anxiety disorder, obsessive-compulsive disorder, somatic symptom disorder and, for relapse prevention, alcohol use disorder, both in its disorder-specific clinical practice guidelines and in its dedicated psychotherapies guideline (IPS_CPG 2020). Culturally adapted CBT, associated with Naeem and colleagues, modifies the content, language, idioms of distress, degree of family involvement and explanatory models for South Asian settings, and has feasibility and randomised-trial-level evidence for depression and psychosis; it is best framed as a promising adaptation with a developing evidence base rather than as a distinct guideline-endorsed therapy. The practical constraint in India is supply, not demand: trained CBT therapists are scarce relative to need, which is why guideline

attention has turned to brief, low-intensity and task-shifted delivery by non-specialist health workers.

INDIA

The IPS psychotherapies guideline (IPS_CPG 2020) and the disorder-specific CPGs make CBT the default first-line psychotherapy for the common disorders, but the workforce to deliver it is thin. Culturally adapted CBT (Naeem and colleagues) and community-delivered, non-specialist-led brief CBT are the realistic Indian answers; state both the guideline endorsement and the delivery gap, because an examiner who asks about CBT in India is usually testing whether you know the second half.

GOOD TO REMEMBER

- **Cognitive behaviour therapy (the therapy):** the model is that interpretation, not the event, drives emotion, physiology and behaviour, so identifying and modifying maladaptive automatic thoughts, intermediate beliefs and core beliefs changes the response; the lead indication is major depression and the anxiety disorders, where CBT is first-line and the best-evidenced psychotherapy of all; the one signature technique is cognitive restructuring via the thought record, delivered through collaborative empiricism.

HOLD THIS

CBT is structured, time-limited, present-focused and collaborative; its cognitive model holds that the automatic thought, not the situation, drives the emotional, physiological and behavioural response; Beck's cognitive triad has exactly three components (self, world, future); the therapy is delivered through cognitive restructuring, Socratic questioning and behavioural experiments within collaborative empiricism, on a fixed session structure of mood check, agenda, homework review, the work, new homework and feedback; and it is the most-evidenced psychotherapy, first-line across the widest range of disorders.

4 · Behaviour therapy

Behaviour therapy is the oldest of the empirically grounded psychotherapies and the one whose logic an examiner can test in a single line: it takes the laws of learning theory out of the animal laboratory and applies them, directly and without recourse to the unconscious, to observable maladaptive behaviour. Where psychoanalysis seeks buried meaning and cognitive therapy targets appraisal, behaviour therapy targets the behaviour itself, the antecedents that cue it and the consequences that maintain it, on the premise that what was learned can be unlearned. Two engines drive everything below, classical conditioning (Pavlov, applied to therapy by Wolpe) and operant conditioning (Skinner); fix which engine powers which technique and the whole topic becomes orderly.

How to use this page. Learn the two conditioning paradigms first, then the classical-conditioning techniques built on extinction of a conditioned fear, the exposure family and aversion, then the operant techniques built on reinforcement and its withdrawal, then the assessment method that precedes all of them, functional analysis. The single error this page is built to prevent is the cardinal viva trap of confusing **flooding** (maximal exposure, no hierarchy)

with **systematic desensitisation** (graded hierarchy, paired with relaxation). Get that discrimination clean and most of the marks are secured.

4.1 Learning theory: the two engines of behaviour therapy

Classical conditioning acquires the fear; operant conditioning maintains the avoidance. Classical conditioning, described by Pavlov, is learning by association: a neutral stimulus repeatedly paired with a stimulus that already produces a response comes itself to produce that response. Operant conditioning, formalised by Skinner in the nineteen-fifties and anticipated by Thorndike's law of effect, is learning by consequence: behaviour followed by a favourable consequence is strengthened, behaviour followed by an unfavourable one is weakened. The two combine in Mowrer's two-factor theory of fear, the conceptual backbone of the anxiety treatments: a phobia is first acquired by classical conditioning (a neutral object paired with a frightening event becomes a conditioned trigger) and then maintained by operant conditioning (avoiding the object removes the fear, and that relief negatively reinforces the avoidance, so the fear never extinguishes). Behaviour therapy works by breaking that second, maintaining loop.

Unconditioned stimulus (UCS)

A stimulus that naturally and without learning elicits a response (food evoking salivation).

Unconditioned response (UCR)

The unlearned, reflexive response to the UCS (salivation to food).

Conditioned stimulus (CS)

A previously neutral stimulus that, after repeated pairing with the UCS, comes to elicit the response (the bell).

Conditioned response (CR)

The learned response now produced by the CS alone (salivation to the bell).

Extinction (classical)

Weakening and loss of the CR when the CS is presented repeatedly without the UCS; the mechanism most exposure treatments exploit.

RULE **Behaviour, not insight, is the target.** Behaviour therapy applies learning theory to change observable behaviour and its contingencies directly; it does not require the patient to understand why the behaviour arose.

4.2 Systematic desensitisation: Wolpe's graded hierarchy and relaxation

A ladder of feared situations climbed one rung at a time while the body stays relaxed. Systematic desensitisation is the flagship classical-conditioning technique, devised by Joseph Wolpe, whose *Psychotherapy by Reciprocal Inhibition* (Wolpe, nineteen fifty-eight) grounded it in learning theory. It rests on reciprocal inhibition: if a response incompatible with anxiety is made to occur in the presence of the anxiety-provoking stimulus, the bond between that stimulus and anxiety is weakened, because a person cannot be deeply relaxed and anxious at the same instant (Wolpe; Companion to Psychiatric Studies). The relaxation is the incompatible response. The procedure has three classic steps: first, training in deep muscular relaxation; second, collaborative construction of an *anxiety hierarchy*, a rank-ordered list of feared situations from the least to the

most anxiety-provoking; third, graded pairing, in which the relaxed patient is exposed, in imagination or in vivo, to the lowest item until it evokes no anxiety, then to the next, ascending the hierarchy only as each rung is mastered. The lead indication is **specific phobia**, and exposure-based treatment of this kind is first-line for it (CANMAT 2014).

WORKED EXAMPLE

A student with a spider phobia is first taught progressive muscular relaxation. Together with the therapist she builds a hierarchy of roughly ten steps, from looking at a cartoon spider (mildly anxiety-provoking) to letting a live spider walk across her hand (the peak). Relaxed, she pictures the cartoon spider until it no longer disturbs her, then a photograph, then a spider in a jar across the room, moving up only when each rung has been neutralised. The anxiety attached to each image is inhibited by the relaxation with which it is paired, and the hierarchy is dismantled from the bottom up.

PEARL

Hold reciprocal inhibition as the one-line mechanism of systematic desensitisation: **relaxation and anxiety cannot coexist**, so pairing the feared item with relaxation drains the fear out of it. The hierarchy is graded and the pace is set by mastery, never by the clock.

4.3 Graded exposure, flooding and implosion: the exposure family

All expose the patient to what is feared; they differ in gradient and intensity. Graded exposure, typically delivered in vivo (in real life rather than imagination), is the modern workhorse: the patient confronts feared situations step by step along a hierarchy and remains in each until anxiety subsides, so that *habituation* and extinction of the conditioned response occur. Unlike systematic desensitisation it does not formally pair each step with trained relaxation; the therapeutic ingredient is staying in contact with the feared stimulus long enough for anxiety to fall of its own accord, which is why *response prevention*, blocking the escape or safety behaviour, is essential. At the opposite pole sits flooding: exposure that is immediate and maximal, beginning with the most feared item and holding the patient there, with no hierarchy and no gradual ascent, until the anxiety peaks and then habituates. Its imaginal cousin is implosion (implosive therapy, Stampfl), maximal exposure conducted entirely in imagination. The detailed exposure and response-prevention protocols for obsessive-compulsive disorder and the trauma-focused exposure work are developed in the Anxiety, OCD and trauma-related disorders notes.

TECHNIQUE	HIERARCHY	RELAXATION PAIRED	INTENSITY AND MODE	PROTOTYPE USE
Systematic desensitisation	Graded, least to most	Yes (reciprocal inhibition)	Gradual; imaginal or in vivo	Specific phobia
Graded exposure	Graded, least to most	No (habituation-based)	Gradual; in vivo	Agoraphobia, phobic and obsessional disorders
Flooding	**None; most-feared first**	No	Maximal; in vivo	Phobias, rapid treatment
Implosion (implosive therapy)	**None; most-feared first**	No	Maximal; imaginal	Phobic and anxiety disorders

The exposure family: systematic desensitisation is graded and relaxation-paired; flooding and implosion are maximal with no hierarchy.

TRAP **Flooding is not systematic desensitisation.** Flooding uses maximal exposure to the most-feared item with no hierarchy and no relaxation; systematic desensitisation is graded up a hierarchy and paired with relaxation. Swapping these two definitions is the single commonest behaviour-therapy error in the viva.

4.4 Aversion therapy and covert sensitisation

Pair the unwanted behaviour with something unpleasant so its pull declines. Aversion therapy is the classical-conditioning technique that runs in the opposite direction to exposure: instead of extinguishing an unwanted fear, it deliberately conditions an unwanted *attraction* to an aversive state by pairing the target behaviour with a noxious stimulus, classically a subthreshold electric shock or an emetic such as apomorphine. Its imaginal form is *covert sensitisation*, in which the patient repeatedly imagines the unwanted behaviour immediately followed by a vividly unpleasant consequence (nausea, disgust), so the pairing is rehearsed in the mind rather than in the body. Historically applied to alcohol dependence (disulfiram exploits the same aversive logic pharmacologically), to the paraphilias and to other appetitive problems, aversion therapy has fallen sharply out of routine use on both effectiveness and ethical grounds and now occupies a small, tightly consented niche. It is examinable chiefly as the counter-example that shows conditioning can build an aversion as readily as it can dissolve a fear.

4.5 The operant techniques: reinforcement, shaping, chaining, extinction, time-out

Change the consequences and you change the frequency of the behaviour. The operant half of behaviour therapy manipulates what follows a behaviour. Reinforcement always *increases* a behaviour and punishment always *decreases* it, and each comes in a positive form (a stimulus is added) and a negative form (a stimulus is removed). The two-by-two of consequences below is worth holding as a grid, because the label that trips candidates, negative reinforcement, is not punishment at all.

OPERANT CONSEQUENCE	INCREASES BEHAVIOUR	DECREASES BEHAVIOUR
Stimulus added	Positive reinforcement (praise, reward)	Positive punishment (aversive stimulus)
Stimulus removed	**Negative reinforcement (relief of an aversive state)**	Negative punishment (response cost, time-out)

The four operant consequences: reinforcement raises a behaviour, punishment lowers it; positive means add, negative means remove.

On this base sit the operant procedures used to build up or strip away behaviour.

Shaping

Building a new behaviour by reinforcing successive approximations to the target, rewarding ever-closer attempts until the full behaviour appears.

Chaining

Linking discrete learned behaviours into an ordered sequence, taught either forwards from the first step or backwards from the last.

Extinction (operant)

Withholding the reinforcer that has been maintaining a behaviour so that the behaviour gradually declines; expect a transient extinction burst first.

Time-out

Brief, contingent removal of the person from all sources of positive reinforcement following an unwanted behaviour; a form of negative punishment, widely used in child behaviour work.

Prompting and fading

Supplying a cue that triggers the desired behaviour, then gradually withdrawing the cue as the behaviour becomes independent.

> COMMON TRAP
>
> **Negative reinforcement is not punishment.** Negative reinforcement *removes* an aversive state and therefore *increases* the behaviour that ended it (taking a painkiller relieves pain, so pill-taking is reinforced). Punishment decreases behaviour. If the behaviour goes up, it was reinforcement, whatever was added or taken away.

4.6 The token economy and contingency management

Structured, ward-wide operant systems that reward adaptive behaviour on a schedule. The **token economy** is the most developed operant application, a structured contingency-management system devised by Ayllon and Azrin for chronic inpatient and rehabilitation settings. Tokens, functioning as secondary (conditioned) reinforcers exactly as money does, are earned immediately for specified target behaviours (self-care, attendance, participation) and later exchanged for backup reinforcers such as privileges or goods; the immediacy of the token bridges the delay to the real reward. Its classic home is the long-stay ward, chronic institutionalised schizophrenia with negative symptoms and self-care deficits, and intellectual disability and children's units. Its close relative, contingency management, delivers tangible incentives (typically vouchers) contingent on an objectively verified target such as a drug-negative urine screen, and is

a well-evidenced operant treatment in the addictions, developed in the Substance use disorders notes.

GOOD TO REMEMBER

- **Token economy (the technique):** the model is operant, a structured contingency-management system in which tokens act as secondary reinforcers earned for target behaviours and exchanged for backup reinforcers; the lead indication is chronic inpatient and rehabilitation settings (chronic institutionalised schizophrenia, intellectual disability); the one technique is immediate tokens redeemed later, attributed to Ayllon and Azrin.

4.7 Behavioural assessment and functional analysis

No technique is chosen until the behaviour has been analysed in context. Behaviour therapy begins not with a diagnosis but with a functional analysis, a systematic description of the problem behaviour together with the conditions that trigger and maintain it. The organising frame is the *ABC* sequence: the *Antecedents* that cue the behaviour, the *Behaviour* itself defined in observable, measurable terms (frequency, duration, intensity rather than inference), and the *Consequences* that follow and thereby reinforce or punish it. The clinician gathers this from interview, direct observation, self-monitoring diaries and rating scales, establishes a baseline, and only then designs an intervention aimed at the maintaining contingency, most often a consequence that is inadvertently reinforcing an unwanted behaviour. This functional, here-and-now analysis is what makes behaviour therapy a targeted procedure rather than a generic conversation, and the same measured behaviours provide the outcome data.

MNEMONIC

A-B-C

Functional analysis reads the behaviour in its context: **A**ntecedents (what cues it), **B**ehaviour (defined observably), **C**onsequences (what maintains it). Change the C, and the behaviour changes.

4.8 Social-skills and assertiveness training

Deficient interpersonal behaviours are taught the way any skill is taught. Where the problem is not an excess of anxiety or an unwanted habit but a *deficit* in interpersonal repertoire, behaviour therapy supplies *social-skills training* and its focused subset *assertiveness training*. Both use a standard behavioural teaching package, instruction and modelling of the target skill, rehearsal through role-play, corrective feedback and reinforcement of successful attempts, and homework to generalise the skill into real settings. Assertiveness training specifically builds the capacity to express needs, refuse unreasonable demands and stand up for oneself without aggression or passivity, and Wolpe regarded assertive responses as themselves reciprocally inhibiting of interpersonal anxiety. These methods are staples of the rehabilitation of chronic schizophrenia (remediating negative-symptom social withdrawal), of social anxiety, and of skills-building work across many conditions.

4.9 Indications, the evidence base and behaviour therapy in India

Robustly evidenced, above all as exposure for the phobic and obsessional disorders. The examinable summary is that behaviour therapy is strongly evidenced where a behaviour or a conditioned fear is the target, and that its techniques are also the active behavioural ingredients inside cognitive behaviour therapy. Exposure-based treatment is the first-line treatment of choice for *specific phobia* (CANMAT 2014), with applied muscle tension added for the blood-injection-injury type; graded exposure is recommended for *agoraphobia* (CANMAT 2014). Exposure and response prevention is a first-line acute psychological treatment for *obsessive-compulsive disorder* (BAP 2014 grade A; CANMAT 2014), and prolonged exposure is a recommended trauma-focused psychotherapy for *post-traumatic stress disorder* (NICE 2018; VA_DOD 2023), both carried in full in the Anxiety, OCD and trauma-related disorders notes. Behavioural activation, the operant-flavoured re-engagement technique, is a first-line psychological treatment for *major depressive disorder* (CANMAT 2016; IPS_CPG 2017 grade A) and is developed with the depression therapies. The token economy and contingency management hold their niche in chronic rehabilitation and the addictions respectively.

1958	2	3
WOLPE'S PSYCHOTHERAPY BY RECIPROCAL INHIBITION	FACTORS IN MOWRER'S TWO-FACTOR THEORY OF FEAR	STEPS OF SYSTEMATIC DESENSITISATION (RELAX, HIERARCHY, GRADED PAIRING)

INDIA

The Indian Psychiatric Society names behavioural activation among the strongest-evidence psychotherapies for depression in its depression guideline (IPS_CPG 2017), and its obsessive-compulsive disorder guidance places exposure and response prevention first-line. India also has a long institutional behaviour-therapy tradition, with behavioural and behavioural-medicine work established at NIMHANS; state the guideline endorsement confidently and frame the wider tradition as an established service history rather than citing a specific trial.

GOOD TO REMEMBER

- **Systematic desensitisation (the technique):** the model is classical conditioning via reciprocal inhibition (Wolpe), pairing a graded anxiety hierarchy with relaxation so fear cannot coexist with the relaxed state; the lead indication is specific phobia; the one technique is graded, relaxation-paired ascent of the hierarchy, contrasted sharply with flooding.
- **Behaviour therapy (the modality):** the model applies learning theory, classical and operant conditioning, to modify observable maladaptive behaviour and its contingencies directly; the lead indication is the phobic and obsessional disorders treated by exposure, with the token economy for chronic institutional behaviour; the one signature technique is graded exposure, the disciplined confrontation of the feared stimulus until anxiety extinguishes.

HOLD THIS

Behaviour therapy applies learning theory to observable behaviour: classical conditioning yields systematic desensitisation (Wolpe, a graded hierarchy paired with relaxation via reciprocal inhibition) and flooding (maximal exposure, most-feared first, no hierarchy), while operant conditioning yields reinforcement, shaping, extinction and the token economy (Ayllon and Azrin); exposure is first-line for specific phobia and, as response prevention, for obsessive-compulsive disorder.

5 · Psychoanalysis and psychodynamic psychotherapy

This is the oldest of the talking treatments and the one that gave the field its whole vocabulary: **unconscious conflict**, **transference**, defence, insight. Freud's psychoanalysis is rarely practised in its pure, five-times-a-week form in Indian psychiatry, yet the examiner returns to it every year, because its concepts underpin the mental status interview, the formulation, and every dynamic therapy that followed. What is tested is not the philosophy but the scaffold: the two models of the mind, the three clinical phenomena (transference, **counter-transference**, resistance), the named techniques, and the spectrum that runs from classical analysis down to brief dynamic work.

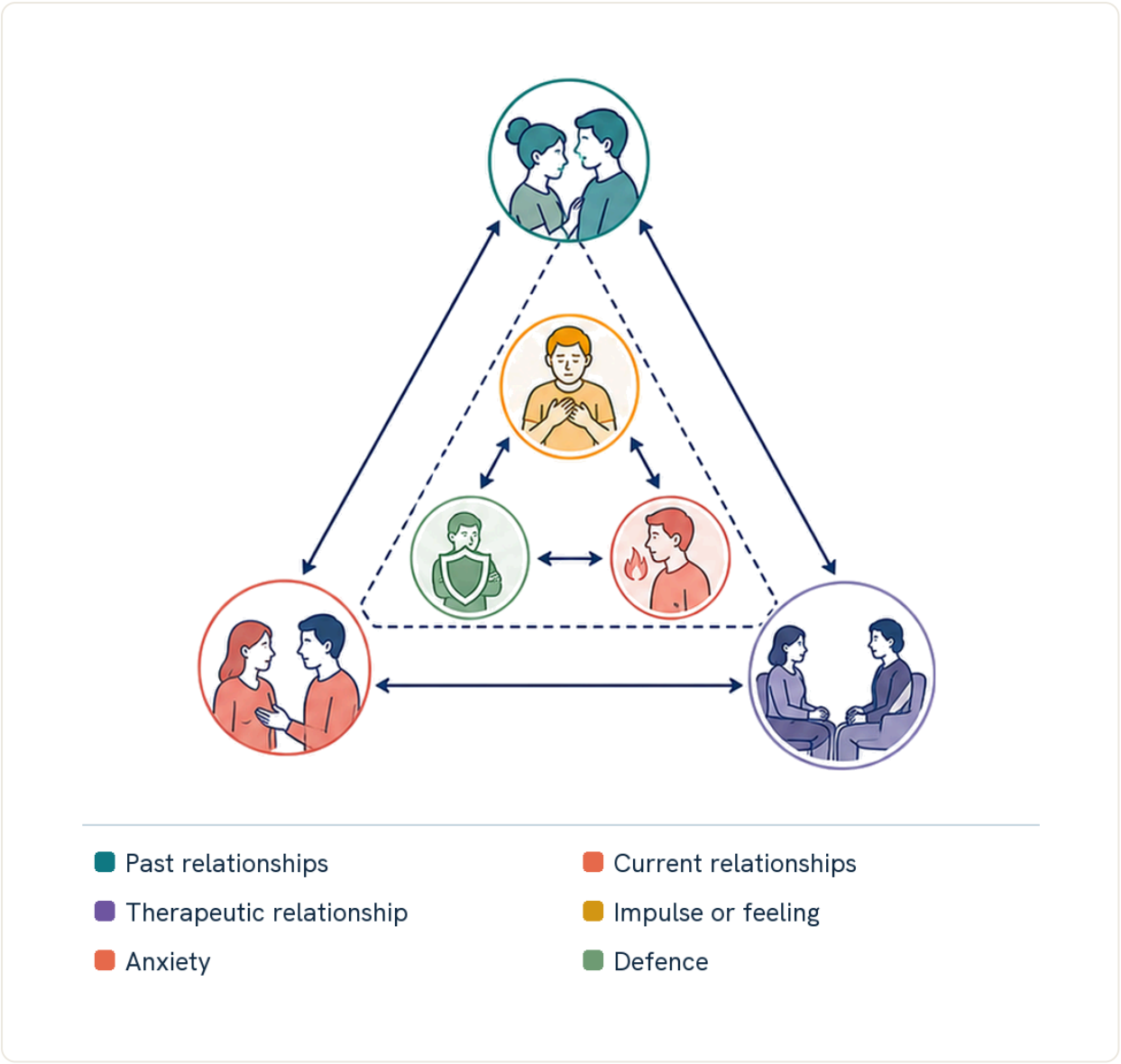


Fig 19.4 Psychodynamic formulation often uses two linked triangles: recurring patterns across past relationships, current relationships and the therapeutic relationship; and the sequence from impulse or feeling through anxiety to defence.

How to use this page. Learn the two maps first, the **topographic model** and the **structural model**, because everything else hangs on them. Then fix the three clinical concepts and the technique list, where the marks live. Then place the modality honestly on the evidence: classical **psychoanalysis** is a guideline first-line treatment for no disorder, whereas short-term **psychodynamic psychotherapy** is a reasonable second-line or alternative option, so do not overstate it. The deeper Freudian and post-Freudian metapsychology, and the descriptive vocabulary of slips and parapraxes, are developed in the Psychometry, Assessment and Descriptive Psychopathology notes.

5.1 The topographic model: three systems of the mind

Conscious, preconscious, unconscious, ranked by their relation to awareness. Freud's first map of the mind, the topographic model, classified mental events by their degree of awareness rather than by any anatomical seat (Kaplan and Sadock CTP 2024). It has three systems. The *system conscious* is what is in awareness now. The *system preconscious* is the antechamber, material

not conscious at this moment but retrievable at will, and it acts as a censor, admitting a forbidden wish to consciousness only if it is disguised past recognition. The *system unconscious*, the deepest layer, holds the wishes and drive-representations that are unacceptable to the person; it is governed by the **pleasure principle** and primary-process thinking, which ignores logic and time, tolerates contradiction, and knows no negatives. This is the model behind the popular iceberg image; the accompanying figure sets the three systems out in that form. Its clinical value is the claim that symptoms, dreams and slips are disguised derivatives of unconscious wishes, not random noise.

5.2 The structural model: id, ego and superego

Three agencies, introduced in *The Ego and the Id* (1923). Freud found the topographic model could not explain why the very defences that produced repression were themselves unconscious, so he rebuilt the map as the tripartite structural model (Kaplan and Sadock CTP 2024). Its three agencies do not map cleanly onto the three systems: the ego and superego each straddle conscious and unconscious. Hold them by their governing principle and their job.

AGENCY	NATURE AND PRINCIPLE	ITS ROLE IN THE CONFLICT
Id	Wholly unconscious reservoir of sexual and aggressive drive; pleasure principle, primary process	**The impulse that presses for discharge**
Ego	Largely unconscious, part conscious; reality principle, secondary process	**The mediator; deploys the defences against the impulse**
Superego	Largely unconscious; internalised parental and moral standards; source of conscience and guilt	**The prohibition; the moral objection to the impulse**

The structural model: a symptom is a compromise between the id impulse, the superego's prohibition and the ego's defence (Kaplan and Sadock CTP 2024).

The clinical pay-off is the idea of **unconscious conflict**: a symptom is a *compromise formation*, the best bargain the ego can strike between a forbidden id impulse, the superego's prohibition and external reality. Neurotic anxiety is the signal that this bargain is failing. Every dynamic formulation you will ever write is, at root, a statement of that three-way conflict.

5.3 Transference and counter-transference

The patient's feelings toward the therapist are a re-run of formative relationships. Transference is the displacement onto the therapist of feelings, wishes and expectations first formed in the patient's early, formative relationships, usually with parents (Kaplan and Sadock CTP 2024). The patient does not experience it as a repetition; a positive transference feels like real gratitude and trust, a negative transference like real suspicion and grievance. Its systematic analysis is what Freud held to be the single feature separating **psychoanalysis** from every other psychotherapy. Counter-transference is the mirror phenomenon: the therapist's own emotional response to the patient. Freud first saw it as an obstacle, a contamination to be analysed away in

the therapist's own analysis; the modern view, informed by object-relations and intersubjective theory, treats the clinician's disciplined counter-transference as a source of data about what the patient evokes in others. Both are worked with, not acted on.

WORKED EXAMPLE

A patient becomes coldly contemptuous whenever the therapist ends a session on time, complaining of being "processed like a case". The therapist notices an urge to over-explain and apologise. The dynamic reading is a negative **transference**: the punctual ending revives an early experience of a preoccupied, withholding parent, and the pull to placate is the therapist's **counter-transference**. The move is not to defend the clock but to interpret the pattern, linking the feeling in the room to its formative template.

RULE **Transference analysis is the heart of the method.** The systematic interpretation of the transference is the one feature that distinguishes psychoanalysis from every other form of psychotherapy.

TRAP **Reversing the direction.** Transference runs patient to therapist; counter-transference runs therapist back to patient. Swapping the two is the classic examination error.

5.4 Resistance, the alliance and the unconscious conflict

Everything in the patient that opposes the surfacing of unconscious material. Resistance is the name for all the ways, mostly out of awareness, in which the patient avoids a topic, blocks an affect, comes late, falls silent or otherwise opposes the treatment (Kaplan and Sadock CTP 2024). It is not obstinacy to be overcome by force but the defences seen in action, and analysts of every school agree that a large part of the work is helping the patient recognise resistance as an obstacle to be understood. Set against it is the therapeutic alliance, the real, reality-based, collaborative bond between the patient's observing ego and the therapist; it is distinct from the transference and is the most consistent predictor of good outcome across every therapy. The three concepts interlock: resistance defends the **unconscious conflict**, the transference displays it, and the alliance is what makes examining it bearable.

Transference

Displacement onto the therapist of feelings from formative early relationships.

Counter-transference

The therapist's own emotional response to the patient; an obstacle in the classical view, a source of data in the modern one.

Resistance

The patient's largely unconscious opposition to the surfacing of unconscious material; the defences in action.

Therapeutic alliance

The real, collaborative working bond, distinct from transference; the strongest common predictor of outcome.

Unconscious conflict

The clash of id impulse, superego prohibition and ego defence that generates anxiety and symptom.

5.5 The techniques: free association to working through

The patient's one task, and the analyst's graded toolkit. The patient is bound by a single instruction, the *fundamental rule*: to say whatever comes to mind, however trivial, repellent or illogical, without censoring. This is free association, the method that, as Freud abandoned hypnosis, became the true creation of **psychoanalysis** (Kaplan and Sadock CTP 2024; Wolberg). Alongside it the analyst reads the *royal road* of dreams and the tell-tale slips and parapraxes of everyday speech, treating each as a disguised derivative of the unconscious. The analyst's own interventions form a graded ladder from surface to depth, and the terms are examinable in their own right.

INTERVENTION	WHAT IT DOES	DEPTH
Clarification	Pulls together and sharpens what the patient has already said, bringing vague material into focus; adds no new inference	**Surface**
Confrontation	Directs the patient's attention to something being avoided or not attended to, typically a defence or a pattern	**Surface to middle**
Interpretation	Offers a hypothesis making the unconscious conscious, linking a current feeling or act to an unconscious wish, defence, the past or the transference; the chief agent of change	**Deep**
Working through	The repeated, effortful re-application of an insight across many situations and over time until change becomes durable; not a single act	**Consolidation**

The interpretive ladder: clarification and confrontation address the surface and the defences, interpretation reaches the unconscious, and working through embeds the gain (Kaplan and Sadock CTP 2024; Gabbard).

Working through is where insight becomes change. A single well-timed **interpretation** rarely cures anything; **working through** is the slow, repetitive labour of meeting the same conflict again and again, in the transference and in outside life, until the patient can respond differently by habit rather than by effort. It is the reason analytic work is long, and the reason a good interpretation delivered too early, before the alliance and the working-through capacity are in place, tends to feed resistance rather than insight.

PEARL

Read the ladder as ascending in depth, not in worth. Clarification and confrontation are not lesser tools; they prepare the ground. An **interpretation** is only as good as its timing, and premature depth is a technical error, not a virtue. The rule of thumb is to interpret the resistance and the defence before the hidden impulse, and to work from the surface down.

5.6 The analytic frame and neutrality

The fixed conditions that make the transference legible. The *frame* is the set of contractual conditions of treatment: the fixed time, place and fee, and the use of the couch (Kaplan and Sadock CTP 2024). Classical analytic sessions run 45 to 50 minutes, three to five times a week, with the patient reclining on the couch and the analyst out of sight, a deliberate arrangement that loosens censorship and encourages the regression and *transference neurosis* the work depends on. The analyst holds a stance of *neutrality* (taking no side among the patient's id, ego, superego and reality), *anonymity* (revealing little of the self, so the transference is the patient's own creation), and *abstinence* (declining to gratify the transference wishes directly). Any deliberate departure from the standard technique, such as sitting the patient up or meeting less often, is called a *parameter*, and is itself explored for its meaning rather than slipped in silently.

5.7 The spectrum: classical analysis to brief dynamic therapy

One family, graded by intensity, regression and focus. The dynamic therapies sit on a single continuum. At the intensive pole is classical **psychoanalysis**: frequent, couch-based, open-ended, aiming at broad structural change through regression and the analysis of a full transference neurosis. In the middle is **psychodynamic psychotherapy**, its briefer and less regressive derivative: once or twice weekly, face to face, with the same core concepts but a lighter touch on regression and more attention to the here and now (Tasman; Gabbard). At the focused pole are the brief dynamic therapies, time-limited and organised around a single dynamic focus agreed at the outset.

FEATURE	CLASSICAL PSYCHOANALYSIS	PSYCHODYNAMIC PSYCHOTHERAPY	BRIEF DYNAMIC THERAPY
Frequency	Three to five times a week	Once or twice a week	**Once a week, time-limited**
Position	Couch, analyst unseen	Face to face, upright	**Face to face, upright**
Regression	Encouraged; full transference neurosis	Limited	**Actively discouraged**
Focus	Open-ended, whole personality	Broad but bounded	**A single agreed dynamic focus**
Goal	Structural change through insight	Insight plus adaptation	**Resolution of the focal conflict**

The dynamic spectrum from classical analysis to brief dynamic therapy; the accompanying figure renders it as a single graded bar (Tasman; Gabbard).

The brief dynamic therapies are named after their pioneers. The classic short-term dynamic psychotherapies share time limits and a focus but differ in tactics. Sifneos developed short-term anxiety-provoking psychotherapy, an Oedipally-focused treatment of **10** to **20** sessions using high activity and a positive transference. Malan, from Balint's Tavistock group, organised the work around two triangles, the triangle of conflict (impulse, anxiety, defence) and the triangle of the person (therapist, current figures, past figures), holding to a 40-session upper limit; his enduring research finding is that the more interpretations linking the transference to the past and present, the better the outcome. Davanloo's intensive short-term dynamic psychotherapy drives at resistance through a central dynamic sequence of technical steps, including his "head-on collision" with the patient's defences. Mann's time-limited psychotherapy fixes treatment at exactly **12** sessions, using the deadline itself as a lever on the conflict around separation and loss.

MNEMONIC

SMDM: Sifneos, Malan, Davanloo, Mann

The four classic brief dynamic pioneers, easiest held by their signatures: **S**ifneos, anxiety-provoking and Oedipal; **M**alan, the two triangles; **D**avanloo, the head-on collision with resistance; **M**ann, the fixed twelve-session frame built on time and loss.

5.8 Evidence and indications: keep the modality honest

No first-line role for classical analysis; a second-line role for its brief derivative. The evidence base is thinner than for CBT, and it must be stated carefully. Classical, long-term **psychoanalysis** is a guideline first-line treatment for no disorder. Short-term psychodynamic psychotherapy (STPP) has a moderate base and appears in guidelines as an option or a second-line choice, never as the reference-standard therapy. STPP is one of several psychotherapy options for major depression (VA_DOD 2022; brief psychodynamic therapy, WHO_mhGAP 2023), taking its place beside the interpersonal and cognitive therapies covered in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes. Focal psychodynamic therapy is a later-line option for adults with anorexia nervosa when first-line treatments fail (NICE 2017). STPP is an alternative for social anxiety in patients who decline CBT (NICE 2013), and a second-line psychotherapy for somatisation (IPS_CPG 2020), whose place is set out in the Somatic-symptom, sexual, impulse-control disorders and suicide notes; psychodynamic interpersonal therapy is offered to reduce repetition of self-harm (RANZCP 2016). The best-evidenced psychoanalytically derived therapy is mentalisation-based treatment (MBT) of Bateman and Fonagy for borderline personality disorder, taken up with transference-focused psychotherapy in the Personality disorders notes.

COMMON TRAP

Presenting **psychoanalysis** as an evidence-based first-line treatment. Only short-term **psychodynamic psychotherapy** reaches the guidelines, and always as an option or second-line choice. Classical, long-term analysis carries no guideline first-line indication for any disorder; claiming one is a marked error.

3-5	1923	12
WEEKLY SESSIONS IN CLASSICAL PSYCHOANALYSIS	THE EGO AND THE ID: FREUD'S STRUCTURAL MODEL	SESSIONS IN MANN'S TIME-LIMITED THERAPY

INDIA

Formal, high-frequency **psychoanalysis** is scarce in Indian practice; what the guidelines actually endorse is its brief, focused derivative. The Indian Psychiatric Society lists short-term **psychodynamic psychotherapy** as a second-line psychotherapy for somatisation and undifferentiated somatoform disorder (IPS_CPG 2020), and has published a dedicated Clinical Practice Guideline on psychotherapies (Agarwal, Nischal, Praharaj, Menon, Kar; Indian J Psychiatry 2020). Frame dynamic work in the Indian setting as a bounded, focal treatment delivered by trained clinicians, not as open-ended analysis.

5.9 The ego defence mechanisms, named here

The ego's unconscious strategies against the forbidden impulse. The defences are the ego's automatic, unconscious manoeuvres for keeping an unacceptable impulse or affect out of awareness; they are the very machinery that **resistance** puts on display in the room. They are named here for completeness and developed in full, with Vaillant's mature-to-primitive hierarchy, in the topic that follows on the ego defence mechanisms.

Repression

The cornerstone; the active keeping of an unacceptable impulse or memory out of awareness.

Denial

Refusal to register an external reality that is too painful to face.

Projection

Attributing one's own disowned impulse or feeling to another person.

Reaction formation

Converting an unacceptable impulse into its conscious opposite.

Displacement

Shifting a feeling from its true object onto a safer substitute.

Sublimation

Channelling an impulse into a socially valued activity; a mature defence.

Splitting and projective identification

The primitive defences central to borderline personality organisation.

GOOD TO REMEMBER

- **Psychoanalysis and psychodynamic psychotherapy (the modality):** a treatment that makes **unconscious conflict** conscious by analysing the **transference**, **resistance** and defence to produce insight and change, mapped by the topographic model (conscious, preconscious, unconscious) and the structural model (id, ego, superego); classical **psychoanalysis** is intensive and couch-based, while **psychodynamic psychotherapy** is its briefer, face-to-face derivative. Its lead role is as a second-line or alternative option: short-term psychodynamic psychotherapy for major depression, somatisation (IPS_CPG 2020) and social anxiety in those declining CBT (NICE 2013), with MBT for borderline personality disorder as its best-evidenced offshoot; classical analysis is guideline first-line for no disorder. The one technique to name is **interpretation** of the transference, built on the patient's **free association**.

HOLD THIS

Psychoanalysis works by making the unconscious conscious through the analysis of TRANSFERENCE, RESISTANCE and defence; its two maps are the TOPOGRAPHIC model (conscious, preconscious, unconscious) and the STRUCTURAL model (id, ego, superego); classical analysis is intensive (couch, three to five weekly sessions, regression) while psychodynamic psychotherapy is its briefer face-to-face derivative, and INTERPRETATION of the transference, built on free association and consolidated by working through, is the one technique that defines the method.

6 · The ego defence mechanisms

This is one of the highest-yield grids in the whole psychodynamic syllabus, and it earns its place because the examiner almost never wants a loose description; the marks are in the *hierarchy*, being able to name a defence, place it on its maturity level, define it in a line and give a clean clinical example. The **ego defence mechanisms** are the unconscious mental operations the ego deploys to keep unacceptable impulses, and the anxiety they generate, out of awareness. Every person uses them; what distinguishes health from disorder is not their presence but their *maturity* and *rigidity*. The single organising idea is the maturity hierarchy, which sorts the two-dozen named **defence mechanisms** into four ranked levels and, crucially, maps them onto personality organisation.

How to use this page. Fix the definition and the short history first, then learn the four-level frame, then drill the four defs lists (**mature defences**, **neurotic defences**, **immature defences** and **psychotic defences**) with one crisp example each. The consolidated grid near the end is your single-glance revision table; the final subtopic is where the marks hide, because it links the grid to Kernberg's levels of personality organisation and to the clinical stance the examiner expects.

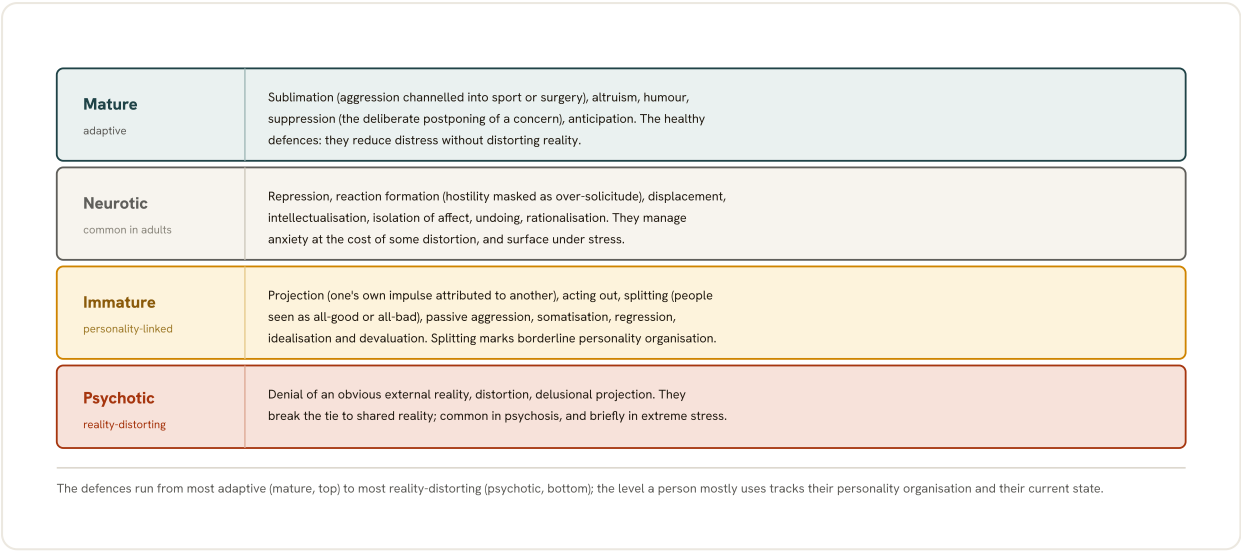


Fig 19.5 The ego defence mechanisms by level of maturity. Defences are unconscious mental operations that protect against anxiety and unacceptable impulses, and they are ranked by how adaptive they are. The mature defences reduce distress without distorting reality and are the mark of health. The neurotic defences, common in everyone and more prominent under stress, manage anxiety at the cost of some distortion. The immature defences, prominent in the personality disorders, distort relationships and reality more heavily, with splitting the hallmark of borderline organisation. The psychotic defences break the tie to shared reality altogether. Which level a person mostly relies on is one of the most useful things the examination and the formulation can establish.

6.1 What a defence mechanism is

An unconscious, involuntary operation against anxiety, not a conscious coping strategy. A defence mechanism is an automatic psychological process that protects the ego against anxiety and against the awareness of internal or external dangers or stressors (Kaplan and Sadock CTP 2024; DSM-5-TR glossary). Three features define it and each is examinable. It is **unconscious**: the person does not know they are doing it, which separates a defence from a deliberate coping tactic. It is **involuntary**: it is triggered automatically by conflict, not chosen. And it is **anxiety-reducing**: its function is to manage the affect thrown up when an unacceptable wish, feeling or piece of reality presses toward consciousness. Defences are universal and, in themselves, adaptive; a life without them is not possible. Pathology enters only when a defence is too primitive for the situation, too rigid to yield, or so costly that it distorts reality or relationships.

RULE **The defence is unconscious; its maturity, not its presence, is what is pathological.** Everyone uses defences all the time; the clinical question is never "is there a defence" but "at what level, and how rigidly".

6.2 A short history: Freud, Anna Freud and the maturity hierarchy

From a single mechanism to a ranked catalogue. Sigmund Freud first used the term "defence" in *The Neuro-Psychoses of Defence* in 1894, then for years let it be eclipsed by **repression**, before reinstating "defence" as the general class in *Inhibitions, Symptoms and Anxiety* in 1926, with repression demoted to one member of it. His daughter Anna Freud, in *The Ego and the Mechanisms of Defence* in 1936, gave the founding systematic catalogue and moved the ego, rather than the drives, to the centre of clinical attention. The developmental and empirical ranking that examiners want is Vaillant's: from his longitudinal study of adult development he arranged the defences into **four** levels of adaptiveness, **mature**, **neurotic**, **immature** and **psychotic**

(pathological), a hierarchy later echoed by the DSM-IV Defensive Functioning Scale, which ranked defences by their adaptive value. The accompanying figure draws these four levels as an ascending ladder from psychotic denial at the base to sublimation at the top.

6.3 Mature defences

The adaptive summit: they gratify the impulse in a way that also serves the self and others. The **mature defences** are the hallmark of healthy adult functioning and of the well-integrated personality; they let the person handle conflict without distorting reality, damaging relationships or paying a symptomatic price (Vaillant; Kaplan and Sadock CTP 2024). They can, of course, be recruited pathologically in excess, but as a group they are what good adaptation looks like.

Sublimation

Channelling an unacceptable impulse into a socially valued or creative activity; the impulse is expressed, not blocked. A person with strong aggressive urges becomes a surgeon or a competitive boxer.

Altruism

Meeting one's own needs vicariously through constructive service to others. Someone deprived in childhood devotes themselves to feeding and schooling street children.

Humour

Overt expression of feeling that names a painful truth without discomfort to self or others. A patient given a grave diagnosis makes a wry joke that acknowledges the fear rather than denying it.

Suppression

The conscious or semi-conscious decision to postpone attention to a distressing impulse or feeling, intending to return to it. A candidate deliberately sets worry about a sick relative aside until the examination is over.

Anticipation

Realistic planning and emotional rehearsal for future inner discomfort. Before surgery a patient reads about the procedure and mentally rehearses the recovery, blunting later distress.

MNEMONIC

SOME ADULTS HAVE SUPER APTITUDE

The five **mature defences** in order: **S**ublimation, **A**ltruism, **H**umour, **S**uppression, **A**nticipation. The trap the phrase guards against is suppression, the only one on this list that is partly conscious; hold it against repression below.

6.4 Neurotic defences

The middle band: common in everyone under stress, and the signature of the neurotic (repression-based) personality. The **neurotic defences** keep conflict out of awareness at a cost that is usually private rather than reality-distorting, and they cluster around a firm repression barrier (Vaillant; Gabbard, *Long-Term Psychodynamic Psychotherapy*). Several map directly onto symptom pictures, most famously undoing onto obsessional rituals and isolation of affect onto the obsessional's flat recounting of distressing material.

Repression

Unconscious exclusion of an unacceptable idea, feeling or memory from consciousness; the foundational defence. A woman abused as a child has no accessible memory of the events yet reacts with unexplained anxiety to reminders.

Reaction formation

Transforming an unacceptable impulse into its conscious opposite. A person with unacceptable hostility toward a sibling becomes conspicuously doting and over-solicitous.

Displacement

Redirecting a feeling from its true object onto a safer substitute. A man humiliated by his employer goes home and shouts at his children.

Intellectualisation

Using abstract reasoning and detail to keep the affect of a conflict out of awareness. A newly diagnosed patient discusses survival statistics and cell biology fluently but shows no feeling.

Isolation of affect

Separating a feeling from the idea or event it belongs to, so the event is recalled without its emotion. A patient describes a horrifying accident in flat, factual detail.

Undoing

A symbolic act meant to cancel or atone for an unacceptable thought or deed; the mechanism behind obsessional rituals. A person with intrusive aggressive thoughts performs repeated counting or checking to "cancel" them.

Rationalisation

Offering plausible but false reasons to justify a feeling or act whose real motive is unacceptable. A rejected applicant decides the job was beneath them anyway.

> **COMMON TRAP**
>
> **Suppression is not repression.** Suppression is a mature defence and is *conscious* or semi-conscious: the person knows the worry exists and deliberately shelves it. Repression is a neurotic defence and is *unconscious*: the material is barred from awareness altogether and cannot be retrieved at will. The conscious-versus-unconscious contrast is the single most-asked discriminator in this topic.

6.5 Immature defences

The primitive band: seen in children, in adolescence, and prominently in the personality disorders. The **immature defences** distort reality and relationships more openly and provoke the reactions in others that keep the pattern going (Vaillant; Kaplan and Sadock CTP 2024). Their persistence into adult life, and above all their dominance, is what marks the more disturbed personality organisations.

Projection

Attributing one's own unacceptable impulses, feelings or thoughts to another person; the precursor of paranoia. A man with unacknowledged jealousy accuses his partner of being unfaithful.

Acting out

Expressing an unconscious wish or impulse directly through action, to avoid being aware of the feeling behind it. An adolescent who cannot bear feelings of abandonment absconds or self-harms rather than voicing the distress.

Splitting

Experiencing self and others as all-good or all-bad, unable to hold contradictory qualities together; the pattern oscillates. A patient adores one nurse as perfect and condemns another as cruel, then reverses the two the following week.

Passive aggression

Expressing aggression toward others indirectly, through non-compliance, procrastination, inefficiency or covert obstruction. A resentful employee repeatedly "forgets" tasks and hands work in late.

Somatisation

Converting intrapsychic distress into bodily symptoms and seeking medical rather than psychological help. A man unable to grieve develops disabling headaches and chest pain with no organic cause.

Regression

Retreating to an earlier developmental level of functioning to escape present demands. A hospitalised adult becomes clingy, demanding and childlike.

Idealisation / devaluation

Attributing exaggeratedly positive, or abruptly negative, qualities to another; the two poles of splitting in action. A patient insists a new therapist is the only one who ever understood them, then dismisses them as useless.

6.6 Psychotic defences

The most primitive band: they abolish reality itself, and they are normal only in early childhood and in dreams. The **psychotic defences** alter the person's perception of external reality rather than merely their inner experience of it, and their presence in an adult signals psychotic-level functioning (Vaillant; Kaplan and Sadock CTP 2024).

Denial

Refusal to accept an aspect of external reality that is obvious to others because it is too threatening; at this level the reality is abolished, not merely minimised. A woman with an advanced, visible tumour insists nothing is wrong and declines all investigation.

Distortion

Grossly reshaping external reality to fit inner need, including sustained wish-fulfilling or grandiose misperception. A man is convinced, against all evidence, that he has a special mission and cannot fail.

Delusional projection

Frank delusional, usually persecutory, beliefs about external reality, in which projected content is experienced as a real external threat. A patient is certain that neighbours are pumping poison gas into the flat to kill him.

PEARL

Denial is the classic "trick" answer: it exists at more than one level. Mild denial (minimising a piece of bad news for a while) is seen across the milder levels, but the full-blown abolition of an obvious external reality, as in the woman denying a visible tumour, is the *psychotic*-level defence. When the examiner asks "what level is denial", the safe answer names the psychotic level while noting that milder denial is not by itself psychotic.

6.7 The consolidated maturity grid

One table, the whole answer. This is the grid to reproduce under exam pressure: the level, the defence, its one-line definition and a clean example (Vaillant; Tasman; Gabbard). Learn it column by column, because a viva will pick a random cell (name the level of undoing; define isolation of affect; give an example of sublimation).

LEVEL	DEFENCE	ONE-LINE DEFINITION	EXAMPLE
Mature	Sublimation	**Impulse channelled into valued activity**	Aggressive urges expressed as a surgical career
	Altruism	Own needs met through service to others	A deprived person devotes life to feeding children
	Humour	Painful feeling named without discomfort	A wry joke about one's own grave diagnosis
	Suppression	**Conscious postponing of a distressing feeling**	Shelving family worry until the exam is done
	Anticipation	Realistic emotional rehearsal of future distress	Reading up and rehearsing recovery before surgery

LEVEL	DEFENCE	ONE-LINE DEFINITION	EXAMPLE
Neurotic	Repression	**Unconscious barring of ideas from awareness**	No memory of childhood abuse, only unexplained anxiety
	Reaction formation	Impulse turned into its conscious opposite	Hostility to a sibling shown as doting concern
	Displacement	Feeling redirected onto a safer object	Shamed by the boss, shouts at the children
	Intellectualisation	Abstract reasoning used to avoid affect	Discussing cancer statistics, showing no feeling
	Isolation of affect	Feeling divorced from its idea	Recounting a horror in flat, factual detail
	Undoing	Symbolic act to cancel an unacceptable thought	Counting rituals to "cancel" aggressive thoughts
	Rationalisation	Plausible false reasons for the real motive	The rejected applicant decides the job was beneath them
Immature	Projection	**Own impulses attributed to another**	Jealous man accuses the partner of infidelity
	Acting out	Impulse discharged in action, not felt	Absconding or self-harm instead of voicing distress
	Splitting	**Self and others seen as all-good or all-bad**	One nurse idealised, another condemned, then reversed
	Passive aggression	Aggression shown as covert non-compliance	"Forgetting" tasks and handing work in late
	Somatisation	Distress converted into bodily symptoms	Ungrieved loss becomes headaches and chest pain
	Regression	Retreat to an earlier level of functioning	A hospitalised adult turns clingy and childlike
	Idealisation / devaluation	Exaggerated all-positive then all-negative views	The therapist is the only one who understands, then useless

LEVEL	DEFENCE	ONE-LINE DEFINITION	EXAMPLE
Psychotic	Denial	**Obvious external reality abolished**	A visible tumour insisted to be nothing
	Distortion	External reality grossly reshaped to inner need	Grandiose certainty of a special, unfailing mission
	Delusional projection	Projected content lived as real external threat	Certainty that neighbours are gassing the flat

The four-level maturity hierarchy of the ego defence mechanisms, with a one-line definition and a clinical example for each (Vaillant; Tasman; Gabbard). The accompanying figure renders these levels as an ascending ladder.

6.8 Clinical relevance: defences map to personality organisation

The grid is a diagnostic instrument, not a curiosity. The examinable payoff is that a person's *habitual, predominant* defences locate them on a spectrum of personality organisation (Kernberg; Gabbard). A personality run mainly on repression-based **neurotic defences** sits in the **neurotic** organisation, with intact reality-testing and an integrated sense of self and others. A personality run mainly on primitive, immature defences, above all **splitting** with its satellites of projective identification, idealisation and devaluation, primitive denial and acting out, sits in the **borderline** organisation, where identity is diffuse and others cannot be held as whole, contradictory people. Splitting originates developmentally in Melanie Klein's paranoid-schizoid position, and its dominance is the single best pointer to borderline organisation. The therapeutic corollary is equally examinable: supportive therapy deliberately *bolsters* a patient's existing adaptive defences and does not probe them, whereas expressive and psychodynamic work *interprets* them, and you never strip away a defence the patient still needs to stay integrated. The fuller treatment of splitting, and of the dialectical behaviour and schema therapies built to work with it, belongs to the Personality disorders notes.

WORKED EXAMPLE

A young woman on the ward telephones her registrar late at night to say he is the only doctor who has ever truly cared for her, and in the same week complains to the nursing station that a different registrar is heartless and negligent. On the round she recalls a serious overdose in a flat, unemotional voice. Two defences are on display: **splitting** with idealisation and devaluation across the two doctors, and isolation of affect in the account of the overdose. The predominance of splitting, not the single episode, points toward a borderline personality organisation and reframes the "difficult" ward behaviour as a defensive style to be understood rather than a provocation to be punished.

TRAP **Do not diagnose from one defence.** Everyone splits or denies occasionally under stress; personality organisation is read from the *habitual, predominant* defensive level, not from a single act. Calling a patient "borderline" on one instance of splitting is the classic overcall.

4	1894	1936
LEVELS OF THE MATURITY HIERARCHY (VAILLANT)	FREUD FIRST NAMES "DEFENCE"	ANNA FREUD'S FOUNDING CATALOGUE

INDIA

The ego-defence grid is a perennial theory-paper and viva question in the Indian MD and DNB psychiatry examinations, taught straight from Kaplan and Sadock, so the level-by-level list is examined here, not treated as a Western aside. In Indian clinical practice the defensive organisation is most often inferred through the projective testing tradition, the Rorschach and the Thematic Apperception Test, which is a core competency in the NIMHANS clinical-psychology curriculum; the technical detail of those instruments sits in the Psychometry, Assessment and Descriptive Psychopathology notes. A second genuinely Indian anchor is **denial** in alcohol use, where the patient's minimisation of a visible problem is the defence the interview must work around; the motivational approach to exactly that is developed in the Substance use disorders notes.

GOOD TO REMEMBER

- **The principle:** defence mechanisms are unconscious, involuntary ego operations that reduce the anxiety of intrapsychic conflict; they are universal, and only their maturity and rigidity, not their presence, is pathological.
- **The discriminator:** suppression is conscious and mature; repression is unconscious and neurotic. If the person can retrieve the feeling at will, it is suppression, not repression.
- **The one exam fact:** Vaillant ranks defences into four levels, mature, neurotic, immature and psychotic, and a predominance of splitting is the signature primitive defence of borderline personality organisation.

HOLD THIS

Ego defence mechanisms are unconscious, involuntary operations against anxiety; Vaillant ranks them in four levels, mature (sublimation), neurotic (repression), immature (projection, splitting) and psychotic (denial), and it is the predominant level, with splitting marking borderline organisation, that carries the clinical meaning.

7 · Interpersonal psychotherapy

Interpersonal psychotherapy (IPT) is one of only two psychotherapies that sit alongside cognitive behaviour therapy as a *first-line* psychological treatment for depression, and that single fact is the examinable core of the topic. Developed by Gerald Klerman and Myrna Weissman in the nineteen-seventies, originally as the psychotherapy arm of an antidepressant medication trial, IPT is a *brief, time-limited, present-focused, diagnosis-focused* treatment built on one deceptively simple premise: whatever its ultimate cause, a depressive episode arises and is maintained within a **current interpersonal context**, so working on that context relieves the symptoms. Learn IPT as the counterpart to CBT: where CBT reaches for the maladaptive *thought*, IPT reaches for the troubled *relationship*.

How to use this page. Fix the model first, then the machinery. The machinery has two moving parts that examiners love to test: the **three phases** (assessment with its interpersonal inventory,

the middle work, and termination) and the **four problem areas** (grief, role disputes, role transitions and interpersonal deficits), exactly one of which is chosen as the focus of treatment. Close on the evidence, because the payoff sentence is short and hard: first-line for depression, especially perinatal, well evidenced, present-focused, does not target personality. The cardinal error the page guards against is mistaking IPT for open-ended dynamic insight therapy; it is manualised, focal and brief.

7.1 The interpersonal model

Symptoms live in relationships, so relationships are the lever. The interpersonal psychotherapy model holds that psychiatric symptoms, depression above all, arise and are maintained in the patient's *current* interpersonal relationships, and that improving the handling of those relationships lifts the symptoms (Klerman and Weissman; Kaplan and Sadock CTP 2024). IPT makes no claim that interpersonal problems *cause* depression in some ultimate sense; it takes a pragmatic, atheoretical stance, accepting that the illness is multiply determined and simply choosing the interpersonal context as the workable point of entry. Three commitments follow and must be memorised together: the therapy is *time-limited* (a standard acute course runs to about **12** to 16 sessions delivered weekly), it is resolutely *present-focused* (the here-and-now of relationships, not the reconstruction of childhood), and it explicitly *does not target personality*, restructuring neither character nor unconscious conflict. Depression is framed openly as a *medical illness*, and the patient is given the sick role, which names the condition as a treatable illness that is not the patient's fault while obliging them to work actively at recovery.

RULE **Present, relational and brief.** IPT targets the current interpersonal context of a depressive episode across roughly twelve to sixteen weekly sessions; it does not excavate the past and does not attempt to change personality.

7.2 The three phases

Assess and formulate, then work, then say goodbye. IPT runs across **3** defined phases (Kaplan and Sadock CTP 2024). The *initial phase* (roughly the first several sessions) makes the diagnosis, gives psychoeducation and the sick role, takes the interpersonal inventory described below, and ends by naming *one* of the four problem areas as the focus and agreeing an explicit treatment contract. The *intermediate* or *work phase*, the bulk of the therapy, applies the strategies specific to the chosen problem area, keeping every session anchored to the link between the patient's mood and their recent interpersonal events. The *termination phase* (usually four to five sessions in length) reviews and consolidates gains, plans for maintaining them, identifies early warning signs of relapse, and treats the ending itself as a small, real experience of loss, an analogue of grief that is named explicitly rather than glossed over.

7.3 The interpersonal inventory

A structured review of every important relationship, done up front. The interpersonal inventory is the signature assessment procedure of the initial phase: a systematic, relationship-by-relationship review of the significant people in the patient's current life, examining for each the nature of the tie, its frequency and expectations, the satisfying and unsatisfying aspects, and

the changes the patient would want (Weissman; Kaplan and Sadock CTP 2024). Its purpose is not history for its own sake but *formulation*: from the inventory the therapist locates the depressive episode within a relational pattern and derives the interpersonal formulation that pins the illness to one of the four problem areas. The inventory is where the whole subsequent therapy is decided, which is why it belongs to the opening sessions and is done before any change work begins.

7.4 The four problem areas

Every case is worked through exactly one of four templates. IPT organises all its middle-phase work under **4** interpersonal **problem areas**, first specified by Weissman and colleagues, and a defining feature of the method is that the therapist selects a *single* area (occasionally a primary plus a secondary) as the treatment focus. Knowing the four, and being able to tell a role dispute from a role transition, is the most examinable discrimination in the whole topic.

PROBLEM AREA	WHAT IT IS	FOCUS OF THE WORK
Grief (complicated bereavement)	Abnormal, delayed or distorted mourning following the death of a significant person	**Facilitate the delayed mourning, then help rebuild interests and relationships to replace what was lost**
Interpersonal role disputes	A live, non-reciprocal clash of expectations with a significant other who is present (spouse, parent, employer)	Identify the stage of the dispute and the divergent expectations, then renegotiate them or, if truly irresolvable, dissolve the relationship
Role transitions	Difficulty adjusting to a changed life role (marriage, parenthood, a new job, retirement, migration, physical illness)	Mourn the loss of the old role and its attachments, then build mastery of and a positive view of the new one
Interpersonal deficits (sensitivity)	A long history of impoverished, unfulfilling relationships and social isolation	**The residual category, chosen only when the other three do not fit; reduce isolation, using the therapeutic relationship as a model to build new ties**

The four IPT problem areas; exactly one is chosen as the focus, and interpersonal deficits is the default when none of the first three applies and carries the least favourable prognosis.

TRAP **Role dispute is not a role transition.** A *role dispute* is an ongoing conflict of expectations with a person who is still present; a *role transition* is the solo task of adjusting to a role that has itself changed. Divorce conflict is a dispute; becoming a mother is a transition.

7.5 The techniques of the work phase

Focused, affect-oriented, communication-centred. The middle phase uses a small set of named techniques, all bent to the interpersonal focus (Kaplan and Sadock CTP 2024). *Exploratory questions*, mostly open and general, open up the relational material. *Encouragement of affect* helps the patient acknowledge painful feelings, use them to guide interpersonal change, and access emotions they have suppressed. *Communication analysis*, a hallmark technique, walks slowly

through a specific recent interaction or argument to expose the ineffective communication patterns inside it and rehearse better ones. *Decision analysis* weighs the options open to the patient in a stuck situation. And the *therapeutic relationship* itself is used sparingly, chiefly for patients whose focus is **interpersonal deficits** (the therapist's bond becomes a template for relationships outside) or a role dispute (the patient learns how they come across). Throughout, the therapist keeps redirecting unfocused talk back to the tie between recent interpersonal events and the depressive symptoms.

WORKED EXAMPLE

A woman becomes depressed in the months after moving cities for her husband's job, cut off from the friendships that had always sustained her. The interpersonal inventory shows no bereavement and no live conflict, but a clear break between the onset of low mood and the relocation. Her therapist formulates the focus as a *role transition*: together they mourn the support network she left behind and, over the work phase, build concrete steps to form new local relationships. As her isolation eases, her mood lifts, without a single session spent on childhood or on restructuring cognitions.

7.6 The evidence base and the lead indication

First-line for depression, with a special strength in the perinatal period. If one sentence must be exam-ready it is this: IPT is a well-evidenced, first-line psychological treatment for major depression, established through numerous randomised controlled trials including the landmark National Institute of Mental Health collaborative study (Tasman; the guideline evidence). It is named a first-line psychotherapy for major depressive disorder by the Indian Psychiatric Society (IPS_CPG 2017, grade A), CANMAT (2016), VA/DoD (2022) and SIGN (2023). Its most distinctive niche is *perinatal depression*, both antenatal and postpartum, where it is a preferred or first-line option (CANMAT 2016; RANZCP 2020; NICE 2014; VA/DoD 2023), a strength that flows naturally from a therapy built around role transitions and role disputes, the very stuff of new parenthood. IPT is also offered in the continuation phase to reduce depressive relapse (VA/DoD 2022). The comparison of IPT with CBT in depression, and the depression rating scales used to track response, are developed in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes.

PEARL

Two sister therapies, two levers. In a depressed patient, reach for **CBT** if the maladaptive *cognitions* are foreground and **IPT** if the trigger and maintainer is a *relationship* problem, a loss, a dispute or a life transition. Both are first-line and roughly equal in efficacy for depression; the choice is often about fit and availability rather than a difference in evidence grade.

7.7 The adaptations

One method, several named offshoots. IPT's tight structure has made it easy to adapt, and three offshoots are worth naming. IPT-A, interpersonal psychotherapy for adolescents (Mufson), tailors the model to depressed teenagers, adding attention to the transition to adolescence and to relationships with parents, and is an established treatment for adolescent depression.

Interpersonal and social rhythm therapy (IPSRT), developed by Ellen Frank, marries IPT's interpersonal work to the stabilisation of daily *social rhythms* (sleep, meals and activity), on the premise that circadian and social-routine disruption precipitates mood episodes; it is a recommended adjunct to pharmacotherapy in bipolar disorder (IPS_CPG 2017, grade A; VA/DoD 2023) and adds a fifth focus, grief for the lost healthy self, to the original four. IPT has also been delivered successfully in a *group* format and in the perinatal setting. The use of IPSRT in bipolar disorder, and of IPT in unipolar depression, is cross-referenced to the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes.

INDIA

The Indian Psychiatric Society names interpersonal psychotherapy among the three strongest-evidence psychotherapies for depression in its depression clinical practice guideline (IPS_CPG 2017), placing it first-line alongside CBT and behavioural activation, and it endorses IPSRT as an adjunctive treatment in its bipolar guideline (IPS_CPG 2017). The realistic Indian caveat is the same as for CBT: guideline endorsement is firm, but trained IPT therapists are scarce, so access, not evidence, is the limiting factor.

4	3	12-16	4-5
INTERPERSONAL PROBLEM AREAS, ONE CHOSEN AS FOCUS	PHASES (ASSESSMENT, WORK, TERMINATION)	WEEKLY SESSIONS IN A STANDARD ACUTE COURSE	SESSIONS IN THE TERMINATION PHASE

MNEMONIC

GRID

The four problem areas: **G**rief, **R**ole disputes, **I**nterpersonal deficits, **D**evelopmental and life-role transitions. Hold that grief is about the *dead*, a role dispute is a conflict with the *living*, a transition is a change in the *self's role*, and deficits is the isolated *residual* category.

GOOD TO REMEMBER

- **Interpersonal psychotherapy (the therapy):** the model is that a depressive episode arises and is maintained in the patient's current interpersonal context, so a brief, present-focused, personality-sparing course of about twelve to sixteen sessions worked through one of the four problem areas (grief, role disputes, role transitions, interpersonal deficits) relieves the symptoms; the lead indication is major depression, first-line and best-evidenced in the perinatal period; the one signature technique is communication analysis anchored to the chosen problem area.

HOLD THIS

IPT (Klerman and Weissman) is a time-limited, present-focused therapy that links depression to the current interpersonal context and works through exactly one of four problem areas, grief, interpersonal role disputes, role transitions and interpersonal deficits, across three phases (assessment with the interpersonal inventory, the middle work, and a termination of four to five sessions); it is first-line for depression, strongest in the perinatal period, and its bipolar offshoot is IPSRT.

8 · Group psychotherapy

Group psychotherapy is the treatment of several patients together by one or two trained therapists who use the group itself, rather than the therapist alone, as the instrument of change. Its examinable core is not a set of techniques but a mechanism: assembled strangers who share a difficulty become, over time, a small society in which each member's characteristic ways of relating are re-enacted, seen and reworked. The single most tested content on this modality is Yalom's catalogue of therapeutic factors, the ingredients through which a group heals, and the examiner almost always wants the exact count, so anchor it now: there are exactly **11**.

How to use this page. Learn the eleven therapeutic factors as a list you can reel off, with **cohesiveness** understood as the central one; then the main types of group and how they differ in aim, structure and which factors they lean on; then the practical frame, composition, size and the five stages a group passes through; and finally who should and should not be put into a group. The cardinal error the page is built to prevent is treating a leaderless peer self-help meeting as though it were formal group psychotherapy, and the second is forgetting that the acutely psychotic or actively suicidal patient does not belong in an insight-oriented group.

8.1 The group as a social microcosm

The group, not the therapist, is the treatment. The founding idea, developed by Yalom from the interpersonal tradition, is that a therapy group becomes a *social microcosm*: given enough time and freedom, members recreate inside the room the very relational patterns that trouble them outside it (Yalom and Leszcz; Tasman ch. 95). The therapist's task is therefore to work in the here and now, drawing attention to what is happening between members as it happens, so that a maladaptive pattern can first be lived, then noticed through *process illumination*, and finally revised. This is why feedback from a peer often lands harder than the same observation from the therapist, and why a group can expose ego-syntonic blind spots that individual therapy leaves untouched. The group is a delivery format for many therapies, but as a modality in its own right its active agent is member-to-member interaction.

RULE **The therapeutic agent is the interaction between members.** In group psychotherapy the group functions as a social microcosm; change comes from here-and-now interpersonal learning, not from the therapist treating each patient in turn with an audience present.

8.2 Yalom's eleven therapeutic factors

The eleven ingredients through which a group heals. Yalom and Leszcz described the therapeutic factors as the mechanisms of change common to therapy groups; the canonical examinable set numbers eleven, and you should be able to name them and give a one-line gloss for each (Yalom and Leszcz; Kaplan and Sadock CTP 2024). Later formulations subdivide interpersonal learning into an input and an output component and add self-understanding, which is why some texts quote a higher figure, but the count to give unless asked otherwise is **11**.

THERAPEUTIC FACTOR	WHAT IT DOES IN THE GROUP
Universality	The member discovers that others share the same feelings, thoughts and problems, dissolving the sense of being uniquely afflicted or alone.
Instillation of hope	Seeing other members improve, especially those once as unwell as oneself, breeds optimism that recovery is possible.
Imparting information	Didactic instruction and advice from the therapist or fellow members, that is, psychoeducation about illness and coping.
Altruism	Members raise their own self-worth by giving to and helping others, countering the feeling of being useless or a burden.
Corrective recapitulation of the primary family group	The group re-evokes the dynamics of the early family, now available to be re-experienced and worked through in a corrective way.
Development of socialising techniques	The group is a training ground for adaptive social skills, giving feedback that refines how a member communicates and relates.
Imitative behaviour	Members learn by observing and modelling the therapist and one another, a vicarious or observational learning.
Interpersonal learning	Through honest here-and-now feedback the member gains insight into their interpersonal impact and then practises new, more adaptive ways of relating.
Group cohesiveness	**The sense of belonging, trust and togetherness; the group-level analogue of the therapeutic alliance and the precondition on which the other factors depend.**
Catharsis	The open release and expression of strong affect, about past or present experience, within a containing group.
Existential factors	Coming to accept responsibility for one's own life, and to face its ultimate contingencies, mortality, aloneness and the limits of what others can give.

Yalom's eleven therapeutic factors, with group cohesiveness marked as the central mechanism through which the rest operate.

MNEMONIC

Support, Learn, Disclose, Exist

Recall the eleven in four clusters rather than as a flat list. **Support** factors: universality, altruism, instillation of hope, cohesiveness. **Learning** factors: imparting information, imitative behaviour, development of socialising techniques, interpersonal learning. **Disclosure** factors: catharsis and corrective recapitulation of the primary family group. **Existential**: the eleventh, existential factors. Four plus four plus two plus one makes exactly eleven, and a wrong count is the commonest error on this question.

TRAP **A self-help group is not group psychotherapy.** A twelve-step or peer-support group is leaderless, run by fellow sufferers, and is not, strictly, a psychotherapy; formal group psychotherapy has a trained leader, screened members and defined therapeutic factors. They share factors such as universality and cohesiveness but are not the same thing.

8.3 Cohesiveness, the central factor

Cohesiveness is to the group what the alliance is to individual therapy. Of the eleven, cohesiveness is singled out as the central mechanism of action, therapeutic in its own right and the platform on which every other factor rests (Yalom and Leszcz). It is the sense of belonging, trust and togetherness that members feel towards the group and its leader, and it is the group's analogue of the therapeutic relationship; the more cohesive the group, the more members will self-disclose, take interpersonal risks and tolerate feedback. A common misconception is that a cohesive group is a conflict-free one. The opposite is nearer the truth: a securely cohesive group is precisely the one that can voice disagreement and hostility openly, because unexpressed conflict festers into covert hostility that erodes cohesion. Cohesiveness is best thought of as the container that makes the frightening work of the other factors safe enough to attempt.

PEARL

If asked for the single most important therapeutic factor, answer **cohesiveness**, and justify it as the group's version of the therapeutic alliance: it is both curative itself and the precondition for universality, catharsis and interpersonal learning to do their work. A cohesive group is not a quiet one; it is one safe enough to argue in.

8.4 The types of group

One format, several distinct modalities. The main types of group used in practice differ in what they aim for, how they are structured and which therapeutic factors they lean on (Kaplan and Sadock; Tasman Table 95-2). Learn them as a spectrum from the most supportive and symptom-focused to the most exploratory, plus the leaderless peer meeting and the whole-environment community at the two ends.

TYPE OF GROUP	CHIEF AIM	STRUCTURE (SIZE, TEMPO)	LEADING FACTORS	PROTOTYPE
Supportive	Improve adaptation, reduce isolation, shore up coping in the seriously ill	5-15 members, open; once to several times weekly	Cohesion, universality, reality-testing, hope	Inpatient ward group
Interpersonal / process (psychodynamic)	Personality and relational change through insight into maladaptive patterns	5-10, closed; once to twice weekly; long-term	**Interpersonal learning, self-understanding, cohesion**	Outpatient Yalom-style interactional group
Cognitive-behavioural	Symptom relief via skills learned and rehearsed for use outside the group	5-15, closed; once to twice weekly; time-limited, up to six months	Imparting information, behavioural rehearsal, hope	Group CBT for depression or anxiety
Psychoeducational	Impart knowledge and illness-management skills to patients and families	Leader-led, structured; time-limited	Imparting information, universality	Illness-education group for families in psychosis
Self-help	Mutual support, reduced shame, acceptance of a shared condition	Leaderless peers, unlimited, open; variable to daily	Universality, altruism, hope, cohesion	Alcoholics Anonymous and the twelve-step groups
Therapeutic community	The whole living and working milieu as treatment; social learning through communal life	Residential or ward as the unit; flattened hierarchy	Social learning, reality confrontation	Maxwell Jones's therapeutic community; rehabilitation settings

The main types of group, arranged from supportive through exploratory to the leaderless peer group and the whole-environment community.

The therapeutic community, also called milieu therapy, is worth holding as a distinct entity: pioneered by Maxwell Jones, it treats the entire residential environment as therapeutic, flattening the staff-patient hierarchy so that communal meetings and shared decision-making become the vehicle for social learning. The interpersonal or process group, the one most people picture as classical group therapy, is the exploratory modality that pursues genuine relational change, while group CBT, supportive and psychoeducational groups use the group chiefly as an efficient setting for a defined task.

8.5 Composition, size and the stages of group development

How a group is built, and the arc it travels. An interactional outpatient group runs to about seven or eight members, with a workable range of roughly five to ten (Yalom and Leszcz; Tasman Table 95-2); too few and interaction thins, too many and members cannot all be held in mind. It usually meets once a week for sixty to ninety minutes. Composition follows a useful rule of

thumb: groups do best when *homogeneous* for ego strength and level of functioning, so that no one is far out of their depth, but *heterogeneous* for the presenting conflicts and personality styles, so that there is friction to learn from. Groups may be *closed*, admitting no new members once begun, or *open*, replacing members as they leave; and the dropout rate is high, commonly around thirty to forty per cent in the early weeks, which is why careful selection and a pregroup preparation session matter so much.

Well-run groups pass through a recognised developmental sequence. The American Group Psychotherapy Association consolidated the historical models into a five-stage paradigm (Kaplan and Sadock CTP 2024), which maps onto Tuckman's familiar labels: *forming* (preaffiliation, the anxious search for acceptance and similarity), *storming* (power and control, testing the leader and negotiating conflict), *norming* (intimacy, deeper disclosure against a secure base of cohesion), *performing* (differentiation, mature interpersonal work with responsibility shared across members) and *adjourning* (separation, consolidating gains and mourning the ending). Attribute the count precisely: there are **5** stages, and the leader's job is to intervene in a way appropriate to the stage the group is in, since a well-meant confrontation delivered before cohesion has formed can damage a fragile member.

MNEMONIC

Forming, Storming, Norming, Performing, Adjourning

Tuckman's five, in order: the group **forms** (comes together, anxious), **storms** (conflict and control), **norms** (intimacy and trust), **performs** (mature working) and **adjourns** (separation). Same five stages the AGPA paradigm names as preaffiliation, power and control, intimacy, differentiation and separation.

8.6 Indications for group psychotherapy, and the contraindications

Who belongs in a group, and who does not. The indications for group psychotherapy follow from its mechanism. A group is well suited to problems that are fundamentally interpersonal, social withdrawal, loneliness, relationship difficulties and the character pathology that plays out with others, because these are exactly what the social microcosm brings into the room. It is powerful where universality and peer support carry weight, in the addictions, bereavement, chronic medical illness, trauma and other stigmatised or isolating conditions, and where modelling and skills practice help, as in rehabilitation of chronic mental illness. It is also economical, reaching more patients per therapist hour than individual work. A patient does well in an exploratory interactional group if they are reasonably motivated, self-reflective, psychologically minded and able to give and receive feedback; those low on these qualities are better placed in a supportive or skills-based group than excluded outright.

The contraindications are, above all, states that cannot tolerate or would disrupt the group's shared task. The acutely psychotic patient who is not yet stabilised, the actively suicidal patient for whom high group affect could destabilise, and the person preoccupied by an acute crisis are all unsuitable for an insight-oriented interactional group. So too is the patient whose first language is not the group's, and, for the exploratory group, the severely cognitively impaired. Marked

antisocial traits are a classic exclusion from a mixed group, though such patients may be treated in specialised homogeneous groups where the leader and setting are equipped for them.

COMMON TRAP

Do not place an acutely psychotic, actively suicidal or crisis-preoccupied patient into an interpretive, insight-oriented group. The intensity of affect and confrontation can worsen an unstable state; these patients need stabilisation first, and if a group at all, a structured supportive or psychoeducational one, not an exploratory interactional group.

11	5	7-8
YALOM'S THERAPEUTIC FACTORS	STAGES OF GROUP DEVELOPMENT (FORMING TO ADJOURNING)	IDEAL MEMBERS IN AN INTERACTIONAL GROUP

8.7 The evidence base, the lead indications and the Indian setting

Strong as a format, especially group CBT, more modest as a distinct modality. The examinable nuance is that group is chiefly a delivery format: the group version of an evidence-based therapy carries that disorder's evidence, so group CBT inherits CBT's standing, while the evidence for group-specific factors as a stand-alone treatment is more modest (the guideline evidence). On that basis, group CBT is first-line for gambling disorder (NICE 2025) and an option for binge-eating disorder (NICE 2017); group-based cognitive and behavioural therapy is recommended for antisocial personality disorder (NICE 2015); group cognitive stimulation therapy is recommended for mild-to-moderate dementia (NICE 2018 grade A); and group IPT or CBT is an option for perinatal depression (CANMAT 2016). The wider CBT and interpersonal-therapy evidence in depression sits in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes, and the group-based work for personality disorder connects to the Personality disorders notes.

INDIA

The Indian Psychiatric Society guidance names individual or group CBT for inhalant use disorder and group-format psychoeducation for somatic symptom disorder (IPS_CPG 2018; 2020). The therapeutic community and milieu approach is standard in Indian de-addiction and rehabilitation settings, and Alcoholics Anonymous, a self-help group, is among the most widely used community supports for alcohol dependence in India. The motivational and brief work that sits alongside these in the addictions is developed in the Substance use disorders notes.

GOOD TO REMEMBER

- **Group psychotherapy (the modality):** the model is the group as a social microcosm working through Yalom's eleven therapeutic factors, with cohesiveness the central one; the lead indication is interpersonal and relational problems, and, as an efficient format, the group version of an evidence-based therapy (group CBT is first-line for gambling disorder and an option for binge-eating disorder); the one signature technique is here-and-now process illumination and interpersonal feedback within a cohesive group.

HOLD THIS

Group psychotherapy works through Yalom's eleven therapeutic factors, cohesiveness foremost as the group's version of the therapeutic alliance, with the here-and-now group functioning as a social microcosm; interactional groups run about seven or eight members through five developmental stages (forming, storming, norming, performing, adjourning); the interpersonal or process group targets relational change while supportive, cognitive-behavioural, psychoeducational, self-help and therapeutic-community groups each lead on different factors; and the acutely psychotic, actively suicidal or crisis-bound patient is excluded from the insight-oriented group.

9 · Family therapy and couple therapy

Family therapy and **couple therapy** are the psychotherapies that change the unit of treatment: the patient is no longer the person in the chair but the web of relationships around them. Kaplan and Sadock define family therapy as a mosaic of techniques sharing one goal, the direct alteration of maladaptive family processes (Kaplan and Sadock CTP 2024). The examinable core is a single premise, that a symptom is best understood inside the system that carries it, and a small set of named schools that operationalise that premise differently. This is a favourite viva topic because it forces two clean discriminations: structural family therapy against strategic and Milan work, and a family-blaming aetiology (long discredited) against the modern, evidence-anchored idea of expressed emotion.



- Circular causality
- Feedback loop
- Boundaries
- Subsystems
- Alliance
- Reorganisation

Fig 19.6 Family-systems thinking replaces one-way blame with circular causality: symptoms participate in reciprocal feedback shaped by boundaries, subsystems and alliances, which therapy helps the family reorganise.

How to use this page. Fix the systemic premise first, then the structural vocabulary of boundaries and subsystems, then the two great systemic schools (structural and strategic and Milan), then the psychoeducational intervention and expressed emotion, which is where the strongest evidence sits. Learn the genogram and the family life cycle as the assessment tools of the field, and close on **couple therapy** and the guideline-anchored **indications**. The one sentence to carry out is that family and couple therapy is first-line for adolescent anorexia nervosa and a core relapse-reducing treatment in schizophrenia; everything else is model and technique built around those two indications.

9.1 The systemic premise: the family, not the individual, is the unit

The symptom belongs to the system, not only to the symptom-bearer. Systemic therapy rests on general systems theory (von Bertalanffy) and the cybernetics of Bateson: a family is a self-regulating system whose members are so interlocked that one cannot move without moving the others, like the interlocking gears of a clock (Kaplan and Sadock CTP 2024). Three ideas carry the premise. The identified patient is the member the family nominates as "the problem", but the

systemic clinician reads that symptom as a signal of, and a thing maintained by, the whole configuration, the classic instance being a couple's marital conflict detoured through a symptomatic child. **Homeostasis** is the system's tendency to return to its prior state through feedback loops, so that a symptom can paradoxically be doing a job, holding the family in a familiar equilibrium, which is why removing it is resisted. And causality is read as circular, not linear: A does not simply cause B; A and B cause each other in a repeating loop, so the question shifts from "who started it" to "what pattern keeps it going". Treat the pattern of relationships and the communication that sustains it, and the symptom loses its function.

Identified patient

The family member designated as "the problem"; systemically, the symptom-bearer who expresses or absorbs a dysfunction that belongs to the whole system.

Homeostasis

The family's self-correcting tendency, through feedback, to preserve a stable state; a symptom may serve to maintain this equilibrium.

Circular causality

Behaviour understood as mutually reinforcing loops rather than a one-way cause and effect; the focus is the repeating interactional pattern.

Boundaries

The implicit rules governing who takes part, and how, in a subsystem; they range from rigid (disengagement) through clear to diffuse (enmeshment).

RULE **The unit of treatment is the system.** In family and couple therapy the identified patient's symptom is read as a product of, and maintained by, the family system; you intervene in the relationships and the communication, not only in the person who carries the symptom.

The field divides into a handful of named schools, each a different pane on the same family (Kaplan and Sadock CTP 2024). The map below anchors the rest of the page.

SCHOOL	KEY FIGURES	FOCUS AND SIGNATURE TECHNIQUE
Structural	Salvador Minuchin	**Boundaries, subsystems and hierarchy; enactment and re-structuring in the room**
Strategic	Jay Haley, Cloe Madanes	**The symptom's function; directives and paradoxical prescription**
Milan systemic	Mara Selvini Palazzoli	**Beliefs that hold the system; circular questioning and the therapist team**
Psychoeducational	Carol Anderson, Ian Falloon	**Illness education and lowering expressed emotion; the multi-family group**
Experiential and emotion-focused	Carl Whitaker, Virginia Satir, Susan Johnson	**Present-moment affect and attachment; sculpting and enactment of emotion**
Transgenerational	Murray Bowen	**Differentiation of self across generations; the genogram**

The main schools of family and couple therapy; the structural and strategic systemic schools carry most of the examinable weight (Kaplan and Sadock CTP 2024; Tasman).

9.2 Structural family therapy (Minuchin): boundaries, hierarchy, enactment

Redraw the family's structure in the room. Structural family therapy, developed by Salvador Minuchin and colleagues at the Philadelphia Child Guidance Center, holds that a family's problems live in its structure: the invisible organisation of subsystems, boundaries and hierarchy through which it operates (Kaplan and Sadock CTP 2024; Rutter). The family is organised into subsystems, the spousal, parental and sibling subsystems chief among them, and each is bounded. Boundaries that are too rigid produce disengagement (members are emotionally cut off); boundaries that are too diffuse produce enmeshment (members are over-involved, and autonomy is lost). Healthy families keep a clear, generation-respecting hierarchy in which the parental subsystem holds authority. The structural therapist is deliberately leader-centred and active, and works less by talking about the family than by watching and changing it live through enactment, having the family perform its typical interaction in the session so the pattern can be seen and then altered on the spot. The overall aim is restructuring: resetting the boundaries and the hierarchy so the system can function.

Enmeshment

Boundaries too diffuse; over-involvement, poor differentiation, little privacy; the classic structure described in families of adolescents with anorexia nervosa (Minuchin).

Disengagement

Boundaries too rigid; emotional distance and under-involvement, so members function as isolated units.

Enactment

The family is directed to perform its habitual interaction in the room, letting the therapist observe the live pattern and intervene to change it.

Restructuring

The active resetting of subsystem boundaries and hierarchy, through boundary-making, unbalancing and challenging the family's assumptions.

MNEMONIC

JEM-HBUC

Minuchin's structural method proceeds in **seven** steps (Nichols): **J**oining and accommodating (reduce the family's anxiety), **E**nactment (let the pattern play out), structural **M**apping (widen the lens from the identified patient to the whole family), **H**ighlighting and modifying interactions (turn the intensity up or down), **B**oundary-making (realign the subsystems), **U**nbalancing (shift a stuck dyad or triad), and **C**hallenging unproductive assumptions.

WORKED EXAMPLE

An adolescent girl is presented as the problem: she and her mother argue constantly and she is losing weight. In the room the therapist notices the mother answers every question put to the daughter, and the father sits silent and outside. The structure is enmeshed mother-daughter, disengaged father, with the marital conflict routed through the girl. The therapist uses enactment (asks the parents to discuss a decision while the daughter stays out of it), makes a boundary around the spousal subsystem, and unbalances by aligning with the father to bring him in. The symptom is left alone; the structure is changed.

GOOD TO REMEMBER

- **Structural family therapy (the therapy):** Minuchin's model reads the family's problem in its structure, the subsystems, the boundaries (rigid or disengaged versus diffuse or enmeshed) and the hierarchy; its lead indication is the child or adolescent presented as the identified patient, classically the family of an adolescent with anorexia nervosa; the one signature technique is enactment, staging the interaction in the room and restructuring the boundaries live.

9.3 Strategic and Milan systemic therapy: the symptom's function and paradox

Design a specific intervention to interrupt the symptom's role. The strategic school grew from Bateson's Palo Alto group and the Mental Research Institute, with Don Jackson, Jay Haley, Cloe Madanes, John Weakland and Paul Watzlawick, and it is rooted in communication theory (Kaplan and Sadock CTP 2024). Where the structural therapist maps the structure, the strategic therapist asks what the symptom does, treating it as a communication that serves a function in the system, then designs a specific strategy (a directive) to disrupt that function. Madanes set out several parameters to weigh before intervening, among them whether the symptom is voluntary or involuntary, who in the family holds the real power, and whether maintaining the symptom serves a purpose. The signature moves are directives and, most famously, paradoxical interventions: prescribing the symptom (asking the family to perform the very behaviour they came to lose), so that the behaviour either comes under voluntary control or reveals its function; assigning rituals or ordeals that disturb the homeostasis; and reframing a behaviour from

pathological to protective. The Milan systemic group, led by Mara Selvini Palazzoli, added a team of therapists observing behind a screen, circular questioning (asking one member to comment on the relationship between two others, so differences and patterns surface), and hypothesising, neutrality and paradox and counterparadox as its working stance.

PEARL

Hold the two systemic schools by their verbs. The **structural** therapist *restructures*, working in the here and now on boundaries and hierarchy through enactment. The **strategic** therapist *strategises*, working on the symptom's function through directives and paradox. Both are brief, active and directive; the Milan variant adds the team behind the screen and circular questioning.

GOOD TO REMEMBER

- **Strategic and Milan systemic therapy (the therapy):** the model treats the symptom as a communication with a function in the family and designs a targeted strategy to interrupt it (Haley, Madanes; the Milan group under Selvini Palazzoli); its lead use is the rigid, stuck or treatment-refractory family, including families around a life-threatening symptom; the one signature technique is the paradoxical intervention, prescribing the symptom, plus circular questioning in the Milan form.

9.4 Psychoeducational family intervention and expressed emotion

Educate the family and lower the emotional temperature to cut relapse. The psychoeducational family intervention is the best-evidenced family treatment and the mainstay for severe and disabling mental illness (Kaplan and Sadock CTP 2024). Developed by Carol Anderson and Ian Falloon and delivered by McFarlane in a multifamily format of between two and ten families, it teaches the family to see the illness as a biological condition (so as to reduce blame), to recognise early signs of relapse, to support medication and appointments, and, above all, to lower the emotional intensity in the home. Its scientific engine is **expressed emotion**, a construct measuring the amount of criticism, hostility and emotional over-involvement a relative directs at the identified patient (Kaplan and Sadock CTP 2024). Expressed emotion is assessed in research by the Camberwell Family Interview, a semistructured interview conducted with the relative alone that rates **five** dimensions, criticism, hostility, emotional over-involvement, warmth and positive remarks, of which the first three define a high-expressed-emotion household; a briefer proxy is the Five Minute Speech Sample. The examinable payoff is that high expressed emotion robustly predicts relapse, and that psychoeducational work which lowers expressed emotion reduces relapse and rehospitalisation in schizophrenia. The deep clinical use of expressed emotion in psychosis is developed in the Schizophrenia: clinical features and phenomenology notes, and its role in mood relapse in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes.

TRAP **Reading expressed emotion as blaming the family.** The double-bind and the "schizophrenogenic mother" were family-blaming aetiological theories, now discredited; expressed emotion is not an aetiology but a measure of how the family *responds* to an established illness and can buffer or worsen its course (Kaplan and Sadock CTP 2024). Do not present the family as the cause.

3	5	7
COMPONENTS OF HIGH EXPRESSED EMOTION (CRITICISM, HOSTILITY, OVER-INVOLVEMENT)	DIMENSIONS RATED BY THE CAMBERWELL FAMILY INTERVIEW	STEPS OF STRUCTURAL FAMILY THERAPY (NICHOLS)

GOOD TO REMEMBER

- **Psychoeducational family intervention (the therapy):** the model treats the illness as a biological condition and equips the family with information, relapse-recognition and lower expressed emotion (Anderson, Falloon; the multifamily group of McFarlane); its lead indication is schizophrenia and first-episode psychosis, where it is a core relapse-reducing treatment; the one signature target is high expressed emotion, whose reduction cuts relapse and rehospitalisation.

9.5 Assessing the family: the genogram, the life cycle and the McMaster model

Map three generations, place the family in its life stage, and rate its functioning. The genogram is the field's core assessment tool: a graphical map of a family's structure and relationships across three or more generations, resembling a family tree but annotated with relationship quality, illness, deaths and cut-offs (Kaplan and Sadock CTP 2024; Rutter). The technique originates in the transgenerational work of Murray Bowen and its symbols were standardised by McGoldrick and Gerson; drawn in the room, it depathologises the family's struggle by placing it in a longer story. The *family life cycle* (Carter and McGoldrick) frames normal family development as a sequence of stages, leaving home, forming a couple, raising young children, living with adolescents, launching them, and later life, each with a transition that can become a sticking point; symptoms often erupt at these junctions, and reading a presentation against the life cycle is itself an intervention. For structured measurement, the McMaster Model of Family Functioning (Epstein, Bishop and Baldwin) rates the family on six dimensions, problem-solving, communication, roles, affective responsiveness, affective involvement and behaviour control, operationalised in the self-report Family Assessment Device. Together these are the assessment layer that any structural, strategic or psychoeducational treatment is built upon.

GOOD TO REMEMBER

- **The genogram and family assessment (the principle):** the genogram is an assessment and mapping tool, not a therapy, a diagram of three or more generations that surfaces patterns, illness and cut-offs (Bowen; McGoldrick and Gerson); the one discriminator is that the family life cycle reads symptoms against normal developmental transitions, and the one exam fact is the McMaster model's six dimensions of family functioning measured by the Family Assessment Device.

9.6 Couple therapy: behavioural and emotion-focused

Two well-evidenced routes to the same distressed dyad. **Couple therapy** targets the interactional patterns that block intimacy and generate conflict, and two models dominate the examinable ground (Kaplan and Sadock CTP 2024; Tasman). Behavioural couple therapy, developed by Jacobson, treats distress as learned, poorly-rewarding interaction and rebuilds it through behaviour exchange (deliberately increasing pleasing exchanges) and through communication and problem-solving skills training; its later refinement, integrative behavioural couple therapy (Christensen and Jacobson), adds emotional acceptance where change is not possible and matches the outcomes of the purely behavioural form. Emotion-focused couple therapy, developed by Susan Johnson, is an experiential and attachment-based model: it reads the couple's fights as protests against a threatened attachment bond, de-escalates the negative cycle, and restructures the interaction so partners can voice underlying attachment needs and respond to them, forging a more secure bond. Behavioural couple therapy is the option to name for alcohol use disorder (the sober partner supports abstinence and the dyad rebuilds trust), where it is a guideline-endorsed treatment, and couple therapy is offered for depression when relationship distress is driving or maintaining the disorder; the motivational-interviewing style that accompanies couple work in the addictions is developed in the Substance use disorders notes.

FEATURE	BEHAVIOURAL COUPLE THERAPY	EMOTION-FOCUSED COUPLE THERAPY
Originator	Jacobson (integrative form, Christensen and Jacobson)	**Susan Johnson**
Model of distress	Learned, poorly-rewarding interaction	**A threatened attachment bond**
Core technique	Behaviour exchange; communication and problem-solving training	**De-escalate the negative cycle; restructure to voice attachment needs**
Named indication	Alcohol use disorder; depression with relationship distress	**Relationship distress and insecure attachment**

The two dominant couple therapies; behavioural (skills-based) and emotion-focused (attachment-based) (Kaplan and Sadock CTP 2024; Tasman; the guideline evidence).

GOOD TO REMEMBER

- **Couple therapy (the therapy):** two evidence-based models, behavioural couple therapy (Jacobson: behaviour exchange plus communication and problem-solving training) and emotion-focused couple therapy (Johnson: attachment-based de-escalation of the negative cycle); the lead named indication is behavioural couple therapy for alcohol use disorder, with couple therapy also offered for depression complicated by relationship distress; the one technique to name is communication and problem-solving skills training.

9.7 Indications and the evidence base

Two strong indications, several good adjunctive ones. The confirmed **indications** for family and couple therapy cluster around two well-evidenced roles and a set of adjunctive ones (the

guideline evidence). Anorexia-nervosa-focused family therapy (family-based treatment) is first-line for children and young people with anorexia nervosa (NICE 2017, grade A; RANZCP 2014). Family intervention is a core, relapse-reducing treatment in schizophrenia and first-episode psychosis (NICE 2009 and 2014; IPS_CPG 2017; MOH_SG 2011; RANZCP 2016). Family-focused therapy is a recommended adjunct in bipolar disorder (IPS_CPG 2017 grade A; VA_DOD 2023), and family-based therapy for bulimia is offered to young people (NICE 2017). On the couple side, behavioural couples therapy is an option for alcohol use disorder (VA_DOD 2021; WHO mhGAP 2012) and couples-focused therapy is offered for depression with relationship distress (VA_DOD 2022). Generic systemic indications, from the schools above, include the child or adolescent presented as the identified patient, families in crisis at a life-cycle transition, and problems that span the generations.

PRESENTATION	MODALITY	EVIDENCE AND STATUS
Adolescent anorexia nervosa	Family-based treatment (FT-AN)	**First-line for children and young people (NICE 2017, grade A)**
Schizophrenia, first-episode psychosis	Family intervention, psychoeducational	**Core relapse-reducing treatment (NICE 2009 and 2014; IPS_CPG 2017)**
Bipolar disorder	Family-focused therapy	**Recommended adjunct (IPS_CPG 2017 grade A; VA_DOD 2023)**
Bulimia nervosa (young people)	Family-based therapy (FT-BN)	**Offered to young people (NICE 2017)**
Alcohol use disorder	Behavioural couples therapy	**An option (VA_DOD 2021; WHO mhGAP 2012)**
Depression with relationship distress	Couple therapy	**Offered where the relationship drives the disorder (VA_DOD 2022)**

The guideline-anchored indications for family and couple therapy; adolescent anorexia and schizophrenia relapse prevention are the two strongest (the guideline evidence).

INDIA

The collectivist, co-resident Indian family makes family involvement the natural default rather than an add-on. The Indian Psychiatric Society operationalises this: its alcohol-use guideline endorses family-based treatment that uses a co-resident relative as recovery monitor and supervisor of disulfiram (IPS_CPG 2014, grade B), a culturally specific adaptation to Indian family structures, and the IPS psychotherapy guideline (Agarwal, Nischal, Praharaj, Menon, Kar; Indian J Psychiatry 2020) treats family and psychoeducational work as core psychosocial care. The NIMHANS tradition of family-focused management of severe mental illness sits in the same space. State both the guideline endorsement and the cultural fit; an examiner asking about family therapy in India is usually testing the disulfiram-supervision adaptation.

GOOD TO REMEMBER

- **Family and couple therapy (the indications):** the two strongest confirmed roles are family-based treatment for adolescent anorexia nervosa (first-line, NICE 2017 grade A) and family intervention for schizophrenia and first-episode psychosis (core, relapse-reducing); family-focused therapy is an adjunct in bipolar disorder, and behavioural couples therapy an option for alcohol use disorder; the systemic indication is any case where the identified patient's symptom is embedded in the family or couple system.

HOLD THIS

Family and couple therapy treats the SYSTEM, not the individual: the identified patient's symptom is read within the family's homeostasis and circular causality. Minuchin's structural family therapy restructures boundaries, subsystems and hierarchy through enactment; strategic and Milan work (Haley, Madanes, Selvini Palazzoli) targets the symptom's function through directives, paradox and circular questioning; the psychoeducational intervention lowers expressed emotion (criticism, hostility and emotional over-involvement, rated by the Camberwell Family Interview) to cut relapse in schizophrenia; the genogram maps three or more generations; and couple therapy is behavioural (Jacobson) or emotion-focused (Johnson). The two strongest indications are family-based treatment for adolescent anorexia nervosa (first-line, NICE 2017 grade A) and family intervention for schizophrenia relapse prevention.

10 · Brief and crisis-focused psychotherapies

Grouped here are the deliberately short, sharply focused interventions: the **brief and time-limited psychotherapies**, the **crisis intervention** that Gerald Caplan built on Erich Lindemann's grief work, and problem-solving therapy. They matter for the examination out of proportion to their length, because they carry a handful of hard, quotable facts, an eponym or two, and one principle that examiners return to again and again: a *crisis-focused* therapy aims to restore the person to the level they were functioning at before the crisis, not to remake the personality. Learn the family by its shared skeleton first, then hang the named models on it.

How to use this page. The three moving parts are, in order, the shared architecture that makes any therapy *brief* (a single agreed focus, a fixed session limit, an active therapist, careful selection); the named brief dynamic and brief cognitive forms; and crisis intervention with its underlying crisis theory. Keep the discriminator sharp throughout: brief dynamic therapy still reaches, cautiously, for insight, whereas crisis intervention stays resolutely on the surface and on the present emergency.

10.1 The shared architecture of brief therapy

Short is not simply "less of" long. Every brief psychotherapy is defined by four shared commitments rather than by session count alone (Wolberg; Companion to Psychiatric Studies). There is a single *circumscribed focus* agreed by patient and therapist, with deliberate **selective inattention** to peripheral material however tempting; a *time limit*, usually set in advance, with most models running between about twelve and twenty-six sessions; an *active, engaged therapist* who keeps the work on the focus rather than waiting on free association; and *careful patient selection*, since these methods suit the psychologically minded, motivated patient with good ego strength and a focal, not diffuse, problem. Wolberg groups the short therapies into 3 kinds, worth

holding as a spine: *crisis intervention*, *supportive-educational* short-term therapy, and *dynamic* short-term therapy, ascending roughly from surface stabilisation toward the beginnings of personality change. The governing maxim of the supportive-educational band is Wolberg's own: get in fast and get out fast.

RULE **Focus, limit, activity, selection.** A therapy is *brief* because it has one agreed focus, a session limit fixed in advance, an active therapist, and a well-chosen patient, not merely because it has few sessions.

10.2 Brief dynamic and brief cognitive forms

A small pantheon of named focal therapies, plus a cognitive wing. The *dynamic* short-term therapies keep the concepts of psychoanalysis (unconscious conflict, transference, defence, interpretation) but cap the breadth and depth of the work around one focus, with no expectation of a regressive transference neurosis (Companion). The focal therapy tradition begins with Michael Balint's focal psychotherapy and matures in four classic models that are the examinable core of this section. In parallel, the *cognitive* wing simply delivers the standard method in a shortened, present-focused frame: brief CBT and structured counselling over roughly six to eight sessions are established short-term options for mild-to-moderate depression (Companion). The comparison of full-length CBT with interpersonal therapy in depression is developed in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes.

MODEL (ORIGINATOR)	DEFINING FEATURE	SIGNATURE TECHNIQUE OR FRAME
Focal psychotherapy (Balint)	The founding brief-dynamic idea: keep aims limited and work to a single agreed focus	Selective attention to one focal conflict; applied psychoanalysis, made brief by design
Brief / focal therapy (Malan, Tavistock)	Interprets a focal conflict through two triangles	**The 2 triangles: the triangle of conflict (impulse, anxiety, defence) and the triangle of person (transference, current other, past parent)**
Time-limited psychotherapy (Mann)	A fixed, non-negotiable ceiling of **12** sessions with the final date set at the outset	A single "central issue" tied to separation; mastering the ending models mastery of other anxieties
Short-term anxiety-provoking psychotherapy (Sifneos)	Actively raises anxiety to press an oedipal-level focus in high-functioning patients	Anxiety-provoking confrontation and clarification; tight selection criteria
Intensive short-term dynamic psychotherapy (Davanloo)	Relentless, early challenge to defences and resistance	The "trial therapy" as both assessment and treatment; rapid unlocking of the unconscious

The brief dynamic models; Malan's two triangles and Mann's fixed twelve-session frame are the most quotable single facts, and the accompanying figure lays out Malan's two triangles.

Mann's model adds a second quotable list: **4** basic universal conflicts that surface around separation and loss, namely independence versus dependence, activity versus passivity, adequate

versus lost self-esteem, and unresolved grief. Selection is the practical gatekeeper across all of these: a circumscribed focal complaint, psychological mindedness, motivation to change rather than merely to relieve symptoms, and the capacity to form a rapid working alliance.

GOOD TO REMEMBER

- **Brief and time-limited psychotherapy (the therapy):** the model is a psychoanalytically informed but strictly bounded treatment worked to a single focus with a session limit set in advance; the lead indication is a well-selected, psychologically minded patient with a circumscribed focal or neurotic conflict (short-term psychodynamic psychotherapy is also a reasonable option for depression); the one frame to quote is Mann's fixed twelve-session ceiling, or Malan's interpretation through the two triangles.

10.3 Crisis intervention and crisis theory

Restore the pre-crisis equilibrium, nothing grander. A **crisis** is a self-limiting period of psychological disequilibrium set off when a hazardous event, a loss or a threat, overwhelms the person's habitual coping and problem-solving (Caplan; Lindemann's study of acute grief after the Coconut Grove fire). Crises are *time-limited* by nature, usually running their course within about six weeks, and Caplan described them unfolding across **4** phases: an initial rise in tension as usual coping is challenged; mounting tension and disorganisation as those methods fail; mobilisation of internal and external resources with novel, emergency problem-solving; and, if still unresolved, a breaking point with major disorganisation. Caplan also split crises into *developmental* (maturational, such as adolescence or retirement) and *situational* (accidental, such as bereavement or disaster). The goal of crisis intervention follows directly and is the single most examinable line here: to restore the person to the pre-crisis level of functioning, at minimum, occasionally leaving them stronger, but never aiming at personality reconstruction (Wolberg). The stance is active, present-focused and time-limited, typically one to six sessions over the first several weeks, with the therapist mobilising social support, involving family, tackling the concrete precipitant, and, where suicidality is present, building a collaborative safety plan. Because the goals are limited, the method drifts deliberately away from insight work toward practical, behavioural and problem-solving techniques.

TRAP **Crisis intervention is not brief dynamic therapy.** Chasing insight or the unconscious in an acute crisis is the classic error; the goal is restoration of the pre-crisis equilibrium through active problem-solving and support, not interpretation.

WORKED EXAMPLE

A young woman presents in acute distress the week after a sudden broken engagement, tearful, not eating, not sleeping, with fleeting thoughts that life is not worth living but no plan. The crisis-focused response is not to explore her childhood attachments. Over a handful of sessions the therapist names the precipitant, restores sleep and appetite with practical measures, mobilises a sister and two friends as an active support network, agrees a simple safety plan, and helps her rehearse the next concrete steps. Within a few weeks she is back to her baseline; the deeper work, if she wants it, is a separate referral. The suicide risk assessment and the safety-planning tools used here are developed in the Somatic-symptom, sexual, impulse-control disorders and suicide notes.

INDIA

The Indian Psychiatric Society anchors the screening-and-brief-intervention (SBIRT) framework at every psychiatric and primary-care contact and endorses brief, motivation-based psychosocial interventions for alcohol use (IPS_CPG 2014; 2018), a natural fit for busy, under-resourced services; the motivational-interviewing side of this is developed in the Substance use disorders notes. The IPS also recommends brief crisis intervention with a collaboratively agreed crisis plan in borderline personality disorder to reduce hospitalisation (IPS_CPG 2023; NICE 2009), covered further in the Personality disorders notes.

GOOD TO REMEMBER

- **Crisis intervention (the therapy):** the model is Caplan's, a self-limiting crisis (about six weeks, four phases) in which coping is overwhelmed; the lead indication is any acute psychosocial or suicidal crisis, disaster or bereavement; the one technique is active, time-limited problem-solving plus mobilising support, with the fixed goal of restoring the pre-crisis level of functioning.

10.4 Problem-solving therapy

Teach the process, not the answer. Problem-solving therapy (PST), developed by D'Zurilla and Nezu, rests on the idea that stress plus poor coping breaks down a person's problem-solving ability and so feeds depression; the remedy is to train a structured, transferable problem-solving process (Geriatric Psychiatry Study Guide). Its staged sequence runs from a constructive *problem orientation* through *defining and formulating* the problem, *generating alternatives* (brainstorming without early judgement), *decision-making* that weighs the options, and finally *implementing and verifying* the chosen solution in real life. It is brief, structured and highly teachable, which is exactly why guidelines reach for it in hard-pressed settings: structured problem-solving therapy is offered for self-harm (NICE 2022; WHO_mhGAP 2015) and is one recognised psychotherapy option for major depression, with its best evidence in older adults and primary care (VA/DoD 2022).

MNEMONIC

ORIENT, DEFINE, GENERATE, DECIDE, DO

The problem-solving sequence: a constructive **orient**ation to problems, **defin**ing the problem, **generat**ing options, **decid**ing between them, then **do**ing and verifying. The first step, orientation, is the one novices skip and the one that most separates PST from mere advice-giving.

GOOD TO REMEMBER

- **Problem-solving therapy (the therapy):** the model is that depression follows a breakdown in coping with life problems; the lead indication is self-harm and depression, especially in older adults and primary care; the one technique is training the staged problem-solving sequence, orientation, definition, generating options, deciding, and implementing.

12	4	6
SESSIONS, THE FIXED CEILING OF MANN'S TIME-LIMITED PSYCHOTHERAPY	PHASES OF A CRISIS IN CAPLAN'S MODEL	WEEKS, THE USUAL SELF-LIMITING COURSE OF A CRISIS

PEARL

Three overlapping "briefs", one discriminator. All three families are short and focal, but the *aim* separates them: brief dynamic therapy still reaches for a measure of insight into a focal conflict; crisis intervention reaches only for restored pre-crisis functioning; problem-solving therapy reaches for a durable coping skill. When a stem describes an acute emergency and asks for the goal, the answer is restoration of the pre-crisis level, not insight.

HOLD THIS

Crisis intervention (Caplan, building on Lindemann) treats a self-limiting crisis, about six weeks across four phases, with an active, time-limited, problem-solving stance whose single goal is to restore the pre-crisis level of functioning while mobilising the patient's support, and it never aims at personality change.

11 · Relaxation training and biofeedback

Relaxation training and **biofeedback** are the physiological end of the psychotherapies: rather than working on thoughts, relationships or the unconscious, they teach the patient to turn down the body itself, on the premise that a relaxed body cannot easily sustain an anxious mind. They are niche in the examiner's mind but not obscure, because two of them carry firm guideline indications, applied relaxation is a first-choice treatment for generalised anxiety disorder, and relaxation and biofeedback are named first-line for somatoform pain, so a single mis-stated indication is the easiest way to lose a mark here.

How to use this page. Learn the family as one shared principle expressed four ways (Jacobson's muscular route, autogenic self-suggestion, breathing, and applied relaxation as the portable coping form), then learn **biofeedback** as the instrumented cousin that adds one thing the others

lack, a real-time signal of a normally-unconscious body function. Fix which channel treats which disorder, and close on the two indications examiners actually test.

11.1 The relaxation-response model

A relaxed body is incompatible with anxiety, so lower the body to quiet the mind. Every technique on this page rests on one idea: the peripheral physiology of anxiety, raised muscle tension, rapid shallow breathing and sympathetic arousal, can be deliberately down-regulated, and a state of low physiological arousal is reciprocally incompatible with the state of anxiety (the same reciprocal-inhibition rationale that lets relaxation serve as the counter-conditioning partner to graded exposure in systematic desensitisation). Relaxation training is therefore both a stand-alone anxiety-management skill and a building block inside behaviour therapy. The techniques differ only in the door they use into the same relaxed state: skeletal muscle (Jacobson), autonomic self-suggestion (autogenic training), the respiratory cycle (diaphragmatic breathing), or an external instrument (biofeedback).

RULE **Down-regulate the body first.** Relaxation-based methods treat anxiety by damping muscular and autonomic arousal, a physiological state incompatible with anxiety; the portable, real-situation form is applied relaxation, and it is the one with a first-line indication.

11.2 The relaxation family: JPMR, applied relaxation, autogenic training and breathing

One relaxed state, four routes in. The reference technique is Jacobson progressive muscular relaxation, JPMR, described by the American physiologist Edmund Jacobson. Its signature move is the systematic *tense-and-release* of successive muscle groups: the patient deliberately tenses a group (hands, forearms, face, neck, shoulders, chest, abdomen, then the legs), holds the tension, then releases it, learning to discriminate the felt difference between a tense and a relaxed muscle and to reproduce the released state at will. It is often abbreviated progressive muscle relaxation and taught as a daily home practice. Applied relaxation, developed by the Swedish psychologist Lars-Goran Ost, takes that trained skill and makes it usable in the moment: the patient is progressively shaped from full progressive relaxation, through release-only and cue-controlled relaxation, to a rapid, portable version that can be deployed within seconds inside a real anxiety-provoking situation, which is why it, and not lying-down JPMR, is the form with the strongest anxiety-disorder evidence. Autogenic training (the German psychiatrist Johannes Schultz) reaches the same state by silent autonomic self-suggestion, the patient repeating standard formulae to induce sensations of *heaviness* (muscular relaxation) and *warmth* (peripheral vasodilation) in the limbs, plus a calm heartbeat, easy breathing, abdominal warmth and a cool forehead. Diaphragmatic breathing corrects the rapid shallow thoracic overbreathing of anxiety with slow abdominal breaths, reversing the hypocapnia that drives the somatic symptoms of the hyperventilation syndrome.

TECHNIQUE	ROUTE IN / SIGNATURE MOVE	LEAD USE
JPMR (Jacobson)	Sequential tense-then-release of muscle groups, learning to feel tension leave	General anxiety and tension; the relaxation partner in systematic desensitisation
Applied relaxation (Ost)	Shaping to a rapid, cue-controlled skill deployed in the real situation	**Generalised anxiety disorder, a first-choice high-intensity psychological intervention**
Autogenic training (Schultz)	Silent self-suggestion of heaviness and warmth across the six standard exercises	Stress-related and psychophysiological disorders
Diaphragmatic breathing	Slow abdominal breathing that reverses the hypocapnia of overbreathing	**Hyperventilation and panic; somatoform presentations**

The relaxation family; applied relaxation is the portable, in-situation form and the only member with a first-line anxiety-disorder indication.

PEARL

The examiner's discriminator inside the family is **applied relaxation versus JPMR**. JPMR is the foundational drill, tense-and-release done in a quiet room; *applied relaxation* is what you build on top of it, a rapid coping skill the patient uses *while* anxious in real life. When a stem says "first-line psychological treatment for generalised anxiety disorder that is not CBT", the answer is applied relaxation, not plain progressive muscle relaxation.

11.3 Biofeedback: the principle and the channels

Show the patient a hidden body signal, and they learn to control it. Biofeedback attaches an electronic instrument to a physiological parameter the person is normally unaware of, then feeds that parameter back in real time as a sound or a moving display; watching the signal, the patient gradually learns to shift it in the wanted direction, and with practice can reproduce the control without the machine. It is, in effect, operant learning of an autonomic or muscular function, and the feedback signal is its active, defining ingredient. The channels are worth knowing by which body function they read and which disorder they treat.

CHANNEL	SIGNAL FED BACK	TYPICAL INDICATION
EMG (electromyographic)	Muscle tension (microvolts from a muscle group)	**Tension-type headache, muscle-contraction pain, rehabilitation**
Thermal	Peripheral skin temperature (a proxy for blood flow)	**Migraine and Raynaud's phenomenon (learning to warm the hands)**
EEG (neurofeedback)	Cortical rhythms	Epilepsy (sensorimotor rhythm) and attention-deficit disorder
Electrodermal / HRV	Skin conductance, or heart-rate variability	Anxiety, hypertension and general stress arousal

The four common biofeedback channels; the two highest-yield pairings are EMG with tension headache and thermal with migraine.

WORKED EXAMPLE

A patient with frequent tension-type headache is set up with an **EMG** sensor over the frontalis and neck muscles; the instrument turns the muscle tension into a tone that rises with tightening. Over successive weekly sessions she learns to drop the tone by consciously loosening those muscles, first with the machine and then without it, and her headache frequency falls. The instrument taught nothing the muscle could not do on its own; it simply made an invisible signal visible long enough to be brought under voluntary control.

TRAP **Biofeedback is not just relaxation with wires.** Its defining, active element is the instrument feeding a normally-unconscious signal back in real time so the patient learns voluntary control of *that specific parameter*; ordinary relaxation training reaches a low-arousal state with no instrument at all. And JPMR is tense-*then*-release, not relax-only.

11.4 Evidence base and lead indications

Modest and mostly adjunctive, with two firm first-line roles. Across disorders the relaxation methods are best read as effective components or adjuncts rather than powerful stand-alone cures, and controlled evidence for biofeedback being superior to simple relaxation is thin. But two indications are exam-solid. First, applied relaxation is one of two equivalent first-choice high-intensity psychological interventions for generalised anxiety disorder (alongside CBT) in the NICE guidance, delivered over roughly twelve to fifteen weekly sessions. Second, relaxation therapy and biofeedback are named first-line for somatoform (medically unexplained) pain in somatic symptom disorder, with progressive muscular relaxation and diaphragmatic breathing first-line for somatoform presentations generally. Relaxation is also offered for anxiety in intellectual disability, and biofeedback has established uses in tension headache, migraine and Raynaud's; the honest caveat is that guideline bodies have found insufficient evidence to recommend for or against adding biofeedback in major depression. Applied relaxation as an anxiety treatment sits beside the exposure methods developed in the Anxiety, OCD and trauma-related disorders notes, and its somatoform role beside the fuller account in the Somatic-symptom, sexual, impulse-control disorders and suicide notes.

INDIA

The Indian Psychiatric Society somatic-symptom guidance (IPS_CPG 2020) places *progressive muscular relaxation, diaphragmatic breathing and biofeedback* as first-line for somatoform and somatoform-pain presentations, the disorders in which relaxation methods matter most in Indian practice, where somatic idioms of distress are common. This dovetails with the strong indigenous tradition of yoga and breath-regulation practices and the NIMHANS behavioural-medicine tradition, so relaxation-based work is often the culturally most acceptable first psychological step.

2
FIRST-CHOICE HIGH-INTENSITY PSYCHOLOGICAL INTERVENTIONS FOR GAD (APPLIED RELAXATION, WITH CBT)

6
STANDARD AUTOGENIC-TRAINING EXERCISES (HEAVINESS, WARMTH AND THE REST)

MNEMONIC

MET

The three biofeedback pairings to hold: **M**uscle tension → EMG → tension headache; **E**EG → neurofeedback → epilepsy and ADHD; **T**emperature (thermal) → migraine and Raynaud's. If it is a headache, ask muscle (EMG) versus vascular (thermal).

GOOD TO REMEMBER

- **Jacobson progressive muscular relaxation (JPMR):** model is that a relaxed muscle is incompatible with anxiety; lead use is general anxiety and tension and as the relaxation half of systematic desensitisation; the one technique is sequential tense-and-release of muscle groups.
- **Applied relaxation (Ost):** model is a portable coping skill built from progressive muscle relaxation; lead indication is generalised anxiety disorder (a first-choice high-intensity psychological intervention); the one technique is rapid, cue-controlled relaxation deployed in the real anxious moment.
- **Autogenic training (Schultz):** model is autonomic self-regulation by silent self-suggestion; lead indication is stress-related and psychophysiological disorders; the one technique is inducing heaviness and warmth in the limbs.
- **Biofeedback:** model is operant learning of an unconscious body signal made visible by an instrument; lead indications are tension headache (EMG), migraine and Raynaud's (thermal) and somatoform pain; the one technique is real-time feedback of a physiological parameter to gain voluntary control.

HOLD THIS

Relaxation training lowers physiological arousal to a state incompatible with anxiety, and its portable form, applied relaxation (Ost), is a first-choice psychological treatment for generalised anxiety disorder; biofeedback adds a real-time instrument signal so the patient learns voluntary control of a hidden body function, its two signature pairings being EMG for tension headache and thermal for migraine, and relaxation and biofeedback are first-line for somatoform pain in the Indian somatic-symptom guidance.

12 · The third-wave therapies

The **third-wave therapies** are the acceptance-and-mindfulness generation of behaviour therapy: a family of treatments that, instead of arguing a patient out of a distressing thought, teach a new *relationship* to that thought, one of awareness, acceptance and willingness rather than dispute. Where classical cognitive behaviour therapy asks "is this thought true, and can we make it more accurate?", the third wave asks "must this thought be obeyed at all, and can you hold it lightly while you act on what matters?". Three members carry the examinable weight and are widely practised in real clinics, dialectical behaviour therapy (DBT), acceptance and commitment therapy (ACT) and mindfulness-based cognitive therapy (MBCT); each is built on mindfulness, and each has a distinct lead indication that the examiner will expect you to name without hesitation.

How to use this page. Learn DBT in depth first, because it is the most examined and the most clinically important of the three, its biosocial theory, its four modes and its four skills modules,

then its lead indication in borderline personality disorder. Then take ACT through its one idea (psychological flexibility) and its six processes, and MBCT through its one job (preventing depressive relapse). Close on the evidence, kept honest against the guideline evidence, because the trap the whole page is built to prevent is over-claiming: DBT is not ordinary CBT, and ACT and MBCT are not first-line for everything just because they are fashionable.

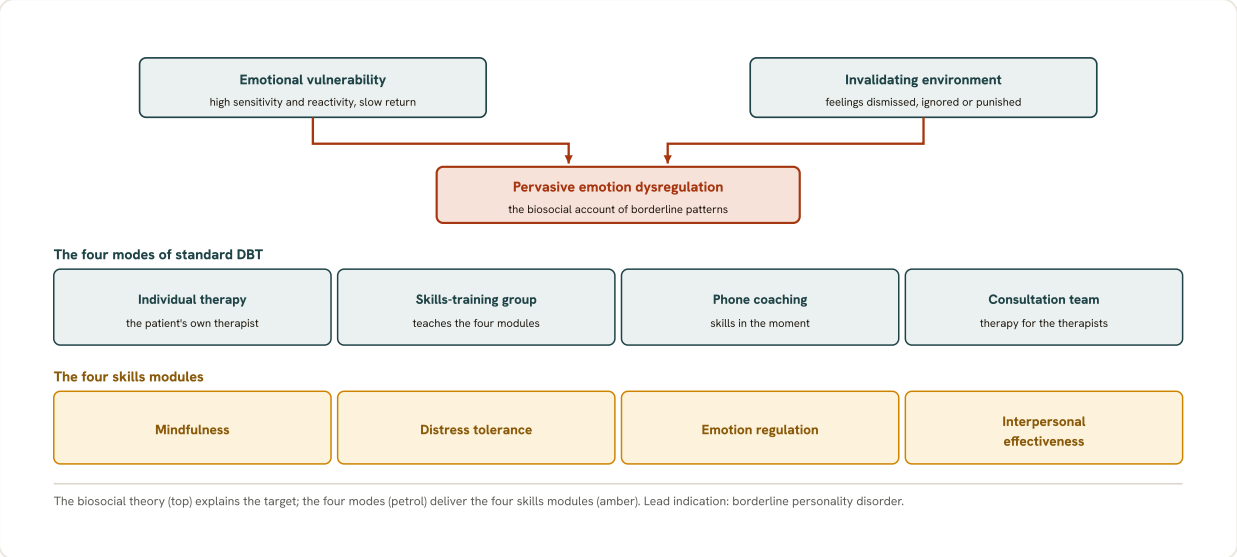


Fig 19.7 Dialectical behaviour therapy: the biosocial theory, the four modes and the four skills modules. Linehan's biosocial theory holds that a constitutional emotional vulnerability meeting a persistently invalidating environment produces the pervasive emotion dysregulation that underlies borderline patterns. Standard DBT treats this through four coordinated modes: individual therapy, a skills-training group, between-session telephone coaching to apply skills in the moment, and a therapist consultation team that keeps the therapists effective. The skills group teaches four modules: mindfulness, distress tolerance, emotion regulation and interpersonal effectiveness. Its strongest evidence and lead indication is borderline personality disorder, taught in full in the Personality disorders notes.

12.1 Three waves of behaviour therapy

First change the behaviour, then the thought, then your relationship to the thought.

Behaviour therapy has moved through three eras, and naming them is the cleanest way to place the third wave (Kaplan and Sadock CTP 2024). The *first wave*, from the mid-nineteen-fifties, was pure learning theory: classical and operant conditioning, the work of Skinner, Wolpe and Eysenck, targeting observable behaviour alone. The *second wave*, from the nineteen-seventies, added cognition, giving Beck's cognitive therapy and Ellis's rational emotive therapy and, in time, the integrated cognitive behaviour therapy that is still the dominant system worldwide; its lever is the *content* of thought. The **third-wave therapies** emerged partly from Jacobson's finding that behavioural activation alone matched full CBT in depression, and they are marked by themes new to behaviour therapy, metacognition, acceptance, mindfulness, dialectics and values. Their shared move is contextual, not content-focused: they change how a person relates to inner experience rather than trying to rewrite the experience itself.

RULE **Acceptance, not disputation, is the defining move.** The third wave changes the patient's *relationship* to thoughts and feelings (awareness, acceptance, willingness), whereas second-wave CBT changes their *content* and accuracy. That single distinction separates DBT, ACT and MBCT from classical CBT.

12.2 Dialectical behaviour therapy: Linehan and the biosocial theory

An emotionally vulnerable temperament meeting a chronically invalidating environment. **Dialectical behaviour therapy** was developed by Marsha Linehan for chronically suicidal and self-harming women, most of whom met criteria for borderline personality disorder, and it synthesises change-oriented behaviourism with acceptance drawn from Zen (Oxford Handbook of DBT). Its aetiological engine is the biosocial theory: a biological *emotional vulnerability*, meaning heightened sensitivity to emotional stimuli, greater reactivity and a slow return to baseline, transacts over years with a pervasively invalidating environment, one that dismisses, punishes or erratically reinforces the child's private emotional experience. The two sides feed each other, the environment amplifying the biology and the intense emotion provoking further invalidation, until the result is pervasive *emotion dysregulation*, which DBT treats as the core problem from which the self-harm, impulsivity and interpersonal chaos of borderline personality disorder all follow. The word "dialectical" names the central tension the therapy holds, radical acceptance of the patient exactly as they are, balanced against a relentless push for change. The accompanying figure sets out this biosocial transaction, vulnerability and invalidation looping into emotion dysregulation.

TRAP **Calling DBT "just CBT for borderline".** DBT adds three things CBT lacks: an explicit dialectic of acceptance and change, mindfulness and acceptance as core skills, and a multi-modal team-delivered structure. Its target is pervasive emotion dysregulation, not a single disorder-specific cognition.

12.3 The four modes of standard DBT

Four modes, each doing a different job. Standard, comprehensive DBT is not one appointment but a programme of exactly **4** modes, and this count is a favourite viva discrimination (Oxford Handbook of DBT). Linehan built each mode to deliver a distinct *function*, so that a patient's motivation, skill, real-world carry-over and the therapist's own resilience are all covered at once. The modes are best learned against those functions, as the accompanying figure lays them out.

MODE OF STANDARD DBT	WHAT HAPPENS IN IT	FUNCTION IT DELIVERS
Individual therapy (weekly)	Targets the treatment-hierarchy behaviours (life-threatening first, then therapy-interfering, then quality-of-life-interfering) using behavioural and solution analysis	**Enhances motivation to change**
Skills-training group (weekly)	Teaches the skills curriculum in a class-like format, run twice across roughly six months	**Enhances capabilities**
Telephone and between-session coaching	Brief out-of-hours contact to coach skills in the moment of crisis, under a twenty-four-hour rule	**Generalises skills to daily life**
Therapist consultation team	"Therapy for the therapists"; the team supports fidelity and manages the emotional demands of the work	**Enhances therapist capability and motivation**

The four modes of standard DBT and the function each is designed to deliver.

PEARL

Hold the modes by their jobs: the patient gets **motivated** in individual therapy, gets **skilled** in the group, gets those skills to **generalise** through phone coaching, and the therapist gets **supported** by the consultation team. Miss any one mode and it is no longer standard DBT, only a fragment of it.

12.4 The four skills modules

Two acceptance skills, two change skills. The skills-training group teaches **4** modules, and their pairing mirrors the dialectic of the whole therapy, two rooted in acceptance and two in change (Oxford Handbook of DBT).

Mindfulness (core mindfulness)

The foundational module, taught first and revisited between the others; non-judgemental, present-moment awareness, observing and describing experience without acting on it. An acceptance skill, and DBT was the first psychotherapy to use **mindfulness** as an explicit skill set.

Distress tolerance

Getting through a crisis without making it worse, through skills for surviving unbearable moments and for radical acceptance of what cannot presently be changed. An acceptance skill.

Emotion regulation

Identifying, understanding and reducing the intensity of unwanted emotions, and building positive experiences so vulnerability to negative mood falls. A change skill.

Interpersonal effectiveness

Asking for what one needs and saying no while keeping the relationship and one's self-respect intact. A change skill.

MNEMONIC

Mindful Dragons Eat Idlis

Mindfulness, **D**istress tolerance, **E**motion regulation, **I**nterpersonal effectiveness. The first two are the acceptance pair (be with the feeling), the last two are the change pair (do something about it), which is the acceptance-and-change dialectic in miniature.

12.5 DBT: the evidence base and the lead indication

The first-choice structured therapy for borderline personality disorder. DBT has the strongest **evidence base** of any psychotherapy for borderline personality disorder, and its signal effect is the reduction of self-harm and suicidal behaviour and of emotion dysregulation (the guideline evidence). It is the recommended psychotherapy in the early stages of borderline personality disorder (IPS_CPG 2023) and the comprehensive programme of choice where reducing recurrent self-harm is the priority (NICE 2009); RANZCP lists it among the therapies that reduce self-harm repetition (RANZCP 2016). The adolescent adaptation, DBT-A, which keeps the same modes and adds family involvement, is offered to young people with significant emotion dysregulation and frequent self-harm (NICE 2022; RANZCP 2016). The fuller treatment of borderline personality disorder, and the place of schema therapy alongside DBT, belongs in the Personality disorders notes; here, learn DBT as the exemplar third-wave therapy and BPD as its lead indication.

GOOD TO REMEMBER

- **Dialectical behaviour therapy (the therapy):** the model is Linehan's biosocial theory, an emotionally vulnerable temperament transacting with a pervasively invalidating environment to produce emotion dysregulation, treated by synthesising acceptance and change; the lead indication is borderline personality disorder, especially where self-harm must be reduced (IPS_CPG 2023; NICE 2009); the signature structure is the four modes (individual therapy, skills group, phone coaching, consultation team) delivering the four skills modules.

12.6 Acceptance and commitment therapy: psychological flexibility and the hexaflex

Stop fighting inner experience; act on your values instead. Acceptance and commitment therapy was developed by Steven Hayes in the nineteen-nineties (originally called comprehensive distancing), and its whole aim is psychological flexibility, the capacity to stay in contact with the present moment and, guided by chosen values, to change or persist in behaviour (Kaplan and Sadock CTP 2024). Its core premise is that suffering is driven by *experiential avoidance*, the unwillingness to feel unwanted thoughts, feelings and sensations, so ACT works not by removing those experiences but by loosening their grip. The model is drawn as a six-pointed hexaflex, and the six interlocking processes are worth holding verbatim; there are exactly **6**.

Acceptance

Actively making room for unwanted private experiences rather than struggling against them, as the alternative to experiential avoidance.

Cognitive defusion

Stepping back to see thoughts *as* thoughts, passing mental events, rather than fusing with them as literal truths or commands.

Contact with the present moment

Flexible, non-judgemental attention to the here-and-now, the mindfulness element of ACT.

Self-as-context

The "observing self", a stable vantage point from which experience is witnessed, distinct from the changing content of experience.

Values

Clarifying the chosen life directions that make behaviour meaningful and give change its purpose.

Committed action

Building patterns of effective, values-guided behaviour, the behavioural-change engine that keeps ACT a behaviour therapy.

COMMON TRAP

Do not promote ACT to a broad first-line therapy. On the guideline evidence it is *one option* among several for major depression (VA_DOD 2022) and a weak-for adjunct in early psychosis and schizophrenia (VA_DOD 2025); its one confirmed first-line role is as an option (with MBCT) for illness-anxiety presentations in the IPS somatic-symptom guideline (IPS_CPG 2020). Say "evidence-supported option", not "guideline first-line".

GOOD TO REMEMBER

- **Acceptance and commitment therapy (the therapy):** the model is that experiential avoidance drives suffering, so the goal is psychological flexibility built through the six hexaflex processes; the lead indication is not a broad first-line status but a values-and-acceptance option across depression and, confirmed as first-line, illness-anxiety presentations (IPS_CPG 2020); the one signature technique is cognitive defusion, holding a thought as a thought rather than a fact.

12.7 Mindfulness-based cognitive therapy: the eight-session programme

Built for one job, preventing the next depression. **Mindfulness-based cognitive therapy** was developed by Segal, Williams and Teasdale in the mid-nineteen-nineties, marrying the mindfulness training of Kabat-Zinn's stress-reduction programme with elements of cognitive therapy (Kaplan and Sadock CTP 2024). It is a group programme delivered over **8** weekly sessions with home practice and a day of practice. Crucially, unlike CBT, MBCT does not try to change the content of thoughts; it teaches *decentring*, the stance that "thoughts are not facts" and "I am not my thoughts", so that low mood no longer recruits the old ruminative machinery that reinstates a full depressive episode. That mechanism is exactly why its indication is narrow and specific: the *prevention of depressive relapse* in people with recurrent depression who are currently well, not the treatment of an acute episode. Its strongest confirmed role is first-line relapse prevention in the maintenance phase of major depression (CANMAT 2016) and an option in the continuation phase for patients at high relapse or recurrence risk (VA_DOD 2022); the acute treatment of depression, with CBT and interpersonal therapy, sits in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes.

GOOD TO REMEMBER

- **Mindfulness-based cognitive therapy (the therapy):** the model is decentring from depressive thought patterns rather than disputing them, mindfulness plus cognitive therapy over eight weekly group sessions; the lead indication is the *prevention of depressive relapse* in recurrent depression in the well phase (CANMAT 2016; VA_DOD 2022), not acute depression and, per NICE 2013, not social anxiety; the one signature technique is mindful decentring, "thoughts are not facts".

12.8 The evidence base across the third wave, and the Indian setting

One strong indication each; do not blur them. The examinable shape of the third wave is that each therapy owns one lead indication and should not be over-generalised beyond it, a point on which the guidelines are strict. DBT is the first-choice structured therapy for borderline personality disorder; ACT is an evidence-supported option rather than a broad first-line therapy; and MBCT is first-line specifically for preventing depressive relapse.

THERAPY	ORIGINATOR	CORE TARGET	LEAD INDICATION (GUIDELINE)
DBT	Linehan	Emotion dysregulation	**Borderline personality disorder, reducing self-harm (IPS_CPG 2023; NICE 2009)**
ACT	Hayes	Experiential avoidance / psychological inflexibility	Option for depression; first-line option for ill-ness anxiety (IPS_CPG 2020; VA_DOD 2022)
MBCT	Segal, Williams and Teasdale	Ruminative relapse to depression	**Preventing depressive relapse in recurrent depression (CANMAT 2016; VA_DOD 2022)**

The three widely-practised third-wave therapies, with the single lead indication each is best evidenced for.

4 MODES OF STANDARD DBT (INDIVIDUAL, SKILLS GROUP, PHONE COACHING, CONSULTATION TEAM)	**4** DBT SKILLS MODULES (MINDFULNESS, DISTRESS TOLERANCE, EMOTION REGULATION, INTERPERSONAL EFFECTIVENESS)	**6** HEXAFLEX PROCESSES IN ACT	**8** WEEKLY SESSIONS IN THE MBCT PROGRAMME

INDIA

The Indian Psychiatric Society embeds the third wave in its guidelines: DBT is the recommended psychotherapy for borderline personality disorder (IPS_CPG 2023), and both ACT and MBCT are named as first-line options for illness-anxiety presentations in the somatic-symptom guideline (IPS_CPG 2020). Mindfulness and meditation-based interventions have deep cultural roots here, and the NIMHANS yoga-therapy research stream has studied adjunctive yoga in depression and schizophrenia, but keep this at the honest level, yoga and meditation are adjuncts, not stand-alone or first-line psychiatric treatments, and that research stream is literature-level rather than guideline-confirmed.

HOLD THIS

The third-wave therapies change your relationship to inner experience, not its content; DBT rests on Linehan's biosocial theory (emotional vulnerability meeting an invalidating environment) and is delivered through four modes, individual therapy, skills group, phone coaching and consultation team, teaching four skills modules, mindfulness, distress tolerance, emotion regulation and interpersonal effectiveness, with borderline personality disorder as its lead indication; ACT builds psychological flexibility through six hexaflex processes; and MBCT is an eight-session programme whose one job is preventing depressive relapse.

13 · Motivational interviewing

Motivational interviewing (MI) is the psychiatry answer to a problem every clinician meets and few are trained for: the patient who knows the drinking is killing them and drinks anyway, who half wants to stop and half does not, and who, the moment you argue for change, argues back for the status quo. Devised by William Miller and Stephen Rollnick from Miller's work with problem drinkers in the nineteen-eighties, MI is defined as a collaborative, person-centred, goal-directed style of communication designed to strengthen a person's own motivation and commitment to change by exploring and resolving **ambivalence**. It is examinable in two registers, as a named psychotherapy with a lead indication in the addictions, and as a general counselling style that underlies every stage of substance-use work, so learn both the machinery and the one-sentence indication.

How to use this page. Fix first that the target of MI is ambivalence, not the substance and not the diagnosis. Then learn the underlying stance (the spirit of motivational interviewing), the four guiding principles that operationalise it, the distinction between change talk and sustain talk that the whole method is built to shift, and the core micro-skills, OARS, that do the shifting. Close on the transtheoretical stages of change that MI is so often paired with, and on the evidence, whose examinable payoff is the phrase "first-line in the addictions". The cardinal error the page is built to prevent is picturing MI as gentle, aimless listening; it is directional and deliberate, it simply reaches its direction by evoking the patient's own arguments rather than supplying the clinician's.

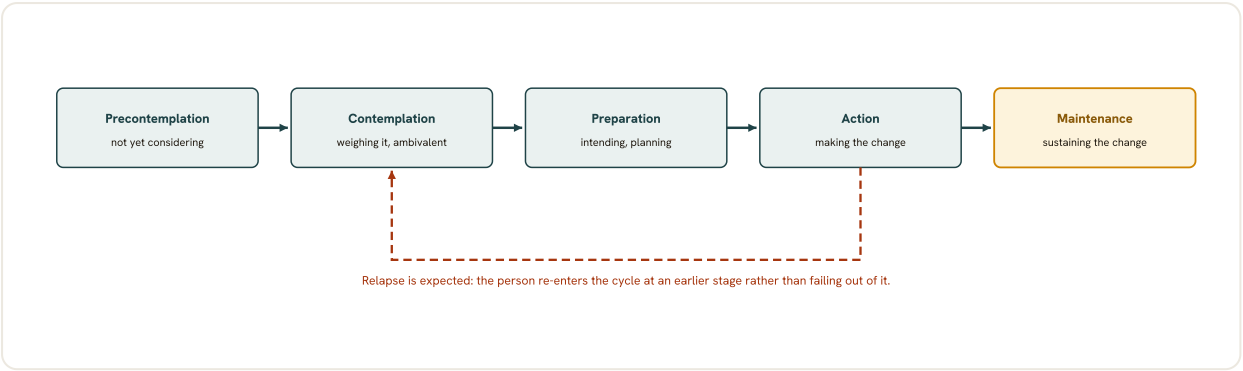


Fig 19.8 The transtheoretical stages of change. Prochaska and DiClemente's model describes readiness for change as a sequence: precontemplation (not yet considering it), contemplation (weighing it, ambivalent), preparation (intending and planning), action (making the change) and maintenance (sustaining it). The clinical value is that the intervention is matched to the stage: raising awareness in precontemplation, exploring ambivalence in contemplation, and supporting action later. Relapse is treated not as failure but as a return to an earlier stage, from which the person moves forward again. This is the map that motivational interviewing works within, meeting the patient at their stage and eliciting their own reasons for change rather than pushing against ambivalence.

13.1 What MI targets: ambivalence, not the substance

The patient already holds both sides of the argument; MI tips the balance from within. The central insight is that a person contemplating change is not unmotivated but *ambivalent*, holding simultaneous and genuine reasons both to change and to stay the same, and that this ambivalence is the normal psychology of change rather than a sign of denial or pathology (Miller and Rollnick; Tasman). Because the arguments for change are already present in the patient, the clinician's task is not to install motivation from outside but to selectively evoke, elaborate and reinforce the patient's own change-favouring statements until they outweigh the arguments for the status quo. This reframes the whole encounter: the person, not the clinician, voices the case for change, which matters because people are more persuaded by what they hear themselves say than by what they are told.

RULE **Evoke, do not install.** MI resolves ambivalence by drawing out and strengthening the patient's own change talk, never by supplying the clinician's reasons; motivation is called forth from the person, not imposed on them.

13.2 The spirit of motivational interviewing

The underlying attitude matters more than any technique. Miller and Rollnick insist that MI is carried less by its methods than by its animating stance, the spirit of motivational interviewing, and in the third edition this spirit has exactly **4** interlocking elements. *Partnership* makes the encounter a collaboration between two experts, the clinician on change and the patient on their own life, rather than an expert acting on a passive recipient. *Acceptance* combines Rogerian accurate empathy, unconditional positive regard, honouring the patient's autonomy to choose, and affirmation of their strengths. *Compassion* commits the clinician to actively promote the patient's welfare and give priority to their needs. *Evocation* assumes the resources and motivation for change already reside within the patient and are to be called out, the opposite of a deficit model in which the clinician fills an empty vessel. Without this spirit the techniques become manipulation; with it they become MI.

MNEMONIC

PACE

The spirit of MI keeps **P** artnership, **A**cceptance, **C**ompassion and **E**vocation. Set the PACE of the conversation with the patient, walking alongside them rather than pulling them.

13.3 The four guiding principles

Express empathy, develop discrepancy, roll with resistance, support self-efficacy. The spirit is enacted through four classic principles that are among the most reliably examined content in this topic (Miller and Rollnick). *Express empathy* through skilled reflective listening, communicating acceptance so the patient feels understood rather than judged. *Develop discrepancy* by helping the patient perceive the gap between their present behaviour and their broader goals and values, because it is this felt mismatch, and not the clinician's disapproval, that powers change. Rolling with resistance means not opposing or arguing against reluctance but reflecting and reframing it, turning what looks like opposition into further exploration. *Support self-efficacy* by building the patient's belief that change is possible and is theirs to achieve, since hope of success is itself a strong predictor of it. Two of these, developing discrepancy and rolling with resistance, are the ones a viva examiner reaches for first.

TRAP **The righting reflex backfires.** The clinician's instinct to correct, warn and argue the patient into change, the righting reflex, predictably provokes the patient to voice the opposite (sustain talk and discord); in MI you suppress that reflex and roll with resistance instead of confronting it.

13.4 Change talk versus sustain talk

Every technique in MI is aimed at increasing one kind of speech and softening the other. Change talk is any patient statement that favours movement toward change; *sustain talk* is any statement that favours the status quo. Because ambivalent people produce both, the clinician listens for change talk, then uses open questions, reflection and affirmation to elaborate and amplify it while gently letting sustain talk pass without reinforcement. Preparatory change talk is captured by the mnemonic DARN, the patient's *Desire* ("I want to cut down"), *Ability* ("I could stop if I tried"), *Reasons* ("my liver is suffering") and *Need* ("I have to do something"); mobilising change talk, which predicts action more strongly, is captured by CAT, *Commitment* ("I will"), *Activation* ("I am ready") and *Taking steps* ("I threw the bottles out"). The clinician's job is to shift the ratio of change talk to sustain talk across the conversation, since that shift, and not any lecture, is what predicts a subsequent change in behaviour.

WORKED EXAMPLE

A man with harmful alcohol use says, "I am not an alcoholic, my father was, but I suppose the mornings have got worse." Instead of correcting the first clause (the righting reflex), the clinician reflects the last, "The mornings are worse than they were," and asks, "What have you noticed?" The patient elaborates on the tremor and the missed work, voicing his own Reasons and Need. Nothing was argued; the clinician simply steered toward the change talk the patient had already offered and let it grow.

13.5 The core skills: OARS

Four micro-skills carry the whole method. The moment-to-moment technique of MI reduces to OARS, a set of **4** communication skills borrowed from client-centred counselling and put to a directional purpose (Miller and Rollnick; Tasman). *Open questions* invite the patient to do most of the talking and to explore rather than answer yes or no. *Affirmations* recognise and reinforce the patient's strengths, efforts and worth, building self-efficacy. *Reflective listening*, the signature skill, feeds back the clinician's best guess at the patient's meaning as a statement, which deepens exploration, conveys empathy and, crucially, lets the clinician selectively reflect change talk. *Summaries* gather the threads of the conversation, and a well-built summary can deliberately collect the patient's change talk into one place so they hear their own case for change spoken back to them. OARS is the examinable acronym; know that reflection, not questioning, is its centre of gravity.

MNEMONIC

OARS

Row the conversation forward with **O**pen questions, **A**ffirmations, **R**eflective listening and **S**ummaries. Reflective listening is the longest of the four oars; lean on it hardest.

13.6 The stages of change: the transtheoretical model

MI meets the patient wherever they sit on the road to change. MI is almost always taught alongside the transtheoretical model of Prochaska and DiClemente, whose stages of change describe how readiness evolves over time. The **5** core stages are *precontemplation* (no intention to change, often unaware of the problem or attending under pressure from others), *contemplation* (aware of the problem and weighing change but not yet committed), *preparation* (intending to act soon, taking small first steps), *action* (making overt behaviour change) and *maintenance* (consolidating gains and preventing relapse). Some formulations add a sixth stage, either *termination* (Prochaska, DiClemente and Norcross) or, in several Indian texts, *relapse*; attribute the core count as five and name the sixth as a variant. The clinical payoff is stage matching: pushing action tasks on a precontemplative patient produces drop-out, so the model tells you when to evoke and when to plan, while MI supplies the how. Change is a spiral, not a ladder, and relapse is treated as an expected loop back rather than a failure. The accompanying figure sets the stages out as a cycle with the spiral of relapse and re-entry marked.

COMMON TRAP

Do not equate MI with the stages-of-change model. They are separate: the transtheoretical model is a *theory of how readiness changes*, MI is a *clinical method for moving it*. MI can be delivered without ever naming a stage, and the stages can be assessed without doing MI; the exam rewards knowing they are complementary, not identical.

13.7 Evidence, MET and the lead indication

First-line in the addictions, as a brief structured therapy and as the foundational counselling style. The examinable sentence is that MI is a well-evidenced, first-line psychological

intervention across the substance-use disorders and, more broadly, in behaviour change (the guideline evidence). Its brief, manualised form, motivational enhancement therapy (MET), delivers the method in about four structured sessions built around personalised assessment feedback, and MET is a first-line psychological treatment for alcohol use disorder (IPS_CPG 2014 grade A; VA_DOD 2021) and first-line psychosocial management for cannabis use disorder (IPS_CPG 2014; VA_DOD 2021). Beyond these, MI is the foundational counselling style used across all stages of substance-use disorder generally (IPS_CPG 2014; WHO mhGAP 2016), is offered for gambling disorder following CBT (RANZCP 2024; NICE 2025), and is a main behavioural treatment for adolescent tobacco use (IPS_CPG 2018). Keep the claim disciplined: strong and first-line in the addictions and for behaviour change, an evidence-based adjunct or preparatory intervention elsewhere, not a first-line stand-alone treatment for the mood or anxiety disorders. The substance-specific detail, the SBIRT framework and the pharmacological pairings live in the Substance use disorders notes.

INDIA

The Indian Psychiatric Society makes MI and MET first-line across the addictions, most firmly for alcohol (IPS_CPG 2014, grade A). The dedicated IPS guideline on psychosocial interventions in addictive disorders in India (Murthy and colleagues, 2018) names motivation-enhancement and relapse-prevention approaches as core and signals a shift toward community-based and home-based delivery, an adaptation to the Indian reality of scarce specialist therapists and family-embedded care. State both the guideline endorsement and the delivery shift; an examiner asking about MI in India is usually testing the second half.

5	4	4
CORE STAGES OF CHANGE (PROCHASKA AND DICLEMENTE)	ELEMENTS OF THE MI SPIRIT (PARTNERSHIP, ACCEPTANCE, COMPASSION, EVOCATION)	STRUCTURED SESSIONS IN MOTIVATIONAL ENHANCEMENT THERAPY

GOOD TO REMEMBER

- **Motivational interviewing (the therapy):** the model is that ambivalence is the normal psychology of change, so the clinician evokes and strengthens the patient's own change talk within a collaborative, autonomy-honouring spirit rather than confronting them; the lead indication is the substance-use disorders and behaviour change, where MI and its four-session form MET are first-line (IPS_CPG 2014 grade A for alcohol); the one signature technique is reflective listening within OARS, used to selectively amplify change talk.

HOLD THIS

MI (Miller and Rollnick) works with ambivalence by evoking the patient's own change talk instead of confronting them; its spirit is partnership, acceptance, compassion and evocation, its principles are express empathy, develop discrepancy, roll with resistance and support self-efficacy, its skills are OARS, and its lead indication is the addictions, delivered first-line as the four-session MET (IPS_CPG 2014 grade A for alcohol).

14 · The Indian and culturally-adapted context

Every therapy on this note was developed and trialled largely in high-income, well-resourced settings, and the examiner will expect you to know what changes when the same therapies meet an Indian clinic: a wide **treatment gap**, a thin specialist workforce, strong family systems, and a living tradition of yoga, meditation and indigenous healing. The examinable shape of the Indian context is that it adds four things to the evidence-based therapies rather than replacing them, its own body of Indian Psychiatric Society guidance, the cultural adaptation of the manualised therapies, an indigenous yoga and meditation-based evidence stream, and a set of brief, task-shared, lay-counsellor delivery models built for scale. Hold each at its honest evidence level; the trap that runs through the whole topic is over-claiming a culturally resonant intervention as a first-line stand-alone treatment.

How to use this page. Learn the IPS psychotherapy guidance first, because it is the most directly examinable Indian fact and it tells you that the evidence-based therapies (CBT, IPT, MI and the rest) remain first-line here too. Then take culturally-adapted CBT as an *adaptation with a developing evidence base*, yoga and meditation as *adjuncts*, and the task-sharing and lay-counsellor stream as the Indian answer to the treatment gap. Close on guru-chela and indigenous healing at the cultural level, and on an honest ledger of what is guideline-confirmed against what is literature-level. The wider transcultural frame of the cultural concepts of distress belongs in the Consultation-liaison, geriatric and transcultural psychiatry notes; here, learn how the therapies themselves are adapted and delivered in India.

14.1 The IPS psychotherapy guidelines and their place

India has its own psychotherapy guidance, and it keeps the evidence-based therapies first-line. The Indian Psychiatric Society has published a dedicated Clinical Practice Guideline on the psychotherapies (Agarwal and colleagues, *Indian Journal of Psychiatry* 2020) and a companion guideline on psychosocial interventions in addictive disorders in India (Murthy and colleagues 2018); in addition, the disorder-specific IPS CPGs embed psychotherapy recommendations for depression (2017), obsessive-compulsive disorder, generalised anxiety disorder (2020), somatic symptom disorder (2020) and borderline personality disorder (2023) (the guideline evidence). What the **IPS psychotherapy** guidance does is important and bounded: it endorses and localises the internationally evidenced therapies rather than inventing new ones, so CBT stays first-line across depression, GAD, OCD and somatic symptom disorder, behavioural activation is named among the strongest options in depression, IPT sits alongside CBT for depression, and motivational interviewing and motivation enhancement therapy are first-line across the addictions (IPS_CPG 2014; 2017; 2020). Do not inflate this into a claim that a single unified all-modality Indian psychotherapy manual exists; the defensible statement is that the IPS has published these specific guidelines and that they cover these areas.

RULE **Adapt the delivery and the idiom, not the evidence base.** In the Indian setting the guideline-anchored therapies (CBT, IPT, MI, behavioural activation) remain first-line; the Indian contribution is to localise, culturally adapt and task-share them, plus add yoga and meditation as adjuncts, not to displace them.

INDIA

A signature Indian adaptation lives in the IPS alcohol-use guidance: family-based treatment that enlists a co-resident relative as recovery monitor and supervisor of supervised disulfiram (IPS_CPG 2014, grade B). This works precisely because the Indian family is typically co-resident and involved, turning a structural feature of Indian households into a therapeutic lever, the kind of cultural tailoring that defines this whole topic. Motivational interviewing in substance use itself sits in the Substance use disorders notes.

14.2 Culturally-adapted CBT in the Indian setting

The same therapy, retuned to language, idiom, family and explanatory model. Culturally-adapted CBT is not a new therapy but a systematic re-tuning of standard CBT for a cultural setting, and the work most associated with South Asian and Indian adaptation is that of Naeem and colleagues (the guideline evidence). The adaptation touches content, not mechanism: the therapist works in the local language, uses local idioms of distress rather than imported metaphors, engages the family instead of assuming an autonomous individual client, respects religious and spiritual explanatory models, and adjusts the balance of guided-discovery versus a more directive, expert stance that many Indian patients expect. The evidence for **culturally-adapted** CBT in South Asian and Indian settings runs from feasibility work up to randomised-trial level for depression and psychosis, which is genuinely promising but is not drawn from a guideline row. Frame it, therefore, as an adaptation with a developing evidence base, not as a guideline-endorsed first-line therapy distinct from CBT.

PEARL

The clean viva line: culturally-adapted CBT changes the *packaging* (language, idioms, family involvement, explanatory model, therapist stance), while keeping the *active ingredients* of CBT intact. That is why it inherits CBT's evidence base in principle but must still be tested locally, and why it is described as promising and developing rather than separately guideline-confirmed.

14.3 Yoga and meditation-based interventions: the Indian evidence stream

Deep cultural roots, real research, but adjunctive evidence. India contributes a distinctive research stream on **yoga** and **meditation-based** interventions, much of it from the NIMHANS yoga-therapy programme, studying adjunctive yoga in depression and in schizophrenia (Tasman and Kaplan and Sadock place yoga, paced breathing and meditation among the mind-body integrative practices). The honest evidence level is *adjunct*, and here the guideline evidence is strict. As an add-on, yoga has guideline-level support: it is offered as an adjunct for the positive and negative symptoms of schizophrenia (VA_DOD 2025, weak-for), exercise including yoga is suggested as an adjunct in major depression (VA_DOD 2022), and yoga and mindfulness are offered for depressive symptoms in the perinatal period (VA_DOD 2023). Equally examinable are the cautions: VA_DOD found insufficient evidence to recommend for or against yoga or meditation for chronic insomnia (VA_DOD 2025) and insufficient evidence for meditation as a major-depression adjunct (VA_DOD 2022). The NIMHANS Indian yoga stream itself sits at the

adjunct level and is literature-based rather than guideline-confirmed. Keep yoga and meditation firmly at "adjunct, not first-line, not stand-alone".

TRAP **Calling yoga, meditation or culturally-adapted CBT a first-line stand-alone treatment.** No source supports yoga or meditation as a stand-alone or first-line psychiatric treatment; their confirmed roles are adjunctive, and culturally-adapted CBT is developing evidence, not a guideline first-line. Say "adjunct" and "promising", never "first-line monotherapy".

14.4 The treatment gap and the case for brief, task-shared, lay-counsellor care

Too few specialists for too many patients forces a different delivery model. The structural fact behind the Indian context is scarcity: the National Mental Health Survey put the current prevalence of any mental disorder near one in ten adults, yet reported an 85% treatment gap for common mental disorders and 73.6% for severe mental illness, against a workforce of only about **0.3** psychiatrists per 100,000 population, most of them urban (National Mental Health Survey 2016; Indian sources). When specialists cannot possibly see everyone, the answer is task sharing: shifting delivery of simple, manualised psychological treatments to trained non-specialists under specialist supervision. The WHO frames this through the Mental Health Gap Action Programme (mhGAP) and its Intervention Guide (mhGAP-IG), used to train primary-care staff to detect and manage priority conditions in low-resource settings. India has generated some of the strongest evidence for this model: brief psychological treatments delivered by trained lay counsellors, developed and trialled by groups such as Sangath in Goa, have shown that lay-delivered, task-shared care can effectively treat depression and reduce harmful drinking in primary care. The accompanying figure sets out this stepped, task-shared pyramid from self-care and community workers up to scarce specialists.

Treatment gap

The proportion of people with a disorder who receive no treatment for it; in India, an 85% gap for common mental disorders and 73.6% for severe mental illness (NMHS 2016).

Task shifting / task sharing

Redistributing tasks from scarce specialists to trained non-specialist or lay providers under supervision; "sharing" keeps the specialist in a supervisory role rather than fully handing over.

mhGAP Intervention Guide

The WHO's simplified, evidence-based protocol for non-specialist detection and management of priority mental, neurological and substance-use conditions in low-resource settings.

Lay-counsellor-delivered treatment

A brief, manualised psychological treatment given by a trained lay person (not a mental-health professional); the Indian trials targeted depression and hazardous drinking in primary care.

WORKED EXAMPLE

A woman with moderate depression presents to a rural primary health centre where the nearest psychiatrist is a day's travel away. Rather than the referral failing into the treatment gap, a supervised lay counsellor delivers a brief, structured psychological treatment (behavioural activation and problem-solving) across several weekly sessions, escalating to the visiting specialist only if she does not improve or risk rises. This is task-shared, mhGAP-style, evidence-based care fitted to the Indian workforce reality, delivering a first-line therapy through a non-specialist rather than diluting it.

85%	73.6%	0.3
TREATMENT GAP FOR COMMON MENTAL DISORDERS, INDIA (NMHS 2016)	TREATMENT GAP FOR SEVERE MENTAL ILLNESS, INDIA (NMHS 2016)	PSYCHIATRISTS PER 100,000 POPULATION, INDIA

14.5 Guru-chela, indigenous healing, and the honest ledger

Name the indigenous frame at the cultural level, and keep the evidence honest. Long before manualised therapy reached India, help for psychological suffering came through indigenous routes, and these still shape where patients seek care first. The guru-chela (teacher-disciple) relationship has been proposed, classically by Neki, as a culturally native paradigm for the therapeutic relationship, an idealised, hierarchical, nurturing bond that maps onto how many Indian patients expect a healer to relate to them; treat it as a conceptual and cultural model of the therapeutic alliance, not as an evidence-based therapy. Alongside it sit the traditional and faith healers, herbalists and religious and spiritual practitioners whom many patients consult in parallel with, or before, biomedical care. Knowing this matters clinically because it shapes explanatory models, help-seeking pathways and adherence, but the research base for indigenous healing is preliminary and largely naturalistic, so it is named and respected at the cultural level rather than recommended as treatment. The honest ledger below is exactly what the examiner is testing: which parts of this stream are guideline-confirmed and which are literature-level.

ELEMENT OF THE INDIAN / CULTURALLY-ADAPTED STREAM	HONEST STATUS	SOURCE LEVEL
IPS psychotherapy CPG (2020) and addiction guideline (2018)	**Indian guideline that endorses and localises the evidence-based therapies**	Guideline-confirmed (IPS_CPG)
Culturally-adapted CBT (Naeem and colleagues)	Adaptation with a developing evidence base, feasibility to RCT-level in depression and psychosis	**Literature-level, not guideline first-line**
Yoga (adjunct)	**Adjunct for schizophrenia (weak-for) and depression; suggested, not first-line**	Guideline-confirmed as adjunct (VA_DOD)
Meditation-based interventions	Adjunct; insufficient evidence as a depression adjunct and for chronic insomnia	VA_DOD cautions
Task-shared, lay-counsellor delivery	**Effective delivery model for depression and harmful drinking; the answer to the treatment gap**	mhGAP; Indian lay-counsellor trials
Guru-chela and indigenous / faith healing	Cultural and conceptual model of the therapeutic bond; shapes help-seeking	Cultural / textbook (Neki), not evidence-based therapy

The honest evidence ledger for the Indian and culturally-adapted stream: what is guideline-confirmed against what is literature-level or cultural.

GOOD TO REMEMBER

- **The defining principle:** the Indian context *adapts and delivers* the evidence-based therapies rather than replacing them; the discriminator to hold is adjunct or developing-evidence against guideline first-line.
- **IPS psychotherapy guidance:** a dedicated IPS psychotherapy CPG (2020) plus an addiction-psychosocial guideline (2018) and disorder-specific CPGs localise CBT, IPT, behavioural activation and MI as first-line; there is no single unified all-modality Indian manual.
- **Culturally-adapted CBT:** retunes language, idioms, family involvement, explanatory model and therapist stance while keeping CBT's active ingredients; promising, developing evidence (Naeem), not separately guideline first-line.
- **Yoga and meditation-based interventions:** adjuncts only (yoga weak-for in schizophrenia and depression, VA_DOD); the NIMHANS stream is literature-level; never stand-alone or first-line.
- **Treatment gap and task sharing:** an 85% gap for common mental disorders and roughly 0.3 psychiatrists per 100,000 drive brief, task-shared, mhGAP-style, lay-counsellor-delivered care (Sangath trials).
- **Guru-chela and indigenous healing:** named at the cultural level as a native model of the therapeutic bond (Neki) and of help-seeking, not as an evidence-based treatment.

HOLD THIS

The Indian and culturally-adapted context keeps the evidence-based therapies first-line and adds four things around them: IPS guidelines that localise them, culturally-adapted CBT (promising, developing evidence), yoga and meditation as adjuncts only, and task-shared lay-counsellor delivery (mhGAP, the Sangath trials) to close an 85% treatment gap, with guru-chela and indigenous healing named at the cultural level rather than as treatments.

15 · Choosing the right therapy

This is the discrimination topic for the whole psychotherapies band, and it is where the marks actually sit. The examiner rarely rewards a rote description of a single modality; the higher-order question is **therapy selection**, given this patient with this presentation, **which therapy** do you offer first and why. **Choosing the right therapy** is therefore a skill of **matching**: you place the presentation against the modality that carries the strongest **indication** for it, then you individualise. The safe answer names the guideline-endorsed first-line therapy before it reaches for the therapist's favourite school, and it grounds the choice in evidence rather than preference.

How to use this page. Fix the four factors that govern the choice first, because every viva answer on selection is really a request to weigh them. Then read the indication grid, the single highest-yield object in the topic, which matches the seven common presentations to their first-line modality, its evidence anchor and its practical fit. Finally hold the principle that this page selects a therapy but does not teach it: the disorder-specific protocol (exposure and response prevention, trauma-focused cognitive behaviour therapy, dialectical behaviour therapy for borderline personality disorder, interpersonal psychotherapy for depression) always lives in the disorder's own chapter, and this topic only points you to the right door.

Presentation	First-line psychotherapy	The evidence and where it is taught
Depression	CBT or IPT	first-line psychological therapies (IPS 2017, CANMAT 2016); behavioural activation an option
Anxiety and OCD	CBT with exposure; ERP for OCD	exposure is the active ingredient; the ERP protocol is taught in the Anxiety, OCD notes
Borderline personality	DBT (also MBT, schema therapy)	DBT has the strongest evidence; taught in full in the Personality disorders notes
Relational or family problem	Family or couple therapy	the system, not the individual, is the unit of treatment
Adjustment or crisis	Supportive; crisis intervention	restore the pre-crisis level of functioning; brief, active and problem-focused
Substance use	Motivational interviewing and CBT	MET and CBT for relapse prevention (IPS 2014); taught in the Substance use disorders notes
Psychosis	Family psycho-education, CBT for psychosis	alongside antipsychotic medication, not instead of it

Match the therapy to the presentation, the evidence and the formulation. The first-line psychotherapy is highlighted; the disorder-specific protocols are taught in their disorder chapters.

Fig 19.9 Choosing the right therapy. The selection of a psychotherapy follows the presentation, the evidence base and the individual formulation. Depression is answered first-line by CBT or interpersonal therapy; the anxiety disorders and OCD by exposure-based CBT, with exposure and response prevention the active ingredient in OCD; borderline personality disorder most strongly by dialectical behaviour therapy; a relational or family problem by family or couple therapy, which treats the system rather than the individual; an adjustment reaction or crisis by supportive therapy and crisis intervention; a substance-use problem by motivational interviewing and CBT for relapse prevention; and a psychotic illness by family psychoeducation and CBT for psychosis, always alongside medication rather than in place of it. The disorder-specific protocols are taught in their own chapters.

15.1 The four factors that decide therapy selection

Weigh four things, in this order. A clean selection answer names four factors and puts the evidence base first (Kaplan and Sadock CTP 2024; New Oxford Textbook). The **disorder and its evidence base** is the first and strongest filter: for most presentations a guideline already names a first-line psychological treatment, and that is the default from which you reason. The **formulation** refines the default: the same diagnosis can point to different therapies depending on the maintaining mechanism, so a depression driven by a bereavement or a role change tilts toward interpersonal work, while one driven by inactivity and hopeless cognition tilts toward behavioural activation or cognitive work. **Patient preference and capacity for the work** matter because they predict engagement and completion: a patient's stated preference improves adherence, and the capacity for insight-oriented work is gated by motivation, cognitive ability and psychological mindedness, the ability to reflect on one's own feelings, motives and relationships and to consider their meaning (Companion to Psychiatric Studies; Tasman). The **availability and setting** factor is the honest constraint: the best-evidenced therapy is worth little if no trained therapist can deliver it, which is why a stepped care logic offers the least intensive effective option first and steps up only if the patient does not improve.

THE FOUR FILTERS OF THERAPY SELECTION

Disorder and evidence base (the guideline first-line is the default); **formulation** (the maintaining mechanism refines the default); **patient preference and capacity** (preference predicts engagement, and psychological mindedness gates insight work); **availability and setting** (what a trained therapist can actually deliver, under a stepped-care logic). Name all four and lead with the evidence base.

RULE **Match the disorder to its evidence base first, then individualise.** The disorder's guideline-endorsed first-line therapy is the default; the formulation, the patient's preference and capacity, and availability refine the choice, but they override a strong first-line only for a stated reason.

PEARL

Capacity is a real gate, not a courtesy. Insight-oriented and reconstructive therapies presuppose motivation, adequate cognitive ability and psychological mindedness; where these are thin, a supportive or structured behavioural approach matches the patient better than an interpretive one, however fashionable the latter. Suitability for the work is part of the indication, not an afterthought.

15.2 The indication grid: matching the presentation to the first-line modality

Seven presentations, seven first-line answers. The core examinable object is the grid below, which pairs each common presentation with the psychotherapy that carries the strongest guideline indication, the evidence anchor for that claim, and the practical reason it fits (the IPS and NICE guidelines). Learn it as a lookup table: the presentation is the stem, the first-line modality is the answer you must name, and the practical-fit column is the sentence that earns the second mark. The accompanying figure lays the same match out as a decision grid.

PRESENTATION	FIRST-LINE MODALITY (THE ANSWER)	EVIDENCE ANCHOR	PRACTICAL FIT
Depression (major depressive disorder)	**Cognitive behaviour therapy, interpersonal psychotherapy or behavioural activation**	IPS 2017 grade A; CANMAT 2016; NICE 2022	Broadest choice; pick IPT for a clear interpersonal trigger (grief, role transition), behavioural activation where withdrawal and inactivity dominate or access is limited
An anxiety or OCD disorder	**CBT; obsessive-compulsive disorder as CBT with exposure and response prevention**	GAD IPS 2020, NICE 2011; OCD IPS 2025 Level 1, BAP 2014 grade A	Graded exposure is the active ingredient; ERP is the OCD-specific package (expose to the trigger, prevent the compulsion)

PRESENTATION	FIRST-LINE MODALITY (THE ANSWER)	EVIDENCE ANCHOR	PRACTICAL FIT
Borderline personality disorder	**Dialectical behaviour therapy**	IPS 2023; NICE 2009	First choice where recurrent self-harm and emotion dysregulation dominate; skills training plus individual therapy; mentalisation-based treatment is the alternative
A relational or family problem	**Family or couple therapy**	Family therapy for adolescent anorexia NICE 2017 grade A; family intervention in psychosis NICE 2014, IPS 2017; couple therapy VA/DoD 2022	The system, not the individual, is the unit of treatment; targets communication, roles and expressed emotion
An adjustment or crisis	**Brief and crisis therapy (problem-solving, crisis intervention, supportive)**	Problem-solving for self-harm NICE 2022; collaborative crisis plan in BPD IPS 2023, NICE 2009	Time-limited and focal; collaborative safety planning; a supportive stance where structured therapy is unavailable
A substance-use problem	**Motivational interviewing and motivational enhancement therapy (four structured sessions)**	IPS 2014 grade A; VA/DoD 2021	Stage-matched to readiness; brief intervention and SBIRT for hazardous use at every contact
A psychotic illness	**Psychosocial adjuncts: family intervention and CBT for psychosis**	Family intervention NICE 2014, IPS 2017; CBT for psychosis IPS 2017 grade B	An adjunct to antipsychotic medication, never a substitute; family intervention reduces relapse

Matching the seven common presentations to the first-line psychotherapy, its guideline anchor and the practical fit; the disorder-specific protocol is taught in the disorder's own chapter. The accompanying figure renders the same match as a decision grid.

TRAP **Offering psychotherapy as a substitute for medication in a severe illness.** In a psychotic illness the family intervention and CBT for psychosis are adjuncts to an antipsychotic, not replacements; naming a therapy as monotherapy for psychosis (or for severe, high-risk depression) is a selection error.

15.3 Reasoning to the match: when the formulation and the patient refine the default

The grid is the default, not a straitjacket. Selection is a two-step move, read the first-line therapy off the evidence, then check whether the formulation, the patient's preference or the setting shifts it. Two worked lines make the reasoning concrete. A patient with a moderate depressive episode that began after a divorce, who talks fluently about the relationship and wants to work on it, is a clean match for interpersonal psychotherapy over cognitive behaviour therapy, not because the evidence separates them (both are first-line, IPS 2017 grade A) but because the

formulation names an interpersonal trigger and the preference predicts engagement. A patient with borderline personality disorder presenting after repeated self-harm is matched to dialectical behaviour therapy, because reducing self-harm and emotion dysregulation is exactly its lead indication (IPS 2023; NICE 2009), and a purely interpretive therapy would be the weaker fit. The discipline of choosing the right therapy is to let the disorder's evidence base set the default and to move off it only with a reason you can state.

WORKED EXAMPLE

A man in his forties presents with hazardous drinking and clear ambivalence, half-wanting to cut down, half-minimising. The matching move is not to prescribe abstinence-focused work to a contemplator but to meet his readiness: motivational enhancement therapy, its brief four-session form, is first-line for alcohol use disorder (IPS 2014 grade A; VA/DoD 2021), and motivational interviewing is the stage-matched style that resolves the ambivalence before any action-stage plan. Reading the stage of change first, and the diagnosis-default second, is the whole of the selection reasoning here.

COMMON TRAP

Procrustean matching, fitting every patient to the one therapy the clinician happens to practise. Selection is driven by the disorder's evidence base and the individual formulation, not by the therapist's training or preferred school; a service that offers only its favourite modality is choosing the therapist's convenience over the patient's indication. The corrective is to name the guideline first-line for the presentation before naming what you would personally deliver.

15.4 The protocol lives in the disorder chapter, not here

Selection points to a door; the room is furnished elsewhere. Once the presentation is matched to a modality, the manualised protocol that delivers it is taught in the disorder's own chapter, and the examinable move is to name the protocol and place it, not to re-teach it here. Exposure and response prevention for obsessive-compulsive disorder, and trauma-focused cognitive behaviour therapy for post-traumatic stress disorder, are developed in the Anxiety, OCD and trauma-related disorders notes. Dialectical behaviour therapy for borderline personality disorder, together with schema therapy, is developed in the Personality disorders notes. Interpersonal psychotherapy and cognitive behaviour therapy as used in depression, with the depression rating scales, sit in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes. Motivational interviewing and motivational enhancement therapy in addiction belong to the Substance use disorders notes. Keeping the selection question and the protocol question separate is what stops a "which therapy" answer from collapsing into an unfocused description of one technique.

15.5 Therapy selection in the Indian setting

Guideline-anchored choice, delivery-constrained supply. The Indian syllabus examines selection directly. The Indian Psychiatric Society has published a dedicated clinical practice guideline on the psychotherapies (Agarwal, Nischal, Praharaj, Menon and Kar; Indian Journal of Psychiatry 2020), and it embeds first-line psychotherapy recommendations across its disorder-

specific guidelines, cognitive behaviour therapy for depression, generalised anxiety disorder and obsessive-compulsive disorder, motivational enhancement therapy for the addictions (IPS 2014 grade A), and dialectical behaviour therapy for borderline personality disorder (IPS 2023), so the matching question is a live one here, not a Western import. The genuine Indian point is that the binding constraint is availability rather than evidence: trained therapists are scarce relative to need, which is why guideline attention turns to brief, low-intensity and task-shifted delivery by non-specialist workers under a stepped-care model, and to culturally adapted cognitive behaviour therapy (associated with Naeem and colleagues), best framed as a promising adaptation with a developing evidence base. Yoga and meditation-based interventions sit at the adjunct level of the evidence, not as stand-alone first-line treatments.

INDIA

An examiner asking about therapy selection in India is usually testing the second half of the answer. State the guideline first-line for the presentation (the IPS psychotherapies guideline, IPS 2020, plus the disorder-specific CPGs), then name the delivery reality: the availability filter dominates, so stepped and task-shifted care, culturally adapted brief cognitive behaviour therapy, and family-inclusive delivery (for example a co-resident relative as recovery monitor in alcohol use disorder, IPS 2014) are the realistic Indian answers. Keep yoga and meditation as adjuncts.

4	3	7
FACTORS WEIGHED IN THERAPY SELECTION (EVIDENCE BASE, FORMULATION, PREFERENCE AND CAPACITY, AVAILABILITY)	PATIENT-SIDE MARKERS OF SUITABILITY FOR INSIGHT WORK (MOTIVATION, COGNITIVE ABILITY, PSYCHOLOGICAL MINDEDNESS)	COMMON PRESENTATIONS IN THE MATCHING GRID

GOOD TO REMEMBER

- **Choosing the right therapy (the principle):** match the disorder to its guideline first-line modality first, then individualise by the formulation, the patient's preference and capacity for the work, and what is actually available; the strong first-lines to name on sight are cognitive behaviour therapy, interpersonal psychotherapy or behavioural activation for depression, CBT with exposure and response prevention for obsessive-compulsive disorder, dialectical behaviour therapy for borderline personality disorder, family therapy for adolescent anorexia and for psychosis relapse, motivational enhancement therapy and motivational interviewing for substance use, and CBT for psychosis only as an adjunct to medication.
- **The one discriminator:** the disorder's evidence base sets the default; patient factors refine it, but a strong first-line is overridden only for a stated reason (declined, unavailable, or a formulation that points elsewhere).
- **The one exam fact:** in a psychotic or severe illness, psychotherapy is an adjunct to pharmacotherapy, never a substitute.

HOLD THIS

Therapy selection is a two-step move: first read off the disorder's first-line psychotherapy from the evidence (cognitive behaviour therapy or interpersonal psychotherapy or behavioural activation for depression, CBT with exposure and response prevention for obsessive-compulsive disorder, dialectical behaviour therapy for borderline personality disorder, family therapy for adolescent anorexia and for psychosis relapse, motivational enhancement therapy and motivational interviewing for substance use, and CBT for psychosis as an adjunct only), then refine by the formulation, the patient's preference and psychological mindedness for the work, and what is available; the protocol itself is always taught in the disorder's own chapter, not here.

Psychiatric assessment and rating scales

16 · The psychiatric history and the mental state examination

The psychiatric clinical assessment has two limbs, and keeping them apart is the single most examinable habit in this paper. The first limb is the **history**, a longitudinal narrative of the person and the illness assembled from what the patient and the informants report; the second is the mental state examination (MSE), a cross-sectional description of the patient's mental functioning here and now, as observed and elicited during the interview. The history tells you what has happened over time; the MSE tells you what is present in the room. Neither, on its own, is a diagnosis. A viva will test the MSE hardest, because it is the psychiatrist's equivalent of the physical examination, a disciplined, ordered survey of observable phenomena, and the one skill that most reliably separates a trained candidate from an untrained one.

How to use this page. Learn the shape of the history first, quickly, then spend the bulk of your attention on the MSE, because that is where the marks and the errors both sit. Fix the domains in their examined order, **appearance and behaviour**, then **speech**, then **mood and affect**, then thought (**thought form** and **thought content**), then **perception**, then **cognition**, and finally **insight** and **judgement**. For each domain, hold two things: what it captures, and the classic error. The vocabulary of descriptive psychopathology that populates these domains, the fine phenomenology of the individual symptoms, and the psychometric theory behind the instruments are developed in the Psychometry, Assessment and Descriptive Psychopathology notes; this page owns the clinical skill of taking a history and conducting the examination.

The domain, in order	What it captures	A classic finding or term
1 **Appearance and behaviour**	grooming and self-care, psychomotor activity, rapport, eye contact, abnormal movements	psychomotor retardation; stereotypy; poor self-care
2 **Speech**	rate, rhythm, volume, tone, quantity and the form of production (not the content)	pressured speech; poverty of speech; mutism
3 **Mood and affect**	subjective mood versus observed affect; the range, reactivity and congruence of affect	blunted, labile or incongruent affect
4 **Thought** form and content	FORM, the flow and structure of thinking; and CONTENT, what is thought (including risk)	loosening of associations (form); a delusion (content)
5 **Perception**	hallucinations by modality, illusions, depersonalisation and derealisation	third-person auditory hallucinations
6 **Cognition**	the bedside screen: attention, orientation and memory (the full examination in the next topic)	disorientation; poor short-term recall
7 **Insight and judgement**	awareness of the illness and the need for care; the appraisal of decisions and their consequences	absent insight; impaired judgement

The one principle to hold
The mental state examination is a cross-sectional, here-and-now examination of the present state. It is not the history, and it is not a diagnosis.

Fig 19.10 The mental state examination: the domains in order. The MSE is examined and recorded in a fixed sequence: appearance and behaviour, speech, mood and affect, thought (both its form and its content), perception, cognition, and finally insight and judgement. Each domain has its own vocabulary and its own classic findings, and the discipline of moving through them in order is what stops a domain being missed. The single principle to hold is that the MSE is a cross-sectional snapshot of the patient's present state, gathered at the interview: it is distinct from the history, which is longitudinal, and it is not itself a diagnosis, but the observations from which a diagnosis and a formulation are built.

16.1 The psychiatric interview and the structure of the history

A single, ordered narrative built from the patient and from those who know them.

Psychiatric history-taking follows a fixed skeleton, and the value of the skeleton is that it forces completeness under time pressure. Open with *identifying data* and the *presenting complaints* in the patient's own words and their duration, then the *history of the present illness*, a chronological account from the first change from the person's normal state through the evolution of every symptom, its onset, course, precipitants and effect on functioning. Then work through the *past psychiatric history* (previous episodes, treatments, admissions and response), the *past medical and surgical history* (illnesses and drugs that cause or colour psychiatric symptoms), the *drug and treatment history* including current and past psychotropics, adherence and substance use, the *family history* (psychiatric illness, suicide and the family structure), the *personal and developmental history* (birth and milestones, childhood, education, occupation, relationships and forensic and sexual history), and the *premorbid personality*, the person's habitual character before the illness against which the current change is measured. Finally, and non-negotiably, the *collateral history* from an informant, because so many psychiatric presentations are marked by impaired insight and the patient alone cannot give the whole account. The examinable principle is that history taking in psychiatry elaborates each psychological symptom in depth rather than cataloguing physical complaints, and that it is always corroborated.

RULE **The history is longitudinal and corroborated.** It is the story of the person and the illness over time, and in psychiatry it is incomplete without a collateral account, because impaired insight is a feature of the very disorders being assessed.

INDIA

The AIIMS *Clinical Methods in Psychiatry* resident's handbook (2024) frames the history of the present illness around the mnemonic **A-B-C-D-E** (Affect and mood, Behaviour, Cognition, Dysfunction / Drugs / Disability, Environment), and formalises two properties of the informant that Indian examiners probe: *reliability* (consistency across informants and over time, absent an ulterior motive) and *adequacy* (enough information for a provisional diagnosis and a plan). Collateral history carries extra weight in Indian practice, where stigma, family-mediated help-seeking and frequent lack of insight mean the accompanying relative often supplies the decisive account. Confidentiality is respected throughout, but the risk of suicide or violence overrides it, and consent to interview the family is taken separately from the patient.

16.2 The mental state examination: a cross-sectional snapshot, not the history and not a diagnosis

The here-and-now examination of mental functioning, in a fixed order. The mental state examination is to the psychiatric assessment what the physical examination is to the medical one: a structured, present-tense description of what the clinician observes and elicits *during the interview itself*. It is deliberately cross-sectional. It does not narrate the past (that is the history's job) and it does not attach a label (that is the diagnosis's job); it is the raw observational data from which, together with the history, a diagnosis is later reasoned. The domains are examined in a conventional order that runs from the most observable to the most inferred: appearance and behaviour, speech, mood and affect, thought form and content, perception, cognition, and insight and judgement, **7** domains in all. The accompanying figure sets these out as the structure map of the examination. Learn the order as a fixed sequence; recording an MSE out of order, or omitting a domain, reads as an incomplete examination.

MSE DOMAIN (IN ORDER)	WHAT IT CAPTURES	COMMON ERROR
Appearance and behaviour	Grooming, physique, psychomotor activity, rapport, eye contact, abnormal movements, attitude to examiner	**Reporting an interpretation ("depressed") instead of the observation ("psychomotor slowing, poor eye contact")**
Speech	Rate, rhythm, volume, tone, quantity and the form of production, described as heard	Recording the *content* of what was said instead of the *form* of the speech
Mood and affect	Subjective, sustained mood versus the observed, moment-to-moment affect, its range, reactivity and congruence	**Collapsing mood and affect into one line, or confusing the two**

MSE DOMAIN (IN ORDER)	WHAT IT CAPTURES	COMMON ERROR
Thought form	The structure and flow of thought: circumstantiality, tangentiality, flight of ideas, loosening of associations	Describing content when asked for form
Thought content	Delusions, overvalued ideas, obsessions, preoccupations, and suicidal and homicidal ideation	Failing to ask about, or to record, suicidal and homicidal ideation
Perception	Hallucinations by modality, illusions, and depersonalisation and derealisation	Not specifying the modality, or missing that the phenomenon is an illusion, not a hallucination
Cognition	The bedside screen: consciousness, orientation, attention, memory and higher functions	Omitting it in a cooperative-seeming patient with a possible organic cause
Insight and judgement	The person's awareness of illness, graded, and the soundness of their decision-making	**Recording insight as merely "present" or "absent" rather than grading it**

The seven domains of the mental state examination in their conventional examined order, what each captures, and the classic recording error. The examination is cross-sectional and observational; it is not the history and it is not a diagnosis.

RULE **The MSE is a cross-sectional here-and-now snapshot.** It describes what is observable and elicitable in the interview, in a fixed order; it is the psychiatric physical examination, distinct from the longitudinal history that precedes it.

TRAP **The cardinal error: confusing the MSE with the history, or treating it as a diagnosis.** Past events, previous episodes and reported symptoms belong in the history, not the MSE; and the MSE yields signs, not a label. Writing "MDD" or "schizophrenia" in the MSE, or importing last year's admission into it, is the classic mistake this examination is built to prevent.

MNEMONIC

A Sad ManThinks Poorly, Cognition Intact?

The seven domains in order: **A**ppearance and behaviour, **S**peech, **M**ood and affect, **T**hought (form and content), **P**erception, **C**ognition, **I**nsight and judgement. Run them in this sequence every time so that no domain is dropped.

16.3 Appearance and behaviour

Everything the clinician can see before a word is exchanged. The first domain records *appearance* (build, self-care and grooming, dress, evidence of self-neglect or of specific states such as the flushed overactivity of mania or the stigmata of alcohol use) and *behaviour*, of which the most examinable element is *psychomotor activity*, either slowed (retardation, as in severe depression or catatonia) or increased (agitation, restlessness, overactivity). Note the quality of *rapport* and *eye contact*, the patient's *attitude to the examiner* (cooperative, guarded, suspicious, hostile, seductive, perplexed), and any *abnormal movements*: tremor, tics, mannerisms, stereotypies, dyskinesias, and the catatonic signs (posturing, waxy flexibility, negativism,

echopraxia). The discipline of this domain is to record *observations*, not conclusions. "Unkempt, malodorous, sitting motionless with downcast gaze" is a description; "looks depressed" is an inference that pre-empts the examination.

COMMON TRAP

Do not let an interpretation masquerade as an observation. Psychomotor retardation, poverty of facial expression and poor eye contact are *observed signs*; "depression" is a conclusion you reach later by weighing them against the history and the rest of the MSE. The mark is for the sign, described.

16.4 Speech

The form of the output, described as heard, not what was said. The **speech** domain captures the physical and formal characteristics of talking: *rate* (fast, as in the pressured speech of mania, or slow), *rhythm* and fluency, *volume* (loud or barely audible), *tone* and prosody (monotonous in depression, over-modulated in mania), *quantity* (voluble and hard to interrupt, or spontaneously mute), and the *form of production*. This domain describes the vehicle of thought; the ideas being conveyed are analysed under thought form and content. A single sample of the patient's actual words, quoted, is worth more than an adjective. The examinable discrimination is between disordered speech that reflects a disordered *thought* process (which is scored under thought form) and disordered speech that reflects a *motor or neurological* problem, such as the slurring of dysarthria or the word-finding difficulty of dysphasia, which points towards an organic cause rather than a formal thought disorder.

16.5 Mood and affect

The sustained inner weather versus the moment-to-moment expressed emotion. The **mood and affect** distinction is a perennial examination favourite. *Mood* is the pervasive, sustained emotional state as *subjectively reported* by the patient ("How have your spirits been?"); it is the climate. *Affect* is the emotional state as *objectively observed* by the clinician from face, posture and voice over the course of the interview; it is the weather. Describe mood in the patient's own terms and note whether it is euthymic, depressed, elevated, irritable or anxious. Then describe affect along four axes: its *quality*, its *range* (full, or restricted, blunted, or flat), its *reactivity* (whether it shifts appropriately with the topic, or is fixed and non-reactive), and its *congruence* with the stated mood and with the content of thought. Incongruent affect, for example giggling while describing a bereavement, is itself a sign. Note also whether the subjective mood and the observed affect agree; a patient may deny low mood while displaying a flat, tearful affect.

WORKED EXAMPLE

A man says his mood is "fine" (subjective mood, reported), but throughout the interview his affect is observed to be restricted in range, non-reactive, and incongruently tearful when he mentions his work. The MSE line reads: "Subjectively euthymic; objectively affect restricted, non-reactive, incongruent, with lability on discussing work." Nothing here is a diagnosis; it is a description of the observed emotional state set against the reported one.

TRAP **Mood is not affect.** Mood is subjective and sustained (what the patient reports over recent weeks); affect is objective and cross-sectional (what you observe now). Range, reactivity and congruence are properties of *affect*. Collapsing the two, or applying "reactive" to mood, is the classic slip.

16.6 Thought form

The structure and flow of thinking, inferred from speech. **Thought form** concerns *how* a person thinks, the organisation and connectedness of their ideas, as opposed to what they think about. It is inferred from the form of speech. The formal thought disorders are the named abnormalities of this stream, and the examinable set turns on one axis: does the train of thought reach its goal, and can you follow the links? Jaspers and the descriptive tradition insist that the psychiatrist attend to the form before the content. The table below fixes the four classic disorders the topic names, plus two more you must recognise.

FORMAL THOUGHT DISORDER	WHAT THE THINKING DOES	REACHES THE GOAL?
Circumstantiality	Over-inclusive, tediously detailed and full of digressions, but the point is eventually made	**Yes, eventually**
Tangentiality	Replies veer off at an angle and drift further from the point with each step	**No, never returns**
Flight of ideas	A rapid, pressured stream leaping between topics on chance links, rhyme, clang and distraction; the thread is followable (classically manic)	Loosely; links are discernible
Loosening of associations	Ideas shift with no logical or comprehensible connection (derailment, knight's-move thinking); the thread is lost (classically schizophrenic)	No; the links themselves are broken
Thought block	A sudden, involuntary cessation of the flow of thought, mid-stream, the mind going blank	Interrupted
Perseveration	Inappropriate persistence or repetition of a word or idea after the context has moved on (often organic)	Stuck

The formal thought disorders, discriminated by whether the train of thought reaches its goal and whether the links between ideas can be followed. Flight of ideas keeps followable links; loosening of associations breaks them.

TRAP **Circumstantiality versus tangentiality, and flight of ideas versus loosening.** Circumstantiality gets there by a long road; tangentiality never arrives. Flight of ideas is fast but its links are traceable (rhyme, pun, distraction); loosening of associations has links you cannot trace at all. The first pair is about arrival; the second pair is about whether the connections make sense.

16.7 Thought content

What preoccupies the mind, from delusions to the ideation that carries risk. **Thought content** records *what* the person is thinking about. Elicit and describe abnormal beliefs and preoccupations, and define them precisely, because the definitions discriminate the diagnoses.

Delusion

A fixed, false belief, out of keeping with the person's social and cultural background, held with unshakeable conviction despite contrary evidence; described by its content (persecutory, grandiose, nihilistic and so on) and whether it is primary or secondary, mood-congruent or incongruent.

Overvalued idea

A comprehensible, strongly held and emotionally invested belief that comes to dominate the person's life; not held with delusional conviction and not resisted as senseless, sitting between a normal belief and a delusion.

Obsession

A recurrent, intrusive, unwanted thought, image or impulse recognised as the person's own and as senseless, resisted (at least initially), and provoking anxiety; distinct from a delusion in that insight into its absurdity is retained.

Preoccupation

A non-delusional, non-obsessional theme that repeatedly draws the mind, such as pervasive worry, rumination or hypochondriacal concern.

The examination of thought content is also where *risk* is formally elicited. Ask directly about *suicidal ideation* (thoughts, intent, plan, preparatory acts and protective factors) and about *homicidal or violent ideation*; both are recorded here, and asking about suicide does not plant the idea. The structured suicide-risk instrument, the Columbia Suicide Severity Rating Scale, and the wider suicide-risk assessment are developed in the Somatic-symptom, sexual, impulse-control disorders and suicide notes; within the MSE, the task is to elicit and document the ideation, its intensity and its associated plan.

> **COMMON TRAP**
>
> An abnormal belief is not a delusion until you have tested three things: its *fixity*, its *falseness*, and its *incongruence with the person's culture*. A belief widely shared within a religious or cultural community is not delusional simply because it is unfamiliar to the examiner. The wider transcultural frame is set out in the Consultation-liaison, geriatric and transcultural psychiatry notes.

16.8 Perception

Disturbances in how the world and the self are apprehended. The **perception** domain covers false or altered percepts, and the definitions again do the discriminating work.

Hallucination

A percept experienced in the absence of any external stimulus, with the full force and quality of a true perception, and located in external space; specify the *modality*, auditory (second-person or third-person voices, running commentary), visual, olfactory, gustatory, tactile or somatic.

Pseudohallucination
A percept experienced in inner subjective space and lacking the substantiality of a true perception, over which the person retains some awareness of its unreality.

Illusion
A *misperception* of a real external stimulus (the dressing gown seen as an intruder), distinguished from a hallucination by the presence of an actual stimulus.

Depersonalisation
A distressing sense of being unreal, detached from or an observer of one's own self, thoughts or body.

Derealisation
The corresponding sense that the external world is unreal, remote or lifeless, as though seen through glass.

The examinable line runs between the *illusion*, which is a distorted reading of a real stimulus, and the *hallucination*, which arises with no stimulus at all; and, within hallucinations, between the true hallucination in external space and the pseudohallucination in inner space. Always record the modality, because the modality carries diagnostic weight (third-person auditory hallucinations point one way, visual and olfactory hallucinations raise the question of an organic cause).

16.9 Cognition

The bedside cognitive screen, and the point at which to reach for a standardised tool. The **cognition** domain is the clinical screen of higher mental function, examined in a rough hierarchy: *level of consciousness*, *orientation* to time, place and person, *attention and concentration* (serial sevens, digit span, months in reverse), *memory* (immediate registration, recent and remote recall), and higher functions (language, praxis, abstraction, executive function). Its purpose in the MSE is to flag the organic, because a cognitive deficit in a patient who otherwise seems to have a primary psychiatric disorder is the finding that redirects the whole assessment. When the bedside screen suggests impairment, quantify it with a standardised instrument. The MMSE (Mini-Mental State Examination; Folstein, 1975) and the MoCA (Montreal Cognitive Assessment; Nasreddine, 2005) are the two brief screens to know, each scored out of a possible 30. A widely cited MMSE threshold for cognitive impairment is a score below 24 out of a possible 30, though the cut-off is education-dependent; the MoCA, which is more sensitive to mild cognitive impairment, uses a threshold below 26 out of a possible 30, with one point added for a person with twelve or fewer years of formal education. The full bedside cognitive examination and the typeset structure of these instruments, with the accompanying scale plate, are developed in the cognitive-examination topic that follows; the deeper psychometric theory of reliability, validity and standardisation sits in the Psychometry, Assessment and Descriptive Psychopathology notes.

7	6	24	26
MSE DOMAINS, EXAMINED IN FIXED ORDER	GRADES OF INSIGHT (COMPLETE DENIAL TO TRUE INSIGHT)	MMSE THRESHOLD: A SCORE BELOW THIS, OUT OF A POSSIBLE 30, SUGGESTS IMPAIRMENT	MOCA THRESHOLD: A SCORE BELOW THIS, OUT OF A POSSIBLE 30, SUGGESTS IMPAIRMENT

16.10 Insight and judgement

Awareness of illness, graded, and the soundness of decision-making. **Insight** is the patient's awareness and understanding of their own condition: that they are unwell, that the illness is psychiatric in nature, and that treatment is needed. It is not usefully recorded as simply "present" or "absent"; it is a graded continuum. The classic scheme runs to **6** grades, from complete denial of illness at one end to true emotional insight at the other.

GRADE	LEVEL OF INSIGHT
Grade I	Complete denial of illness
Grade II	Slight awareness of being sick and needing help, while denying it at the same time
Grade III	Awareness of being sick, but blaming it on others, on external factors or on a physical cause
Grade IV	Awareness that the illness is due to something unknown within the patient
Grade V	**Intellectual insight: admits the illness and that symptoms are due to their own irrational feelings, but cannot apply this to future experience**
Grade VI	**True emotional insight: emotional awareness of the motives and feelings within, which can lead to real change in behaviour**

The six grades of insight, from complete denial (Grade I) to true emotional insight (Grade VI). The examinable discriminator is Grade V versus Grade VI: intellectual insight knows but does not change; true insight is emotionally owned and can change behaviour.

Judgement is the appraisal of the patient's ability to make sound, reasoned decisions in their own and others' interest, assessed from their real-life choices during and around the illness and, where needed, from their reasoning about a hypothetical situation. It bears directly on capacity and on risk, and it can be intact where insight is impaired, or vice versa, so the two are recorded separately.

16.11 Recording and integrating the assessment

The MSE feeds the formulation; it does not replace it. A good MSE is written in observational, present-tense language, domain by domain in order, quoting the patient where a quotation is more precise than an adjective. Its findings are then integrated with the history to build the diagnostic formulation and the differential, but the integration is a separate step: the MSE supplies signs, the history supplies the story, and only their synthesis yields a diagnosis. Two failures recur. The first is importing the history into the MSE, writing past episodes or reported symptoms into a domain that is meant to be here-and-now. The second is closing the MSE with a diagnostic label, as though the description of signs were itself the conclusion. Guard both borders and the examination does its job, which is to be the disciplined observational base on which everything downstream is built.

GOOD TO REMEMBER

- **The principle:** the mental state examination is a cross-sectional, here-and-now, observational survey of mental functioning across seven domains in fixed order (appearance and behaviour, speech, mood and affect, thought form and content, perception, cognition, insight and judgement); it is distinct from the longitudinal history and is not, in itself, a diagnosis.
- **The discriminator:** the history is what the patient and informants *report* over time and must be corroborated by a collateral account; the MSE is what the clinician *observes and elicits* now. Within it, mood is subjective and sustained while affect is objective and cross-sectional.
- **The one exam fact:** the seven domains run appearance and behaviour, speech, mood and affect, thought (form and content), perception, cognition, insight and judgement; insight is graded to six levels; MMSE and MoCA screen cognition out of a possible 30, with thresholds below 24 and below 26 respectively.

HOLD THIS

The MSE is the psychiatric physical examination: a cross-sectional, here-and-now, observational survey of seven domains in fixed order (appearance and behaviour; speech; mood and affect; thought form and content; perception; cognition; insight and judgement), distinct from the longitudinal, corroborated history and never, by itself, a diagnosis.

17 · Higher mental functions and the cognitive examination

This topic teaches the bedside skill that separates a psychiatrist from a symptom-checklist: the structured examination of the **higher mental functions**, the cortical faculties of attention, orientation, memory, language, praxis and executive control. It earns flagship space because it is examined in two registers at once. In the viva the examiner hands you a patient and watches you test, so the marks are in doing the **cognitive examination** in the right order with the right instruction; in the written paper the marks are in the numbers, the domains and the verified cut-offs of the two screening instruments every candidate is expected to reproduce cold. Cognition is also the sixth of the seven mental-state domains (appearance and behaviour; speech; mood and affect; thought; perception; cognition; insight and judgement), so the whole of this page sits inside the mental state examination as a cross-sectional, here-and-now snapshot, never a diagnosis in itself.

How to use this page. Learn the examination as a hierarchy, not a list. Test **attention and concentration** first, because a patient who cannot hold attention cannot be validly tested on anything downstream; then **orientation**, then registration and **memory testing**, then language and praxis, then the **frontal lobe tests** of executive control. Only once the individual faculties are understood do the packaged screens make sense: the MMSE and the MoCA are simply these bedside items bundled and scored. The deeper lobe-by-lobe functional neuroanatomy and the formal test batteries belong to the neuropsychology overview; the reliability and validity of these scales, and the descriptive-psychopathology vocabulary, belong to the Psychometry, Assessment and Descriptive Psychopathology notes. Here we teach the examination itself.

MNEMONIC

ALL SANE MEN THINK PRECISELY CONSIDERING INSIGHT

The seven mental-state domains in their conventional order, so you can locate where the cognitive examination sits: **A**ppearance and behaviour, **S**peech, **M**ood and affect, **T**hought (form and content), **P**erception, **C**ognition, **I**nsight and judgement. Cognition is the **C**, the sixth station; the higher mental functions on this page are what you test when you reach it.

Domain	What is tested	Points
Orientation to time	year, season, month, day, date	5
Orientation to place	country, state, town, building, floor	5
Registration	repeat three named objects	3
Attention and calculation	serial sevens, or spell a word backward	5
Recall	recall the three objects	3
Language	naming, repetition, a three-stage command, reading, writing	8
Visuospatial	copy two intersecting pentagons	1
Total		30

A score below 24 out of a possible 30 suggests cognitive impairment; interpret against age and education. Folstein 1975; permission-required, structure typeset, not reproduced.

Fig 19.11 The Mini-Mental State Examination (MMSE). A brief clinician-administered screen of orientation, registration, attention, recall, language and construction, scored out of a possible 30. A score below 24 suggests cognitive impairment, but the cut-off must be read against the person's age and education: a highly educated person may be impaired while still scoring well, and a person with little formal schooling may score lower without being impaired. It is a screen, not a diagnosis, and it is relatively insensitive to the earliest, mild and predominantly executive deficits. The structure is typeset here from the published instrument; the MMSE is copyright and permission-required, so the form itself is not reproduced.

Domain	What is tested	Points
Visuospatial and executive	trail-making, cube copy, clock drawing	5
Naming	name three animals (lion, rhinoceros, camel)	3
Attention	digit span, target tapping, serial sevens	6
Language	repeat two sentences, verbal fluency	3
Abstraction	similarities between two items	2
Delayed recall	recall five words after a delay	5
Orientation	date, month, year, day, place, city	6
Total		30

26 or above out of a possible 30 is normal; add a point for twelve years or fewer of education. Nasreddine 2005; permission-required, structure typeset.

Fig 19.12 The Montreal Cognitive Assessment (MoCA). A brief screen scored out of a possible 30 that samples visuospatial and executive function, naming, attention, language, abstraction, delayed recall and orientation. A score of 26 or above is taken as normal, with one point added for people with twelve years or fewer of formal education. It is more sensitive than the MMSE to mild cognitive impairment and to the executive and visuospatial deficits of the earliest stages, which is why it is often preferred where an early or subtle decline is the question. The instrument is copyright and, in most current editions, requires training or certification to administer, so the structure is typeset here rather than the form reproduced.

17.1 Attention and concentration: the gateway faculty

Test attention first, because everything else rests on it. Attention is the capacity to focus on a stimulus, and concentration is the capacity to sustain that focus over time; together they are the substrate on which registration, memory and language testing depend, which is why they are examined at the very start of **bedside cognition** (Clinical Methods in Psychiatry, AIIMS 2024; Fish and Sims). Three bedside tasks carry the load. The digit span is the purest measure: random digits are read one per second and repeated back, and a healthy adult manages about seven forwards and five in reverse, so a forward span below five points to an attentional deficit; the reverse span additionally taxes working memory. The **serial sevens** asks the patient to subtract seven serially from one hundred (100, 93, 86, 79, 72, 65), and spelling the word WORLD backwards is the standard less numerate alternative. **Reciting the months of the year backwards** is a quick, education-light screen of sustained attention. Impaired, fluctuating attention is the single signature of delirium, and its presence should stop you reading a poor memory score as amnesia until attention is restored.

RULE **Attention is the gateway; test it first.** A patient who cannot attend cannot be validly tested on memory, language or executive function. Inattention that fluctuates is the hallmark of delirium, not of dementia, and it invalidates every tier below it.

TRAP **Reading a failed serial sevens as pathology.** The serial sevens is heavily confounded by numeracy and education; a poorly schooled patient may fail it while wholly attentive. Corroborate with months backward or digit span before calling attention impaired, and never rest a conclusion on the serial sevens alone.

17.2 Orientation: time, place and person

The most sensitive bedside marker of an acute organic state. Orientation is the patient's awareness of the situation across three axes, and it is tested and recorded in a fixed order: **time** (day, date, month, year, season, approximate time of day), **place** (building, town, floor, kind of place) and **person** (their own identity and that of those around them). The clinically useful fact is the gradient of vulnerability: orientation to time is lost first and recovers last, place follows, and orientation to person is the most robust, surviving into severe global impairment. Disorientation to time out of proportion to any memory deficit is an early and sensitive sign of delirium, which is why it opens the cognitive screen. The reverse pattern is a red flag for a non-organic picture: a patient who does not know who they are while remaining fully oriented to time and place is far more likely to be presenting a dissociative or functional disturbance than an organic amnesia.

> **PEARL**
>
> Follow the gradient, time before place before person. When it is inverted, when a patient is disoriented to their own identity yet knows the day and the ward, suspect a functional or dissociative process rather than delirium or dementia, because organic disorientation almost never takes out person while sparing time.

17.3 Registration and memory: immediate, recent and remote

Separate encoding from storage from retrieval, and separate the time-frames. Memory testing walks three temporal windows. **Immediate memory (registration)** is tested by naming three unrelated words (for example apple, table, penny) and having the patient repeat them at once; this is really a test of attention and encoding, not of memory storage. **Recent memory** is the critical amnestic measure: after a few minutes of distraction the patient is asked to recall those same three words, and impaired delayed recall that does not improve with category cues is the signature of the hippocampal-type amnesia of Alzheimer disease. **Remote memory** is probed through well-anchored autobiographical and general events (schooling, marriage, prime ministers, major public events), and in the typical amnestic gradient recent memory fails while remote memory is relatively preserved. Two further distinctions are examinable: **anterograde** amnesia (a failure to lay down new memories after an insult) versus **retrograde** amnesia (loss of memories from before it); and **verbal** memory (word lists, stories, a left-temporal function) versus **visual** memory (recalling and reproducing a figure, a right-temporal function), the latter tapped at the bedside by asking the patient to copy and later redraw a design.

TRAP **Confusing registration with recall.** Failing the immediate three-word repetition is an attention or encoding failure; failing the delayed recall of words that were registered is the true amnestic sign. Only the second, uncued delayed recall, discriminates early Alzheimer-type memory loss, and only if attention was intact when the words went in.

17.4 Language and praxis

Six language channels and the two apraxias. Language is examined across a fixed set of channels, and testing them in order localises the lesion. **Spontaneous speech and fluency** (is output effortful and non-fluent, as in a Broca-type picture, or fluent but empty and paraphasic, as

in a Wernicke-type picture); **comprehension** (following graded one-, two- and three-step commands); **repetition** (repeating a phrase such as "no ifs, ands or buts", the channel selectively spared in transcortical and lost in conduction aphasia); **naming** (confrontation naming of objects and their parts, the most sensitive and earliest-affected language function, its failure being anomia); **reading**; and **writing**. Praxis, the ability to carry out a learned, purposeful movement when the elementary motor and sensory systems are intact, is tested separately and is the classic parietal-frontal sign.

Ideomotor apraxia

The idea of the movement is intact but cannot be mapped onto the motor engrams: the patient fails to perform a gesture to command ("show me how you would wave goodbye", "how you would use a comb") yet may perform it spontaneously.

Ideational apraxia

The concept of the act itself is lost or degraded, so a sequence of actions (filling and lighting a pipe, preparing a letter for posting) cannot be organised, even though each isolated element may be possible.

WORKED EXAMPLE

A right-handed patient names a watch but calls its strap and winder a "thing", follows a one-step command but not a three-step one, and cannot mime striking a match to instruction though he does it when handed a real matchbox. The early anomia and the gesture-to-command failure with preserved spontaneous use are ideomotor in type and point the examination toward the dominant temporo-parietal cortex, to be pursued with the fuller batteries in the neuropsychology overview.

17.5 The frontal-executive tests

The functions the MMSE forgets. Executive control, the planning, set-shifting, abstraction and inhibition mediated by the prefrontal cortex, is invisible to the older screens and must be sought deliberately with the **frontal lobe tests**. **Verbal fluency** comes in two forms: phonemic (as many words as possible beginning with a given letter, classically F, A and S, in a minute each) and semantic or category fluency (as many animals as possible in a minute); reduced output, especially disproportionately reduced phonemic fluency, signals frontal dysfunction. The Luria three-step, the fist-edge-palm motor sequence, tests motor programming and perseveration. The **go/no-go** paradigm (tap once when I tap once, do not tap when I tap twice) tests inhibitory control, and the related conflicting-instruction task tests sensitivity to interference. **Abstraction** is drawn out by similarities (how are an apple and an orange alike; the impaired answer is concrete, "both are round", rather than the categorical "both are fruit") and by **proverb interpretation**, where a concrete reading of "a rolling stone gathers no moss" betrays loss of abstraction. These are packaged into the Frontal Assessment Battery (FAB) of Dubois and colleagues (2000), six subtests scored from 0 to 3, giving a score out of a possible 18.

FAB SUBTEST	FRONTAL FUNCTION PROBED	BEDSIDE TASK
Similarities	Conceptualisation	**In what way are a banana and an orange alike (category, not appearance)**
Lexical fluency	Mental flexibility	**Words beginning with S in sixty seconds**
Motor series	Programming	**Luria's fist-edge-palm sequence**
Conflicting instructions	Sensitivity to interference	**Tap twice when I tap once**
Go / no-go	Inhibitory control	**Tap once when I tap once; do not tap when I tap twice**
Prehension behaviour	Environmental autonomy	**Does the patient grasp the examiner's proffered hands despite instruction not to**

The six subtests of the Frontal Assessment Battery, each scored from 0 to 3, for a bedside frontal screen out of a possible 18 (Dubois et al 2000; Lishman's Organic Psychiatry).

17.6 The Mini-Mental State Examination (MMSE)

The classic global screen, and what it misses. The **MMSE** of Folstein and colleagues (1975) is the most widely used bedside cognitive screen, taking five to ten minutes and scored out of a possible 30 across five domains: orientation, registration, attention and calculation, recall and language (with a visuoconstructive copy). The domain weighting is worth holding, because the accompanying scale plate typesets the permission-required form in full and the examiner is expected to know how the marks are distributed. The conventional cut-off is **24**: a total below 24, that is at or below 23, suggests cognitive impairment, though this must be read against the patient's age and education. Two caveats are examinable. Highly educated patients may score a perfect 30 out of a possible 30 while already declining, a ceiling effect that masks early disease; poorly educated or elderly patients may fall below the cut-off without pathology, so age- and education-adjusted norms are preferred over the raw threshold. Critically, the MMSE has few memory items and no executive or frontal items at all, which is exactly why it under-detects both mild cognitive impairment and frontal-predominant dementias.

MMSE DOMAIN	POINTS	SAMPLE BEDSIDE ITEM
Orientation	10	**Time (year, season, date, day, month) and place**
Registration	3	**Repeat three named objects immediately**
Attention and calculation	5	**Serial sevens or WORLD spelt backwards**
Recall	3	**Recall the three objects after a delay**
Language and praxis	9	**Naming, repetition, a three-stage command, reading, writing, copying**

The five scored domains of the MMSE, totalling out of a possible 30; the accompanying scale plate carries the typeset form (Folstein et al 1975; Clinical Methods in Psychiatry, AIIMS 2024).

TRAP **Treating a low MMSE as a diagnosis.** The score is a cross-sectional measure of impairment, not a diagnosis of dementia. Delirium, depressive pseudodementia, low education, sensory deficit, language barrier and poor cooperation all pull it down; a single number never diagnoses, and a normal number never excludes early or frontal disease.

17.7 The Montreal Cognitive Assessment (MoCA)

The screen built to catch what the MMSE misses. The **MoCA** of Nasreddine and colleagues was developed in the late 1990s specifically to remedy the MMSE's insensitivity to mild cognitive impairment, and it is scored out of a possible 30 across seven domains, adding the executive, abstraction and richer delayed-recall items the MMSE lacks. Its cut-off is **26**: a total at or above 26 is taken as normal, and below 26 as impaired. A single point is added to the total for anyone with twelve years or fewer of formal education, a built-in correction absent from the MMSE and one that matters greatly in populations of variable schooling. Because it loads on delayed free recall and on frontal-executive tasks (trail-making, clock drawing, phonemic fluency, abstraction), the MoCA is the more sensitive of the two to mild cognitive impairment and early Alzheimer disease, at some cost in specificity. Like the MMSE it is permission-required and now requires certified training to administer; the accompanying scale plate carries the typeset structure.

MOCA DOMAIN	POINTS	WHAT IT ADDS OVER THE MMSE
Visuospatial / executive	5	**Trail-making, cube copy and clock drawing, absent from the MMSE**
Naming	3	**Low-frequency animals (lion, rhinoceros, camel)**
Attention	6	**Digit span, vigilance tap-test and serial sevens**
Language	3	**Sentence repetition and phonemic fluency**
Abstraction	2	**Similarities (train and bicycle; watch and ruler)**
Delayed recall	5	**Five words, uncued, the key memory load**
Orientation	6	**Date, month, year, day, place, city**

The seven scored domains of the MoCA, totalling out of a possible 30, with one point added for twelve years or fewer of schooling; the accompanying scale plate carries the typeset form (Nasreddine et al; Kaplan and Sadock CTP 2024).

RULE **For suspected mild cognitive impairment, reach for the MoCA.** Its executive load and its five-word uncued recall catch the early decline the MMSE ceilings past; the price is lower specificity, so a below-cut-off MoCA screens in, it does not diagnose.

24	26	1	18
MMSE CUT-OFF FOR IMPAIRMENT (OUT OF A POSSIBLE 30)	MOCA CUT-OFF FOR IMPAIRMENT (OUT OF A POSSIBLE 30)	EXTRA MOCA POINT FOR TWELVE YEARS OR FEWER OF SCHOOLING	FAB MAXIMUM, SIX SUBTESTS SCORED 0 TO 3

INDIA

The education and language caveats are not academic in the Indian setting, where literacy varies widely and the raw MMSE and MoCA cut-offs travel poorly. The Hindi Mental State Examination (HMSE) was developed as a culturally and linguistically adapted screen for low-literacy and non-literate Indian populations and is listed alongside the MMSE, MoCA and Addenbrooke's examination in the standard Indian bedside repertoire (Clinical Methods in Psychiatry, AIIMS 2024), and it appears in Indian medicolegal capacity assessments of elderly individuals. Vernacular adaptations of the MoCA and the ACE, and the indigenous neuropsychological batteries developed in the NIMHANS and AIIMS traditions, exist for the same reason: to keep the cognitive examination valid across the country's languages and schooling levels rather than importing a Western cut-off wholesale.

GOOD TO REMEMBER

- **The principle:** the cognitive examination is a hierarchy, attention first, then orientation, memory, language and praxis, then executive function, because a deficit at any tier invalidates the tiers below it, and the whole is a cross-sectional snapshot of the higher mental functions, never a diagnosis on its own.
- **The discriminator:** the MMSE (out of a possible 30, cut-off 24) has no executive items and misses mild cognitive impairment; the MoCA (out of a possible 30, cut-off 26, plus one point for twelve years or fewer of schooling) adds executive and delayed-recall load and is the more sensitive to mild cognitive impairment.
- **The one exam fact:** attention is tested first, and fluctuating inattention, not amnesia, is the signature of delirium.

HOLD THIS

Examine the higher mental functions in hierarchical order (attention, orientation, memory, language and praxis, executive), because inattention, the hallmark of delirium, invalidates everything below it; then bundle them into the two screens whose cut-offs must be reproduced cold, the MMSE at 24 out of a possible 30 (blind to executive function and to mild cognitive impairment) and the MoCA at 26 out of a possible 30 with a one-point allowance for twelve years or fewer of schooling (the more sensitive to mild cognitive impairment), remembering that a score measures impairment, it never makes the diagnosis.

18 · The biopsychosocial and 4-Ps formulation

The single skill that binds the whole of this chapter, the history, the mental state examination and the diagnostic label, into one usable clinical product is the **case formulation**. Where a diagnosis places a patient in a category, a formulation tells the story of why *this* person developed *this* problem at *this* moment, and it is the formulation, not the diagnosis, that a management plan is actually built on. It is also the most reliably examined assessment skill on the paper: the long case and the viva reward the candidate who can move past "the diagnosis is a depressive episode" to "here is a middle-aged man, vulnerable for these reasons, tipped over now by these events, kept unwell by these, and protected by these, so here is what I would do first".

How to use this page. Fix the diagnosis-versus-formulation distinction first, because the commonest exam error is to offer a diagnosis when a formulation is asked for. Then learn the **biopsychosocial model** as the vertical axis (biological, psychological, social) and the **four Ps** as the horizontal axis (predisposing, precipitating, perpetuating, protective); the two axes cross to make the grid that the accompanying figure lays out, and that grid is the answer template for almost any "formulate this case" question. Finally see how the grid generates the plan: the perpetuating column is what treatment attacks, the protective column is what treatment mobilises.

The 4 Ps	Predisposing	Precipitating	Perpetuating	Protective
Biological	genetic loading, family history, birth or developmental insult	a physical illness, substance use, a medication change	chronic pain, ongoing substance use, poor adherence	good physical health, no substance use, a good treatment response
Psychological	early adversity, maladaptive schemas, low self-esteem	a loss, a failure, a threat to self-worth	cognitive distortions, avoidance, hopelessness	insight, coping skills, psychological-mindedness
Social	childhood neglect, poverty, migration	bereavement, job loss, relationship breakdown	isolation, high expressed emotion, financial strain	supportive relationships, employment, a faith community

Fig 19.13 The formulation grid: the biopsychosocial model and the 4 Ps. A formulation is the individual account of why this person has this problem at this time, and it is what turns a diagnosis into a plan. The grid crosses the three biopsychosocial levels, biological, psychological and social, against the four temporal factors: predisposing (the long-standing vulnerabilities), precipitating (what tipped it over now), perpetuating (what keeps it going) and protective (the strengths and supports to build on). Working through the twelve cells forces attention to factors a diagnosis alone would miss, and the perpetuating and protective columns in particular point directly to what the treatment should target and what it can lean on.

18.1 Diagnosis versus formulation: the category and the individual account

A diagnosis is nomothetic, a formulation is idiographic. A **diagnosis** is a shared category: it matches the patient's symptom pattern to the criteria of ICD-11 or DSM-5-TR and answers the question "what is the disorder?". It is deliberately impersonal, because its value is precisely that it is the same for every patient who meets the criteria, which is what lets it carry a prognosis and an evidence-based treatment. A case formulation answers a different and complementary question, "why this person, why this problem, why now?", and its value is precisely that it is unique to the individual in front of you. Formulation is not a competitor to diagnosis but its clinical partner: the diagnosis says what treatments have worked for this *kind* of problem, the formulation says how to deliver them to *this* patient and what else must be addressed. A formulation is, in Jaspers' terms, an exercise in both understanding (an empathic grasp of the patient's experience) and explaining (an evidence-based account of the contributing causes), and following Jaspers the two must be held together rather than collapsed into one. Crucially, a formulation is a hypothesis: it is provisional, iterative and revised as new information arrives, whereas the diagnosis, once criteria are met, is comparatively stable.

FEATURE	DIAGNOSIS	FORMULATION
What it is	The disorder category the illness belongs to (ICD-11, DSM-5-TR)	**The individualised account of why this person has this problem now**
Question answered	"What is the disorder?"	**"Why this person, why this problem, why now?"**
Level	Nomothetic: shared across all who meet criteria	Idiographic: specific to the individual
Content	Symptom pattern matched to operational criteria	Predisposing, precipitating, perpetuating and protective factors across the biological, psychological and social domains
Status	Relatively fixed once criteria are met	A working hypothesis, revised with new information
What it drives	Prognosis and evidence-based treatment selection	The individualised, sequenced management plan

The diagnosis names the category; the formulation explains the individual. They are partners, not rivals: the diagnosis carries the evidence base, the formulation carries the delivery.

RULE **A diagnosis labels, a formulation explains.** When the examiner asks you to "formulate", give the individualised causal account across the biopsychosocial domains and the four Ps, not the ICD or DSM category; naming the disorder is a necessary first line, never the whole answer.

18.2 The biopsychosocial model: the vertical axis (Engel, 1977)

Three domains, and an argument against dualism. The biopsychosocial model, proposed by George Engel (Science, 1977), holds that illness is never purely "physical" or purely "mental": every presentation is shaped simultaneously by **biological**, **psychological** and **social** factors, and a complete account must weigh all three. It was framed explicitly as a corrective to the Cartesian biomedical model, which split mind from body and so mishandled exactly the mixed presentations psychiatry sees. For the formulation this model supplies the vertical axis, the three rows into which any causal factor is sorted. The biological row covers disease and physiology (genetic loading, the brain, physical illness, substances and drugs). The psychological row covers cognition, mood and behaviour (temperament, attachment and early experience, beliefs and schemas, coping style, personality). The social row covers the interpersonal, the social and occupational, and the health-care system (family, relationships, work, housing, culture, access to care).

Biological

Disease and physiology: genes and family history, the brain and its neurochemistry, physical illness, substances and medication.

Psychological

Cognition, mood and behaviour: temperament, attachment and early experience, beliefs and maladaptive schemas, coping and defensive style, personality.

Social

Interpersonal, social and occupational, and the health-care system: family and relationships, work and finances, housing, culture and community, access to care.

INDIA

In Indian practice the social row carries unusual weight, and the family sits at its centre. The co-resident family is routinely a predisposing factor (high expressed emotion, enmeshment), a perpetuating factor (conflict, stigma, treatment interruption) and, most importantly, a protective factor and treatment ally: the Indian Psychiatric Society's alcohol-use guidance formalises this by naming a co-resident relative as the recovery monitor and supervisor of supervised disulfiram (IPS_CPG 2014). A culturally competent formulation also captures the patient's explanatory model and idiom of distress in the social row; the wider transcultural frame of the cultural concepts of distress is developed in the Consultation-liaison, geriatric and transcultural psychiatry notes.

18.3 The 4-Ps grid: the horizontal axis

Four factor-classes, set on a time axis. The **four Ps** are the horizontal axis of the formulation, sorting every factor not by its domain but by the *role* it plays in the illness across time. There are four, and the exam expects all four by name. A predisposing factor is a long-standing background vulnerability that set the stage (the "why this person"). A precipitating factor is the recent trigger that brought the problem on now (the "why now"). A perpetuating factor is what maintains the problem and blocks recovery once it has begun. A protective factor is a strength or resource that buffers the person and improves the prognosis. Setting the vertical biopsychosocial axis against this horizontal four-Ps axis produces the grid the accompanying figure draws: three rows by four columns, twelve cells, each prompting a specific question and together making the standard template for a written or spoken formulation.

Predisposing

Long-standing vulnerabilities that set the stage, from before the illness (genes, early adversity, temperament, chronic disadvantage). The "why this person".

Precipitating

Recent triggers that brought the problem on at this point (an acute stressor, a loss, a physical illness, a substance). The "why now".

Perpetuating

Factors that maintain the problem and impede recovery (ongoing substance use, avoidance, rumination, unemployment, conflict, non-adherence). The treatment target.

Protective

Strengths and resources that mitigate the illness and aid recovery (insight, social support, engagement with care, employment, faith and community). The prognosis and the plan's allies.

DOMAIN	PREDISPOSING	PRECIPITATING	PERPETUATING	PROTECTIVE
Biological	Family history, genetic loading, obstetric or developmental insult, chronic physical illness	Substance intoxication or withdrawal, an acute illness, a medication change	**Continued substance use, poor physical health, medication non-adherence**	Good physical health, no substance dependence, prior treatment response
Psychological	Insecure attachment, early trauma, maladaptive schemas, personality traits, low self-esteem	A recent loss, a perceived failure or narcissistic injury	**Cognitive distortions, avoidance, rumination, hopelessness**	Psychological-mindedness, insight, adaptive coping, motivation to change
Social	Childhood adversity, poverty, disrupted or chaotic family	Bereavement, job loss, relationship breakdown, migration	**Unemployment, marital conflict, high expressed emotion, isolation, stigma**	Supportive family, stable work and housing, a community or faith network

The biopsychosocial 4-Ps grid: the three Engel domains (rows) crossed with the four Ps (columns) give twelve cells, each with a prompting question. The perpetuating column (shaded) is what treatment attacks; the protective column carries the prognosis.

MNEMONIC

PREDISPOSING · PRECIPITATING · PERPETUATING · PROTECTIVE

The four Ps, in time order: what made the person **vulnerable** (predisposing), what **triggered** it now (precipitating), what **keeps** it going (perpetuating), and what **helps** (protective). Some schemes add a fifth P for the presenting **Problem** itself; the core examinable set is four.

TRAP **Confusing predisposing with precipitating, and forgetting protective.** A long-standing trait belongs under predisposing; the recent event that tipped the patient over belongs under precipitating. Filing a recent job loss as "predisposing" is the classic slip. The equally common error is omitting the protective column altogether, which is where prognosis and the patient's own resources live.

3	4	12	1977
BIOPSYCHOSOCIAL DOMAINS (ENGEL: BIO, PSYCHO, SOCIAL)	PS OF THE FORMULATION (PREDISPOSING, PRECIPITATING, PERPETUATING, PROTECTIVE)	CELLS IN THE GRID (THREE DOMAINS BY FOUR PS)	ENGEL'S BIOPSYCHOSOCIAL PAPER (SCIENCE)

18.4 The aetiological and the longitudinal formulations

Two further lenses that overlay the grid. The grid is the workhorse, but two related formats are worth naming. The aetiological formulation is essentially the predisposing, precipitating and perpetuating columns read as a causal chain of vulnerability, trigger and maintenance; the classical teaching (Shorter Oxford; Companion to Psychiatric Studies) is that the perpetuating causes are the usual target for treatment of the established illness, while the predisposing and precipitating causes are the ones relevant to prevention. The longitudinal formulation (also called

the developmental formulation) tells the story chronologically instead of by category: it traces the patient's life epoch by epoch, showing how temperament, attachment, early adversity, later stresses and current supports accumulated into the present presentation. In an Indian long case the developmental history feeding this longitudinal account is a graded skill in its own right; the descriptive-psychopathology vocabulary and the deeper psychometric theory that the interview and mental state examination draw on are developed in the Psychometry, Assessment and Descriptive Psychopathology notes. Both formats are just re-cuts of the same biopsychosocial and four-Ps material, not new content to memorise.

18.5 From formulation to the management plan

The plan mirrors the grid. The formulation is not an academic flourish; it directly generates the management plan, and it does so along the same two axes. Reading down the biopsychosocial rows gives a plan that is itself biological, psychological and social (for example medication, a specific psychotherapy, and a social or family intervention), which is why a good management answer is structured biopsychosocially. Reading across the four Ps tells you what each part of the plan is *for*: treatment concentrates on the **perpetuating** factors, because those are what is keeping the patient unwell and are the most modifiable now; the **protective** factors are deliberately mobilised and strengthened (engaging a supportive spouse, building on the patient's motivation); and the predisposing and precipitating factors, largely historical, inform prevention and relapse-planning rather than the acute plan. Where the presentation carries risk, the same four Ps are applied to the risk itself (predisposing, precipitating, perpetuating and protective factors for suicide), a formulation-driven approach developed with the suicide risk assessment and the C-SSRS as used inside the MSE in the Somatic-symptom, sexual, impulse-control disorders and suicide notes.

WORKED EXAMPLE

A middle-aged man presents with a depressive episode (the diagnosis). The **formulation**: *predisposing*, a family history of depression and perfectionistic, self-critical traits; *precipitating*, a recent enforced redundancy; *perpetuating*, social withdrawal, rising alcohol use and escalating marital conflict; *protective*, a supportive wife, no established alcohol dependence, and that he sought help himself. The plan follows directly: an antidepressant and a review of alcohol use (biological), cognitive behaviour therapy targeting the self-critical cognitions and withdrawal (psychological), and couple work plus support with re-employment (social), aimed squarely at the perpetuating column while mobilising the protective factors already present.

GOOD TO REMEMBER

- **The principle:** a formulation is the individualised, idiographic account of why this person has this problem now, built by crossing Engel's three biopsychosocial domains with the four Ps; it partners the diagnosis rather than replacing it, and it is a revisable hypothesis.
- **The one discriminator:** predisposing = long-standing vulnerability ("why this person"); precipitating = the recent trigger ("why now"); perpetuating = what maintains it (the treatment target); protective = strengths and resources (the prognosis and the plan's allies).
- **The one exam fact:** perpetuating factors are the usual target of treatment while predisposing and precipitating factors inform prevention (Shorter Oxford; Companion), and the model itself is Engel's 1977 biopsychosocial approach.

HOLD THIS

A diagnosis names the category; the formulation crosses Engel's three domains (biological, psychological, social) with the four Ps (predisposing, precipitating, perpetuating, protective) to explain why this person is ill now, and the management plan then attacks the perpetuating column and mobilises the protective column.

19 · The rating scales

A clinical interview *describes* a patient; a **rating scale** *quantifies* what the interview finds, converting a symptom picture into a number that can be tracked, compared against a threshold, and read against an evidence base. The rating scales are therefore not a substitute for the mental state examination but its metric complement: the examination tells you a patient is depressed, the scale tells you how depressed, and whether the treatment has moved the needle. On the paper this is a compact, high-yield topic that rewards precise recall, because almost every question is of one shape, name the scale for a construct, state who rates it, say how it is built, and give its verified cut-off, and a single wrong number loses the mark.

How to use this page. Fix two cross-cutting distinctions first, since they organise the whole field: whether an instrument is **clinician-rated** or **self-report**, and whether its job is screening, diagnosis or severity and outcome measurement. Then work through the catalogue family by family, the mood scales, the psychosis scales, the anxiety and OCD scales, the cognitive instruments, and the global-functioning and outcome instruments, learning for each what it measures, how it is structured, and its verified band or threshold expressed *out of a possible* maximum. Finally learn the selection step, how to **pick the right scale** for the construct and the setting. The instrument forms themselves are not reproduced here; each is gathered in the accompanying catalogue and the scales appendix at the back, and the deeper machinery of reliability, validity, sensitivity and specificity, standardisation and norms that decides whether any of these numbers can be trusted is developed under reliability and validity above and, in full, in the Psychometry, Assessment and Descriptive Psychopathology notes.

19.1 The two distinctions that sort every scale: who rates it, and what it is for

Classify a scale before you use it, along two axes. The first axis is the *rater*. A clinician-rated (observer-rated) instrument is scored by a trained interviewer who applies clinical judgement to anchored descriptions, so it captures signs the patient may not report and resists exaggeration, at

the cost of time and the need for training and inter-rater reliability; the Hamilton scales, the PANSS, the YMRS and the Y-BOCS are of this kind. A self-report (patient-rated) instrument is completed by the patient, is quick and cheap, needs no trained rater and gives the patient's own perspective, but depends on literacy, insight and candour and is vulnerable to over- or under-reporting; the GAD-7, the PHQ-9 and the Beck inventories are of this kind. The second axis is the *purpose*. A **screening** scale is a brief, high-sensitivity net cast over an unselected population to flag possible cases for further assessment; a **diagnostic** instrument (typically a structured interview such as the SCID or MINI) operationalises criteria to confirm or exclude a disorder; and a **severity and outcome** scale, the largest group here, assumes the diagnosis is already made and measures how ill the patient is and how that changes with treatment. The commonest error on the paper is to blur these purposes, so hold them apart from the outset.

AXIS	TYPE	WHAT IT MEANS, AND THE EXEMPLARS
Rater	Clinician-rated	**Scored by a trained interviewer against anchors; captures signs, resists faking; needs training and inter-rater reliability (HAM-D, MADRS, YMRS, PANSS, BPRS, HAM-A, Y-BOCS)**
	Self-report	**Completed by the patient; fast, cheap, gives the patient's view; limited by literacy, insight and candour (GAD-7, PHQ-9, BDI, GDS)**
Purpose	Screening	Brief, high-sensitivity case-finding in an unselected population; a positive screen triggers fuller assessment (GAD-7, AUDIT, EPDS)
	Diagnostic	A structured interview operationalising criteria to confirm or exclude a disorder (SCID, MINI)
	Severity / outcome	**Assumes the diagnosis; grades severity and tracks change with treatment (HAM-D, MADRS, YMRS, PANSS, Y-BOCS)**

Every instrument in the catalogue sits at the crossing of a rater axis (clinician-rated versus self-report) and a purpose axis (screening, diagnostic, or severity and outcome). Naming both for a given scale is half the answer.

RULE **Rater and purpose first, number second.** Before quoting a cut-off, state whether the scale is clinician-rated or self-report and whether it screens, diagnoses or measures severity; a severity scale grades an established diagnosis, it does not make one.

19.2 The mood scales: HAM-D, MADRS and YMRS

Three severity scales carry the mood chapter: two for depression, one for mania, all clinician-rated. The Hamilton Depression Rating Scale (HAM-D, HDRS; Hamilton, 1960) is the oldest and most-used depression scale in trials. The original had 21 items, but Hamilton advised counting only the first 17, so the **17**-item version is standard, each item scored either 0 to 4 or 0 to 2, giving a total out of a possible 52. Scores at or below 7 mark remission; a widely used severity scheme reads 8 to 13 as mild, 14 to 18 as moderate, 19 to 22 as severe and 23 and above as very severe, and a response is conventionally a fall of at least half from baseline. Its known weakness is a heavy loading of somatic and insomnia items, which can flatter sedating drugs. The Montgomery Asberg Depression Rating Scale (MADRS; Montgomery and Asberg, 1979) answers that weakness: a leaner 10-item clinician-rated scale, each item scored 0 to 6, giving a total out of a possible 60, weighted toward psychological rather than somatic symptoms and expressly built to be sensitive to change, which is why it is favoured as a primary antidepressant-trial outcome. Here a score at or below 10 indicates remission and a score above 30 to 35 indicates severe depression. For the manic pole the Young Mania Rating Scale (YMRS; Young and colleagues, 1978) is the gold standard: 11 clinician-rated items, seven scored 0 to 4 and four core items (irritability, speech, thought content, and disruptive or aggressive behaviour) double-weighted 0 to 8, giving a total out of a possible 60, with remission usually set at 12 or below. Because a few items can score modestly in euthymia, a "normal" YMRS is not necessarily zero. All three, together with the HAM-D, MADRS and YMRS as applied at the bedside, belong with the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes.

HAM-D (HDRS)

Clinician-rated depression severity; 17-item standard form, out of a possible 52; remission at or below 7; somatic-item heavy.

MADRS

Clinician-rated, 10 items each 0 to 6, out of a possible 60; psychologically weighted and change-sensitive; remission at or below 10.

YMRS

Clinician-rated mania scale; 11 items, four double-weighted, out of a possible 60; gold standard for manic severity; remission at or below 12.

> **PEARL**
>
> When an examiner asks why the MADRS, not the HAM-D, is the modern antidepressant-trial workhorse, the answer is its psychological weighting and superior sensitivity to change: three of the seventeen HAM-D items are sleep items, so a sedating drug can lower the HAM-D without truly lifting mood, a bias the MADRS largely escapes.

19.3 The psychosis scales: PANSS and BPRS

Two clinician-rated interviews grade psychotic symptom severity, one the modern standard, one its parent. The Positive and Negative Syndrome Scale (PANSS; Kay, Fiszbein and Opler, late 1980s) is the gold-standard outcome measure in schizophrenia trials. It has 30 items across three subscales, seven for positive symptoms (delusions, hallucinations), seven for negative symptoms

(blunted affect, withdrawal, avolition), and 16 for general psychopathology, and each item is rated on a seven-point anchored scale running from 1 (absent) to 7 (extreme). A subtle but examinable point follows: because the floor of every one of the 30 items is 1, not 0, the total runs from a floor at 30 up to a ceiling out of a possible 210, so the lowest possible PANSS is 30 rather than zero, and there is no single official diagnostic cut-off, the scale being read as change and by subscale. It is semi-structured, needs specific rater training, and takes roughly half an hour to forty minutes. The Brief Psychiatric Rating Scale (BPRS; Overall and Gorham, 1962) is the older, shorter parent from which the PANSS grew: 18 items covering both psychotic and non-psychotic symptoms, each rated on a seven-point scale, giving a total out of a possible 126. Its strength is brevity; its weakness is limited coverage of negative symptoms, the very gap the PANSS was designed to close. The PANSS and BPRS in clinical use are developed with the Schizophrenia: clinical features and phenomenology notes.

TRAP **Quoting the PANSS minimum as zero.** Every item is anchored at 1 for "absent", so a fully asymptomatic patient still scores 30. The PANSS runs from 30 to a possible 210, and a "50 percent reduction" in a trial is measured from that floor, not from zero.

19.4 The anxiety and OCD scales: HAM-A, GAD-7 and Y-BOCS

One clinician-rated anxiety scale, one self-report screen, and the OCD gold standard. The Hamilton Anxiety Rating Scale (HAM-A; Hamilton, 1959) is the clinician-rated severity and outcome measure for generalised anxiety: 14 items, each scored 0 to 4, giving a total out of a possible 56, split across psychic and somatic anxiety clusters. A total in the high teens (a threshold near 17 to 18) marks clinically significant anxiety, and a common scheme reads up to 17 as mild, 18 to 24 as mild to moderate and 25 to 30 as moderate to severe. The GAD-7 (Spitzer and colleagues, 2006) is its self-report counterpart, and the standard primary-care screen for anxiety: seven items, each scored 0 to 3, giving a total out of a possible 21, with 5, 10 and 15 marking mild, moderate and severe, and a score at or above 10 the usual threshold to prompt fuller assessment. For obsessive-compulsive disorder the Yale-Brown Obsessive Compulsive Scale (Y-BOCS; Goodman and colleagues, 1989) is the undisputed gold standard: a 10-item semi-structured scale (five items for obsessions, five for compulsions) rating time, interference, distress, resistance and control, each 0 to 4, giving a total out of a possible 40 that is independent of symptom content. Its bands are worth memorising, 0 to 7 subclinical, 8 to 15 mild, 16 to 23 moderate, 24 to 31 severe and 32 to 40 extreme, and a score at or above 16 is the threshold that marks clinically symptomatic OCD in treatment trials. The Y-BOCS as used to track exposure and response prevention belongs with the Anxiety, OCD and trauma-related disorders notes.

HAM-A

Clinician-rated anxiety severity; 14 items each 0 to 4, out of a possible 56; threshold for significance in the high teens.

GAD-7

Self-report anxiety screen; 7 items each 0 to 3, out of a possible 21; screen-positive at or above 10 (bands at 5, 10, 15).

Y-BOCS

Semi-structured OCD gold standard; 10 items each 0 to 4, out of a possible 40; clinically symptomatic at or above 16.

19.5 The cognitive instruments: MMSE and MoCA

Two brief cognitive screens, both scored out of a possible 30, differing in what they catch. The Mini-Mental State Examination (MMSE; Folstein, Folstein and McHugh, 1975) is the classic bedside cognitive screen: an 11-question instrument sampling five domains, orientation, registration, attention and calculation, recall, and language, scored out of a possible 30 and taking five to ten minutes. A score at or below 23 is the conventional threshold indicating cognitive impairment. Its limitations are examinable: it is insensitive to frontal-executive and subcortical deficits, shows a ceiling effect in the well-educated, and is confounded by low literacy and language, so a normal MMSE does not exclude early or executive impairment. The Montreal Cognitive Assessment (MoCA; Nasreddine and colleagues, 2005) was built precisely to catch what the MMSE misses, mild cognitive impairment in people who score in the normal range on the MMSE. It also runs out of a possible 30, adds executive, visuospatial and abstraction tasks, and takes about ten minutes; the authors' recommended clinical cutoff is 26, meaning a score at or above 26 is read as normal and below 26 as impaired, with one point added for twelve or fewer years of education. As these are permission-required instruments, their domains and scoring are set out on the accompanying scale plate rather than reproduced here.

TRAP **Treating a normal MMSE as a normal cognition.** The MMSE ceilings in educated patients and barely samples executive function; a patient with early frontal or subcortical impairment can score above 23 and still be impaired. Reach for the MoCA (cutoff 26) when mild or executive impairment is the question.

30	23	26	16
MMSE AND MOCA MAXIMUM (EACH SCORED OUT OF A POSSIBLE 30)	MMSE AT OR BELOW THIS INDICATES COGNITIVE IMPAIRMENT	MOCA RECOMMENDED CUTOFF (AT OR ABOVE 26 IS NORMAL)	Y-BOCS AT OR ABOVE THIS MARKS CLINICALLY SYMPTOMATIC OCD

INDIA

Imported cognitive screens travel badly across India's languages and literacy levels, so the field re-standardises rather than borrows. The Hindi Mental State Examination (HMSE) is the vernacular adaptation of the MMSE for low-literacy Indian populations, and the NIMHANS Neuropsychology Battery is the indigenous instrument set for deeper testing (verbal fluency, working memory, set-shifting), alongside the PGI and AIIMS batteries. For disability itself India has its own device: the Indian Disability Evaluation and Assessment Scale (IDEAS), developed by the Indian Psychiatric Society's Rehabilitation Committee in 2002, scores four domains (self-care, interpersonal activities, communication and understanding, and work) each 0 to 4 and, with duration of illness, yields the global disability score used for statutory certification of mental illness. The principle that a cut-off is only valid in the population its norms were drawn from is developed in the Psychometry, Assessment and Descriptive Psychopathology notes, and the statutory disability frame in the Mental health legislation and forensic psychiatry notes.

19.6 The global-functioning and outcome instruments, and the substance, somatic and suicide pointer

Beyond symptoms, three instruments grade global functioning and change. The Global Assessment of Functioning (GAF) is a single clinician-rated number from 1 to a possible 100, higher meaning better psychological, social and occupational functioning; it was the old DSM Axis V. DSM-5 retired it as too unreliable and confounded by symptoms, replacing it with the WHODAS 2.0 (the World Health Organization Disability Assessment Schedule, second edition), a 36-item instrument covering six domains, cognition, mobility, self-care, getting along with people, life activities and participation, available in self, proxy and interviewer forms and validated in Hindi. The Clinical Global Impression (CGI; ECDEU, 1976) is the pragmatic trial workhorse: a clinician's global rating with a severity limb (CGI-S) and an improvement limb (CGI-I), each on a simple one-to-seven scale, valued precisely because a single expert judgement often tracks change as well as a long scale. Beyond these, the catalogue extends into families pointed to elsewhere: for substances, the self-report AUDIT (out of a possible 40, screen-positive at or above 8) and CAGE belong with the Substance use disorders notes; the C-SSRS (the Columbia Suicide Severity Rating Scale) for suicide-risk stratification, and the self-report PHQ-9 for depression in primary care, belong with the suicide risk assessment and the C-SSRS as used inside the MSE in the Somatic-symptom, sexual, impulse-control disorders and suicide notes.

19.7 The scale catalogue and how to pick the right scale (Step 5b)

Selection is a construct-to-instrument match, not a reflex. The final assessment step, choosing an instrument, follows a fixed logic that the accompanying catalogue is built to serve. First name the *construct* (which symptom dimension, and which disorder). Second name the *purpose* (to screen, to diagnose, or to grade severity and track outcome). Third fix the *setting and rater* (a busy clinic favours a brief self-report; a trial or a medicolegal assessment demands a trained clinician-rated interview). Fourth match the *population and language* (a validated, locally normed translation, never a raw import). Run those four filters and the instrument is usually determined: to track a depressive episode in a trial, the MADRS; to grade mania, the YMRS; to measure schizophrenia outcome, the PANSS; to follow OCD, the Y-BOCS; to screen anxiety in primary care, the GAD-7; to screen cognition, the MMSE, or the MoCA when mild impairment is the question. This is the discipline of **scale selection**, and being able to **pick the right scale** for the construct and setting is exactly what the arc's Step 5b examines. The consolidated **scale catalogue** below is the reference for that choice; the instrument forms themselves are reproduced in the scales appendix.

SCALE	CONSTRUCT (DISORDER)	RATER	STRUCTURE AND TOTAL (OUT OF A POSSIBLE N)	VERIFIED CUT-OFF OR BAND
HAM-D	Depression severity (mood)	Clinician-rated	17 items; 52	**Remission at or below 7; mild 8–13, moderate 14–18, severe 19–22, very severe 23+**

SCALE	CONSTRUCT (DISORDER)	RATER	STRUCTURE AND TOTAL (OUT OF A POSSIBLE N)	VERIFIED CUT-OFF OR BAND
MADRS	Depression severity, change-sensitive (mood)	Clinician-rated	10 items each 0–6; 60	**Remission at or below 10; severe above 30–35**
YMRS	Mania severity (mood)	Clinician-rated	11 items, 4 double-weighted; 60	**Remission at or below 12; gold standard for mania**
PANSS	Schizophrenia symptom severity	Clinician-rated	30 items each 1–7 (7+7+16); 210	**Floor 30 (not 0); read by change and subscale, no fixed cut**
BPRS	Psychotic and non-psychotic symptoms	Clinician-rated	18 items each rated 1–7; 126	The older, briefer parent of the PANSS
HAM-A	Anxiety severity (GAD)	Clinician-rated	14 items each 0–4; 56	**Significant in the high teens (near 17–18)**
GAD-7	Anxiety screen	Self-report	7 items each 0–3; 21	**Screen-positive at or above 10 (bands 5, 10, 15)**
Y-BOCS	OCD severity	Either (semi-structured)	10 items each 0–4; 40	**Symptomatic at or above 16; 8–15 mild, 16–23 moderate, 24–31 severe, 32–40 extreme**
MMSE	Global cognition screen	Clinician-rated	11 questions, 5 domains; 30	**Impairment at or below 23**
MoCA	Mild cognitive impairment screen	Clinician-rated	Multi-domain; 30	**Normal at or above 26; +1 point if 12 or fewer years' education**
GAF	Global functioning	Clinician-rated	Single rating; 100	Higher is better; the retired DSM Axis V
WHODAS 2.0	Disability and functioning	Self / proxy / interviewer	36 items, 6 domains	DSM-5 replacement for the GAF; Hindi validated
CGI	Global severity and change	Clinician-rated	CGI-S and CGI-I limbs, 1–7 each	Pragmatic trial workhorse
AUDIT	Alcohol-use screen (substance)	Self-report	10 items; 40	**Screen-positive at or above 8**

SCALE	CONSTRUCT (DISORDER)	RATER	STRUCTURE AND TOTAL (OUT OF A POSSIBLE N)	VERIFIED CUT-OFF OR BAND
C-SSRS	Suicide risk (somatic / suicide)	Clinician-rated	Ideation and behaviour subscales	Stratifies severity of ideation and behaviour
PHQ-9	Depression screen (primary care)	Self-report	9 items each 0–3; 27	**Bands at 5, 10, 15, 20; item 9 screens suicidality**

The rating-scale catalogue: for each instrument, its construct, rater, structure, and verified threshold. Every total is stated out of its possible maximum; the mood, psychosis, anxiety and OCD rows cross-reference their disorder chapters.

RULE **Match the construct, the purpose, the setting and the rater.** The right scale is the one whose construct fits the symptom, whose purpose fits the task (screen, diagnose, or track), and whose format fits the clinic and the patient's language; a validated local translation always beats a raw import.

WORKED EXAMPLE

A man with schizophrenia and low mood is entering a clinic trial of an adjunctive antidepressant. Selection runs the four filters. The primary construct is psychotic symptom severity in a trial by a trained rater, so the PANSS. The secondary construct is comorbid depression, needing a scale that does not double-count psychotic items, so a self-report such as the PHQ-9 or BDI rather than the somatic-heavy HAM-D. Global change for the sponsor is captured cheaply by the CGI-I, and cognition, if adjunctive effects are a concern, by the MoCA rather than the MMSE. Four instruments, each chosen because its construct, purpose, rater and format fit, not because it is familiar.

GOOD TO REMEMBER

- **The principle:** a rating scale quantifies a construct an interview has already identified, and every one is defined by four facts, its rater (clinician-rated or self-report), its purpose (screening, diagnostic, or severity and outcome), its structure, and its verified threshold stated out of a possible maximum.
- **The one discriminator:** mood is HAM-D and MADRS for depression (MADRS the change-sensitive, less somatic one) and the YMRS for mania (all out of a possible 60 except the HAM-D's 52); psychosis is the PANSS (floor 30, up to a possible 210) and its parent the BPRS; anxiety and OCD are the HAM-A, the self-report GAD-7 and the Y-BOCS; cognition is the MMSE (impairment at or below 23) and the MoCA (normal at or above 26), both out of a possible 30.
- **The one exam fact:** the two cognitive cut-offs are the crunch, MMSE 23 or below indicates impairment and the MoCA cutoff is 26, both scored out of a possible 30, and the MoCA exists to catch the mild and executive impairment the MMSE ceilings past.

HOLD THIS

Classify every scale by rater (clinician-rated versus self-report) and purpose (screen, diagnose, or track severity) before quoting its number, and memorise the crunch cut-offs out of their possible maxima: HAM-D remission at or below 7 (out of a possible 52), MADRS remission at or below 10 and YMRS at or below 12 (each out of a possible 60), PANSS floored at 30 (up to a possible 210), Y-BOCS symptomatic at or above 16 (out of a possible 40), and the cognitive pair, MMSE impaired at or below 23 and MoCA normal at or above 26 (each out of a possible 30).

20 · Reliability and validity

Every rating scale in this chapter, and every scale reproduced in the consolidated appendix, is only as trustworthy as its **psychometric properties**, and the two that decide whether a score means anything are reliability and validity. The examiner tests this in the plainest possible form: reliability is **consistency**, validity is **accuracy**, and the candidate who can hold those two ideas apart, and state how each is measured, has the marks. This page teaches the properties as they bear on the practical question a clinician actually faces, which is whether to believe a number a scale has produced, and whether to reach for that scale in the first place.

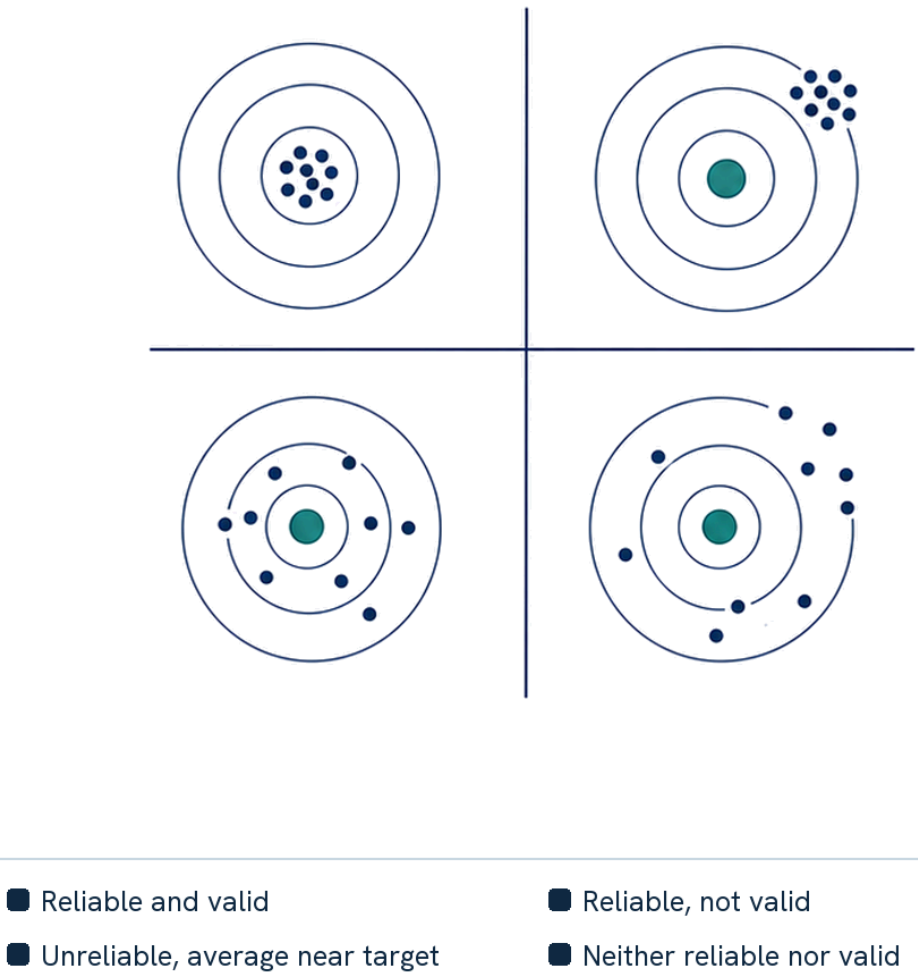


Fig 19.14 Reliability is consistency and validity is accuracy. Measurements may be both reliable and valid, reliably biased, scattered around the target on average, or neither consistent nor accurate.

How to use this page. Fix the headline distinction first, because it is the single commonest confusion on the paper: a scale can be perfectly *reliable* and still be *invalid*, but it can never be valid without first being reliable. Then learn the forms each property takes, since the exam rewards the specific names, the four kinds of consistency and the families of accuracy, not a vague gesture at "the scale is good". Finally see how these ideas become **sensitivity and specificity** and the predictive values when the instrument is a screening test, and how a raw score means nothing until **standardisation** and norms give it a reference point. The deep theory underneath all of this, the mathematics of factor analysis, the mechanics of test construction and item analysis, and standardisation in full, is developed in the Psychometry, Assessment and Descriptive Psychopathology notes; here the treatment is kept to what governs choosing and reading a clinical scale.

20.1 The two questions a scale must answer: consistency and accuracy

Reliability asks "is it consistent?"; validity asks "is it measuring the right thing?". Reliability is the reproducibility of a score: the degree to which the same instrument gives the same answer on

the same unchanged subject, across occasions, across raters, or across the items within it. It is quantified as a correlation coefficient running from 0.00, meaning no reliability at all, to 1.00, meaning perfect reproducibility, and it is a property not of the test in the abstract but of the test scores as produced in a particular sample. Validity is a different and higher demand: the degree to which the score actually corresponds to the construct, the diagnosis or the trait it was built to measure, that is, its accuracy. Reliability is a necessary but not a sufficient quality of a useful scale; a scale must be consistent before it can be believed, but consistency alone never guarantees that what it consistently measures is what you wanted. The classic image, drawn in the accompanying figure, is the marksman: reliability is a tight grouping of shots, validity is a grouping centred on the bullseye, and a tight cluster in the wrong corner is the very picture of a reliable but invalid instrument.

RULE **Reliability is consistency; validity is accuracy.** Reliability asks whether the scale gives the same answer twice; validity asks whether that answer is the truth. Get the two words the right way round and most of this topic is already won.

20.2 The forms of reliability: four ways to test consistency

Consistency is checked across time, across raters, and across items. There are four standard estimates, and the exam expects them by name and by what source of error each one probes. Test-retest reliability administers the same scale to the same people on two separate occasions and correlates the two sets of scores; the resulting coefficient of stability captures consistency across time, and the interval matters, a fortnight being appropriate for a fluctuating state such as depression but a longer gap for a stable trait such as a personality dimension. Inter-rater reliability asks whether two or more clinicians scoring the same patient arrive at the same rating, and is the critical property for any clinician-administered instrument; it is reported as a Kappa coefficient for categorical judgements or an intra-class correlation for continuous scores, with Kappa above **0.70** counted as excellent agreement. Internal consistency asks whether the items of a scale hang together and measure a single underlying dimension, and is expressed as Cronbach's alpha (coefficient alpha), which is mathematically the average of every possible split-half of the test; a clinically usable scale should reach an alpha of **0.80** or higher, nearer 0.90 in practice. The split-half method is the older single-administration version of the same idea: the items are divided, usually odd against even, the two halves correlated, and the value corrected upward for the full test length by the Spearman-Brown formula.

Test-retest reliability

Same scale, same people, two occasions, correlated. The coefficient of stability, capturing consistency over time. Its error source is time sampling.

Inter-rater reliability

Agreement between two or more raters scoring the same subject. Kappa (categorical) or intra-class correlation (continuous). The key property of a clinician-rated scale.

Internal consistency

The degree to which items measure one dimension, indexed by Cronbach's alpha, the mean of all possible split-halves. Its error source is content sampling.

Split-half

A single-administration internal-consistency estimate: correlate one half of the items (odd against even) with the other, then correct with the Spearman-Brown formula.

ESTIMATE	WHAT CONSISTENCY IT CHECKS	STATISTIC AND BENCHMARK
Test-retest	Stability of the score across time (same test, two occasions)	**Correlation (coefficient of stability); interval must suit state versus trait**
Inter-rater	Agreement between different raters scoring one subject	**Kappa or intra-class correlation; Kappa above 0.70 is excellent**
Internal consistency	Whether items cohere as one dimension	**Cronbach's alpha; 0.80 or higher for clinical use**
Split-half	Coherence, from a single sitting (halves compared)	**Half-test correlation, Spearman-Brown corrected**

The four standard reliability estimates: test-retest checks consistency across time, inter-rater across observers, and internal consistency and split-half across the items themselves.

20.3 The forms of validity: from surface appearance to the underlying construct

Validity is a ladder from what a test looks like to what it truly measures. The families run from the weakest to the strongest form of evidence. Face validity is the most superficial: whether the scale simply looks, to the person taking it, as though it measures what it claims. It is not a technical property at all but a matter of acceptability, and its real value is that a test which looks relevant keeps the patient engaged and cooperative. Content validity is the first substantive form: whether the items are a representative sample of the whole behavioural domain being measured, so that an anxiety scale with no item on worry has a content gap; it is judged by expert consensus rather than by statistics. Criterion validity correlates the scale against an external, independent gold-standard measure of the same thing, and comes in two time-framed subtypes. Concurrent validity takes the criterion at the same moment (validating a new brief scale against an established one administered together), while predictive validity takes the criterion in the future (whether today's score forecasts a later outcome, such as response to treatment). Construct validity is the most comprehensive: whether the scale genuinely captures the abstract, unobservable construct, the "depression" or "hopelessness" itself. It is built from two complementary strands, convergent evidence, that the scale correlates with other measures of the same construct, and discriminant validity (divergent validity), that it does *not* correlate with measures of unrelated constructs. Campbell and Fiske's 1959 multitrait-multimethod matrix was designed to demonstrate both at once, and Cronbach and Meehl (1955) argued that construct validity ultimately subsumes the others.

Face validity

Whether the test superficially appears to measure what it claims. A matter of acceptability and rapport, not a technical index.

Content validity

Whether the items representatively sample the full behavioural domain. Judged by expert consensus; non-statistical.

Criterion validity

Correlation of the scale with an external gold-standard criterion of the same variable.

Concurrent validity

Criterion measured at the same time as the test (a new scale validated against an established one).

Predictive validity

Criterion measured later; whether the score forecasts a future outcome.

Construct validity

Whether the scale captures the abstract trait it targets, evidenced by convergent and discriminant findings.

FAMILY	THE QUESTION IT ANSWERS	HOW IT IS ESTABLISHED
Face	Does it look like it measures the right thing?	**Subjective appearance to the test-taker; secures coopera-tion, not proof**
Content	Do the items cover the whole domain?	**Expert consensus that the items sample the construct fully**
Concurrent	Does it agree with a present gold standard?	**Correlate with an established criterion measured at the same time**
Predictive	Does it forecast a future outcome?	**Correlate today's score with a criterion obtained later**
Convergent	Does it track other measures of the same construct?	**High correlation with scales of the same trait**
Discriminant	Does it stay clear of unrelated constructs?	**Low correlation with scales of different traits (Campbell and Fiske, 1959)**

The families of validity, from the surface (face) inward to the construct. Concurrent and predictive are the two subtypes of criterion validity; convergent and discriminant are the two strands of construct validity.

20.4 The cardinal relationship: reliable without valid, never valid without reliable

Reliability is necessary but not sufficient for validity. This is the single most examined line on the topic, and it works in one direction only. A scale can be entirely reliable and yet invalid: if it consistently measures the wrong thing, it will give reproducible, stable, internally coherent scores that simply do not correspond to the intended construct. The bathroom scale that reads three kilograms heavy on every single weighing is perfectly reliable and perfectly wrong; a "depression" questionnaire whose items in fact tap anxiety will show a handsome alpha and good test-retest stability while failing to measure depression at all. The converse, however, is impossible. A scale whose scores scatter unpredictably from one occasion to the next, or on which raters cannot agree, cannot line up with any true criterion, because its own noise swamps any signal;

unreliability sets a ceiling on validity. So reliability is the gatekeeper: it must be present for validity to be even attainable, but its presence never certifies validity on its own.

WORKED EXAMPLE

A team builds a brief "burnout" scale from items that, on inspection, mostly ask about low mood and poor sleep. On piloting it performs beautifully on every reliability index: Cronbach's alpha is 0.91, and the two-week test-retest correlation is 0.86. Reassured, they deploy it, and it flags half the workforce as burned out. The scores are consistent, but they are consistently measuring depression, not burnout: high reliability, poor construct validity. The consistency was real and told them nothing about whether the right thing was being measured. Only a validity study, correlating the scale against an accepted burnout criterion and showing it diverges from a depression measure, would have caught the error.

TRAP **Reading high reliability as proof the scale works.** A stellar alpha and a strong test-retest coefficient show only that the instrument is consistent, not that it measures the intended construct. A reliable scale can be reliably wrong; never let reproducibility stand in for accuracy.

20.5 Sensitivity and specificity and the predictive values of a screening scale

When the scale is a screen, validity is expressed as diagnostic accuracy. A screening instrument is judged against a diagnostic gold standard, and its accuracy is carried by two numbers. Sensitivity is the proportion of people who truly have the condition that the test correctly flags positive, its true-positive rate; a sensitive test misses few genuine cases, that is, it produces few false negatives. Specificity is the proportion of people who truly do not have the condition that the test correctly clears, its true-negative rate; a specific test raises few false alarms, that is, few false positives. Crucially, sensitivity and specificity are intrinsic properties of the test and do not change with how common the disorder is. The predictive values do change. The positive predictive value is the proportion of those who screen positive who genuinely have the condition, and the negative predictive value the proportion of those who screen negative who genuinely do not; both depend heavily on the base rate, so that even an accurate test, applied where the disorder is rare, throws up many false positives and a disappointing positive predictive value. This is why a screen is deliberately tuned for high sensitivity, to catch every possible case and accept some false positives, leaving a later confirmatory assessment to weed them out.

INDEX	WHAT IT MEASURES	CLINICAL READING
Sensitivity	Of those with the disorder, the share the test flags positive	**High sensitivity means few false negatives; good for ruling out**
Specificity	Of those without the disorder, the share the test clears negative	**High specificity means few false positives; good for ruling in**
Positive predictive value	Of those who screen positive, the share who truly have it	**Falls as the disorder gets rarer (base-rate dependent)**
Negative predictive value	Of those who screen negative, the share who truly lack it	**Rises as the disorder gets rarer (base-rate dependent)**

Sensitivity and specificity are fixed properties of the test; the predictive values shift with prevalence. A screen favours sensitivity so as to miss no case, at the cost of false positives.

MNEMONIC

SnNout · SpPin

SnNout: a highly **Sen**sitive test, when **N**egative, rules the diagnosis **out** (few false negatives, so a negative result is trustworthy). **SpPin**: a highly **Sp**ecific test, when **P**ositive, rules the diagnosis **in** (few false positives, so a positive result is trustworthy). Screening leans on SnNout; confirmation leans on SpPin.

20.6 Standardisation and norms: giving a raw score its meaning

A raw score is meaningless until it is referenced. **Standardisation** has two limbs. The first is procedural: administering and scoring the instrument under fixed, uniform conditions for every test-taker, so that a score reflects the person and not the circumstances of testing. The second is the normative reference: establishing, from a large representative standardisation sample, the distribution of scores in the population, which becomes the yardstick against which any individual raw score is read. Those reference data are the *norms*, the average performance of the standardisation sample, and a raw number is converted into a derived score (a percentile, a z-score, a standard score) to locate the person within them. This is norm-referencing, comparing a person to a group; it is distinct from criterion-referencing, comparing a person to a fixed performance standard irrespective of others. The practical corollary is the one that catches candidates out: a cut-off is only valid in the population from which its norms were drawn, which is exactly why an imported threshold cannot be lifted wholesale into a different population.

INDIA

This is where standardisation stops being academic in Indian practice. A scale developed and normed in a Western sample carries Western norms and cut-offs that travel poorly across India's languages, literacy levels and idioms of distress, so before an imported instrument is used it must be translated and back-translated, its reliability and validity re-established, and fresh norms generated on an Indian standardisation sample. The indigenous test-development tradition at NIMHANS and AIIMS exists for precisely this reason, and the Hindi Mental State Examination, built as a culturally and linguistically adapted screen for low-literacy Indian populations, is the standard worked example of a scale re-standardised rather than borrowed. The general principle holds across the rating-scale catalogue: a cut-off is only as good as the population it was normed on.

PEARL

Sensitivity and specificity describe the test; predictive values describe the test *in a population*. When an examiner says a screen "performs poorly" in primary care despite good published sensitivity, the answer is almost always the low base rate dragging down the positive predictive value, not a flaw in the instrument.

0.80	0.70	4	1.00
MINIMUM CRONBACH'S ALPHA (INTERNAL CONSISTENCY) FOR CLINICAL USE, NEARER 0.90 PREFERRED	KAPPA ABOVE WHICH INTER-RATER AGREEMENT IS RATED EXCELLENT	VALIDITY FAMILIES: FACE, CONTENT, CRITERION, CONSTRUCT	A PERFECT RELIABILITY OR VALIDITY COEFFICIENT (0.00 = NONE AT ALL)

GOOD TO REMEMBER

- **The principle:** a scale's worth rests on its psychometric properties, reliability (consistency, checked by test-retest, inter-rater, internal consistency with Cronbach's alpha, and split-half) and validity (accuracy, running from face and content through criterion, both concurrent and predictive, to construct with its convergent and discriminant strands).
- **The one discriminator:** reliability is consistency, validity is accuracy; a scale can be reliable without being valid, but never valid without being reliable, because reliability is necessary but not sufficient for validity.
- **The one exam fact:** for a screening scale, sensitivity and specificity are fixed properties of the test, while the positive and negative predictive values depend on prevalence, so a screen is tuned for high sensitivity (SnNout) and its false positives are cleared by later confirmation.

HOLD THIS

Reliability is consistency and validity is accuracy: a scale can be reliable without being valid but never valid without being reliable, because reliability is necessary but not sufficient for validity, and when the scale is a screen its sensitivity and specificity are intrinsic to the test while its predictive values swing with the base rate.

21 · Neuropsychological and projective testing

Beyond the bedside cognitive screen sits a second tier of assessment that the psychiatrist rarely administers but must be able to order, read and act on: the formal psychological tests run by the

clinical psychologist. Three families are examined. **Projective testing** probes the latent, unconscious layers of personality through ambiguous stimuli; **neuropsychological testing** maps cognition onto brain structure and quantifies deficit; and **intelligence testing** yields a standardised, norm-referenced index of general ability. The examinable marks here are the named instruments and who devised them, the two or three high-yield numbers, the one indication each family answers, and, for the projective tests, the long-running argument over whether their psychometric properties justify their use at all.

How to use this page. Keep it compact and comparative: this is a map of what each test does and when to reach for it, not a manual for administering it. The deep theory underneath, reliability against validity, standardisation, norming, test construction and factor analysis, together with the descriptive-psychopathology vocabulary these interviews rest on, is developed in the Psychometry, Assessment and Descriptive Psychopathology notes; the bedside cognitive examination of the higher mental functions, with the MMSE, the MoCA and the frontal tests, is the screen these batteries extend, covered in its own topic above. Here we cover the formal, psychologist-administered instruments that sit one step beyond that screen.

21.1 Projective testing: the projective hypothesis and its instruments

An ambiguous stimulus becomes a screen for the self. The **projective hypothesis** holds that when a person is shown an unstructured, ambiguous stimulus that permits an almost unlimited range of responses, what they produce is shaped by their own needs, thoughts and conflicts, so the stimulus acts as a blank screen onto which personality is projected (Kaplan and Sadock CTP 2024). Projective tests are therefore indirect, broad-band measures of personality as a whole, aimed at latent and unconscious material, and because the patient cannot see how a response will be scored they are relatively hard to fake, in deliberate contrast to the structured, self-report objective inventories (the true or false items of the MMPI and its kin). Four instruments carry the tradition. The Rorschach inkblot test, devised by the Swiss psychiatrist Hermann Rorschach around 1921, presents ten symmetrical inkblot cards, some coloured and some achromatic, and asks only "what might this be?"; responses are coded by location, determinant and content, with five competing pre-Exner scoring systems (Beck, Hertz, Klopfer, Piotrowski and Rapaport) and Exner's Comprehensive System, which synthesised them, the most widely used and best researched. The Thematic Apperception Test (the TAT), developed by Morgan and Murray in 1935, shows a set of around twenty ambiguous picture cards and asks the patient to tell a story for each, what is happening, what led up to it, what the figures feel and how it will end, revealing recurrent themes, needs and object relations. The **sentence-completion test** is the most direct, semi-projective member: the patient finishes incomplete stems ("My greatest fear is..."), and Rotter's and Sacks' forms are the standard versions. The **Draw-A-Person** and House-Tree-Person drawing tests round out the set.

PROJECTIVE TEST	STIMULUS AND TASK	WHAT IT IS TAKEN TO TAP
Rorschach inkblot test	Ten symmetrical inkblot cards, coloured and achromatic; "what might this be?"	**Perceptual organisation, reality-testing, thought disorder, affect (Exner scoring)**
Thematic Apperception Test (TAT)	Around twenty ambiguous picture cards; make up a story for each	**Dominant needs, motives, object relations and recurrent conflictual themes**
Sentence-completion test	Incomplete sentence stems finished by the patient (Rotter, Sacks)	**Attitudes, conflicts and concerns, elicited semi-directly**
Draw-A-Person / House-Tree-Person	Free drawing of a human figure (or house, tree, person)	**Self-image and body-image; weakest psychometrically**

The four classic projective instruments, from the most to the least researched; all rest on the single projective hypothesis (Kaplan and Sadock CTP 2024; Clinical Methods in Psychiatry, AIIMS 2024).

RULE **The projective hypothesis is the whole logic.** The stimulus is deliberately ambiguous so that structure comes from the patient, not the card; the response is read as a projection of latent personality. Kill the ambiguity and you kill the test, which is why these are unstructured, broadband and interpreted, never scored like a true-or-false inventory.

21.2 The psychometric debate over projective tests

Rich clinically, contested psychometrically. The recurring examination and viva point is that projective tests trade measurement rigour for clinical depth. Reliability and validity are, for most of the set, modest to poor: several Rorschach interpretive systems have unproven validity, and the sentence-completion tests and figure drawings largely lack the reliability and validity studies to support them and are easy to fabricate or distort (Kaplan and Sadock CTP 2024). Scoring and interpretation are time-consuming and examiner-dependent, so two clinicians may read the same protocol differently. Against that, the Rorschach remains the most-researched projective device, standardised administration under Exner's system improved its reproducibility, and the Society for Personality Assessment issued a formal 2005 statement defending its place in clinical and forensic use; many clinicians still combine it with the TAT in a personality workup. The defensible summary is that a projective finding is a hypothesis-generating clue to be corroborated, valuable alongside interview and objective testing, never a stand-alone diagnostic verdict.

TRAP **Confusing reliability with validity.** Reliability is consistency, the same result on repeat or across raters; validity is accuracy, whether the test measures what it claims. A projective test can be made more reliable by standardising the scoring (as Exner did) and still remain of doubtful validity for the trait inferred. The two are separate hurdles, and a test can clear one while failing the other.

PEARL

Read a projective sign the way you read a raised inflammatory marker: it flags that something may be there and points you where to look, but it does not name the illness. The moment a Rorschach response or a drawing is quoted as if it were the diagnosis, the test has been over-read.

21.3 Neuropsychological testing: the batteries and what they add over the bedside screen

Cognition mapped onto the brain, and quantified. A **neuropsychological** test is a task designed to measure a specific cognitive function known to depend on a particular brain structure or pathway, used to detect, localise and quantify impairment after injury or illness (Clinical Methods in Psychiatry, AIIMS 2024). The field organises around two approaches: the fixed, standardised battery, which runs every patient through the same comprehensive set, and the flexible, hypothesis-testing approach, which selects tests to answer a specific referral question. Two fixed batteries are the classic named pair. The Halstead-Reitan Neuropsychological Battery is the comprehensive empirical battery that yields an impairment index and speaks to the presence, lateralisation and localisation of cortical dysfunction; the Luria-Nebraska Neuropsychological Battery operationalises Luria's qualitative, functional-systems method into standardised clinical scales. Alongside the batteries sit domain-specific tests the examiner should recognise: the Wisconsin Card Sorting Test for set-shifting and executive control, the Trail Making and Stroop tests for attention and interference, verbal fluency (the COWA), the Rey Auditory-Verbal Learning Test and the Wechsler Memory Scale for verbal memory, and the Benton Visual Retention Test and the Bender Gestalt test for visuoconstructive ability. What all of this adds over the bedside cognitive screen is decisive: where the MMSE or MoCA return a single number that ceilings out in mild or focal disease, a battery returns a normed, multi-domain cognitive profile with lateralising and localising value, sensitive to the subtle deficits of early dementia, head injury and ADHD, and usable for rehabilitation planning, disability certification and research.

FIXED BATTERY	TRADITION	CHIEF CLINICAL YIELD
Halstead-Reitan	Comprehensive, empirically derived American battery	**Impairment index; presence, lateralisation and localisation of cortical dysfunction**
Luria-Nebraska	Standardisation of Luria's functional-systems method	**Profile of clinical scales across motor, language, memory and executive systems**

The two classic fixed neuropsychological batteries; both are administered whole and read against norms, in contrast to the flexible hypothesis-testing approach (AIIMS 2024).

INDIA

Western cut-offs and norms travel poorly across Indian languages and schooling, so an indigenous neuropsychological tradition was built to replace them. The NIMHANS Neuropsychological Battery (Rao and colleagues, 2004) comprises nineteen tests standardised for Indian adults with norms for ages sixteen to sixty-five, adapted from the Halstead-Reitan model, and now has parallel batteries for children and for the elderly. The AIIMS Comprehensive Neuropsychological Battery in Hindi (Gupta and colleagues, 2000) is built on Luria-Nebraska principles, runs to one hundred and sixty items across ten basic scales with norms for ages fifteen to eighty, and is used to lateralise and localise lesions. The PGI Battery of Brain Dysfunction and the widely used PGI Memory Scale complete the core Indian repertoire, keeping the assessment valid in the settings where the imported batteries are not.

21.4 Intelligence testing: the Wechsler scales and the concept of IQ

General ability, expressed against same-age peers. An **intelligence** test is a norm-referenced instrument that samples a broad range of verbal and performance tasks and compares the person's score against a same-age reference group. The clinical workhorses are David Wechsler's scales, the WAIS for adults, the WISC for children and the WPPSI for the preschool years, each giving verbal and performance indices and a full-scale intelligence quotient. The Stanford-Binet, Terman's revision of the original Binet-Simon scale, is the other historic lineage, and Raven's Progressive Matrices offers a largely non-verbal, culture-reduced estimate. The **concept of IQ** itself has shifted. The original ratio IQ was the ratio of mental age to chronological age multiplied by a hundred, which broke down in adulthood once mental age plateaus. Modern scales use the **deviation IQ** instead: scores are treated as normally distributed and centred on **100** with a standard deviation near **15**, so the number expresses how far a person stands from the population average rather than any age ratio.

Ratio IQ

The historic formula: mental age divided by chronological age, multiplied by a hundred. Serviceable in childhood, invalid in adults once mental age ceases to rise.

Deviation IQ

The modern standard: a standard score placing the person on a normal distribution centred on 100 with a standard deviation near 15 (Wechsler). It expresses relative standing, not an age quotient.

INDIA

Indian intelligence testing runs on adapted and indigenous scales: the Binet-Kamat Test, Malin's Intelligence Scale for Indian Children (MISIC), Bhatia's Battery of Performance Tests of Intelligence and the Seguin Form Board are in routine use, and the Vineland Social Maturity Scale (VSMS) is the adaptive measure drawn on for disability certification in intellectual disability. As with the neuropsychological batteries, the point is to keep the norm relevant to the population being tested.

10	100	19	5
RORSCHACH INKBLOT CARDS (HERMANN RORSCHACH)	DEVIATION-IQ MEAN, WITH A STANDARD DEVIATION NEAR 15	TESTS IN THE NIMHANS NEUROPSYCHOLOGICAL BATTERY	PRE-EXNER RORSCHACH SCORING SYSTEMS, SYNTHESISED BY EXNER

GOOD TO REMEMBER

- **The principle:** projective tests read latent personality off an ambiguous stimulus (the projective hypothesis) and are psychometrically weak; neuropsychological and intelligence tests are norm-referenced, quantified batteries that add a standardised, multi-domain profile the bedside screen cannot give.
- **The discriminator:** projective = unstructured, unconscious, contested validity (Rorschach's ten inkblots, Exner scoring; the TAT's picture-story cards); neuropsychological = brain-behaviour, fixed against flexible battery (Halstead-Reitan and Luria-Nebraska); intelligence = norm-referenced ability, the Wechsler deviation IQ centred on 100 with a standard deviation near 15.
- **The one exam fact:** the Rorschach has ten symmetrical inkblot cards (Hermann Rorschach, around 1921) and the modern deviation IQ is centred on 100 with a standard deviation near 15, replacing the old mental-age ratio.

HOLD THIS

Three test families, three anchors: projective testing reads latent personality off an ambiguous stimulus by the projective hypothesis and is rich but psychometrically shaky (the Rorschach's ten inkblots under Exner scoring, the TAT's story cards); neuropsychological testing maps and quantifies cognition through a fixed or flexible battery (Halstead-Reitan, Luria-Nebraska, and in India the nineteen-test NIMHANS battery); and intelligence testing places general ability on a normal curve centred on 100 with a standard deviation near 15 via the Wechsler deviation IQ.

Nosology and cross-cutting clinical issues

22 · The principles of psychiatric classification and the diagnostic process

Every diagnosis a psychiatrist makes rests on a **classification**, a shared system that carves the continuous mess of human distress into named categories. This page teaches the **principles of psychiatric classification** and the **diagnostic process** that runs on top of them: why we classify at all, where our systems came from, the concepts that hold a classification together, how a clinician actually reaches a diagnosis, and how we judge whether a diagnostic label is any good. The examiner tests this as pure understanding rather than fact-recall, so the marks go to the candidate who can say what a classification is *for*, hold reliability apart from validity, and place the modern systems in the arc that produced them.

How to use this page. Fix the historical spine first, because almost every examinable idea here is a response to a historical problem: Kraepelin's two-disease dichotomy founded the field, the **reliability of diagnosis** collapsed in mid-century, and the operational turn of the nineteen-seventies and -eighties was the cure. Then learn the **purposes of classification**, the building concepts (category, prototype, the polythetic criteria set, the hierarchy, comorbidity), the categorical-versus-dimensional debate, and finally the diagnostic process and the validators that certify a diagnosis. The deep psychometric theory beneath reliability and validity, factor analysis,

test construction and standardisation, belongs to the Psychometry, Assessment and Descriptive Psychopathology notes; here the treatment stays at the level of the classification and the clinical act of diagnosing.

22.1 The history of classification: from Kraepelin to the operational turn

Modern diagnosis begins with a clinician who watched the course of illness. The **history of classification** is the story of psychiatry trying, and repeatedly failing, to carve nature at its joints. Philippe Pinel enumerated four broad forms of madness in the early nineteenth century, but the pivotal figure is Emil Kraepelin, who placed the diagnostic interest of psychiatry at the bedside, on the *course and outcome* of the illness rather than on theory or anatomy. On that basis, in the sixth edition of his textbook, he drew the great dichotomy that still structures psychiatry: dementia praecox, a deteriorating disorder of thought later renamed schizophrenia by Bleuler, set against manic-depressive insanity, a periodic disorder of mood with a comparatively good prognosis. Kraepelin erected a firewall between the two that survives, as major depression against schizophrenia, in every system since.

The twentieth century then split into two traditions. American psychiatry, under psychoanalytic influence, produced the theory-laden DSM-I and DSM-II, and interest in diagnosis waned. The corrective was the **neo-Kraepelinian** revival at St Louis, which insisted that psychiatry return to describable, verifiable clinical syndromes. Its instrument was the *operational* criteria set: an explicit, rule-bound definition specifying exactly which and how many symptoms are required, so that two clinicians applying it to the same patient reach the same diagnosis. Eli Robins and colleagues published such operational criteria in 1972 (the Feighner criteria), Spitzer's group turned them into the Research Diagnostic Criteria, and in 1980 the revolutionary DSM-III operationalised almost every diagnosis at once, stripping out psychoanalytic theory. That operational turn, not any new discovery about the brain, is the single most important event in the modern history of classification. The accompanying figure sets out this spine from Pinel to the present.

MILESTONE	FIGURE AND DATE	WHAT CHANGED
The great dichotomy	Kraepelin, 1899	**Course and outcome split psychosis into dementia praecox and manic-depressive insanity**
The name "schizophrenia"	Bleuler, 1908	Recast dementia praecox as a less deteriorating, any-age disorder
Psychoanalytic era	DSM-I 1952, DSM-II 1968	Theory-laden, unreliable; diagnosis fell into disrepute
Operational criteria	Feighner et al, 1972	**Explicit rule-bound criteria for research; the neo-Kraepelinian instrument**
The operational turn	DSM-III, 1980	**Operationalised almost every diagnosis; removed psychoanalytic theory**
The current systems	DSM-5 2013; ICD-11 in effect 2022	Harmonised metastructure, hybrid categorical-dimensional

The historical spine of psychiatric classification. The pivot is the operational turn: a fix for unreliability, not a discovery about aetiology.

Why the operational turn was needed: the reliability crisis. Through the nineteen-fifties and -sixties, studies of ordinary clinical practice found the **reliability of diagnosis** to be alarmingly poor. In a much-cited English study, five experienced raters who had agreed their criteria beforehand still reached only about **46%** average agreement on the presence of a symptom, barely better than a coin toss. Two forces drove this: *information variance* (clinicians eliciting different facts) and *criterion variance* (clinicians applying different thresholds to the same facts). The transatlantic mismatch, in which American psychiatrists diagnosed schizophrenia where the British saw mania, and the notoriety of pseudopatients admitted and labelled on a single reported symptom, made the crisis public. The remedy was twofold, and it is the examinable pair: the *structured interview* attacked information variance by fixing what is asked, and the *operational criteria set* attacked criterion variance by fixing the threshold. Together they transformed reliability, so that in skilled hands a psychiatric diagnosis is now as reproducible as clinical judgements elsewhere in medicine.

RULE **Operationalisation was a cure for unreliability, not for uncertain validity.** Fixing the criteria (DSM-III) made clinicians agree; it did not prove the agreed-upon categories were real diseases. Reliability was bought; validity was not.

1899 KRAEPELIN'S DICHOTOMY: DEMENTIA PRAECOX VERSUS MANIC-DEPRESSIVE INSANITY

1980 DSM-III, THE OPERATIONAL TURN THAT FIXED CRITERION VARIANCE

2013 DSM-5 PUBLISHED (APA)

2022 ICD-11 CAME INTO EFFECT FOR MORBIDITY (1 JANUARY)

22.2 Why we classify: the purposes of a classification

A classification earns its keep by what it lets us do. The **purposes of classification** are the standard opening to any essay on this topic, and there are five. **Communication** is first and foremost: a diagnostic term compresses a large body of clinical information into a word two clinicians can exchange without misunderstanding. **Prediction** is the clinical pay-off: a valid category forecasts course, prognosis and outcome. **Treatment selection** follows, because if more than one treatment exists we must distinguish one kind of patient from another to use them rationally rather than allocating therapy by whim. **Research** requires that investigators in different centres study the same defined populations, which is impossible without an agreed, reliable classification. **Administration**, the least glamorous purpose, covers health statistics, service planning, epidemiology, insurance and the medico-legal record; it is the reason the World Health Organization maintains the ICD at all.

PURPOSE	WHAT IT DELIVERS
Communication	**A shared shorthand that transfers clinical information between professionals**
Prediction	Prognosis, course and expected outcome from the category
Treatment selection	Rational choice among available treatments for a defined patient type
Research	Comparable, replicable study populations across centres
Administration	Statistics, service planning, epidemiology and the medico-legal record

The five purposes of a psychiatric classification. Communication and prediction are the two most examined; administration is why the ICD exists as a global instrument.

The same power carries costs that a complete answer names. A diagnosis conveys only limited information and can flatten the individuality of a predicament; it is stereotypical, since real patients rarely match the textbook portrait exactly; it can be pejorative, so that terms like "psychopath" become veiled contempt; and it invites *reification*, the error of treating the concept as a discovered thing and treating the "disease" instead of the patient's actual symptoms and disabilities. The examinable stance is that classification is indispensable despite these hazards, because no workable alternative to grouping patients has ever been found.

22.3 The building concepts: category, prototype, polythetic criteria, hierarchy, comorbidity

Five ideas hold a classification together, and each is a stock exam question. Learn them as crisp definitions, because the discriminations between them do the work.

Category

A discrete diagnostic class with a boundary: a patient either meets it or does not. All diagnoses are *concepts*, not discovered things; they survive only as long as they remain clinically useful.

Prototype

The description of a typical, ideal member of a category. On the prototype model a real patient is diagnosed by *resemblance* to the prototype rather than by satisfying a fixed checklist, and members vary in how typical they are. This is how experienced clinicians actually recognise a case, and it is the model ICD-11 adopts.

Polythetic criteria set

A definition listing several features of which the patient need show only a specified subset (for example, any five of nine), so no single feature is necessary or sufficient. It contrasts with a *monothetic* set, where every listed feature is required. Polythetic criteria make a category heterogeneous: two patients can share a diagnosis with few symptoms in common.

Diagnostic hierarchy

A rank ordering in which a higher-placed disorder pre-empts a lower one, so that a single diagnosis is chosen. The classic order is organic disorders over psychotic (schizophrenic) over affective over neurotic and stress-related; any diagnosis excludes the symptoms of those above it and embraces those below.

Comorbidity

The co-occurrence of two or more diagnoses in one patient. Where a strict hierarchy once forbade it, the modern manuals largely abandoned hierarchical exclusions, so comorbidity is now recorded rather than suppressed, at the cost of much apparent overlap.

The hierarchy and comorbidity are two sides of one historical shift. Under the older Jaspers-derived hierarchy, and Schneider's rule that first-rank symptoms were diagnostic of schizophrenia "except in the presence of coarse brain disease", a patient could hold only the highest applicable diagnosis; a depressed patient with an organic cause was "organic", full stop. DSM-III and its successors relaxed most of these exclusions to let clinicians record the full picture, which is why comorbidity rates then appeared to soar. The diagnostic hierarchy nonetheless survives as a clinical *rule of the diagnostic process*, examined below: rule out the organic before you rest on the functional.

TRAP **Confusing polythetic with monothetic.** A polythetic set needs only a subset of its features, so the diagnosis is inherently heterogeneous; a monothetic set needs them all. Assuming everyone with one diagnosis shares the same symptoms is the polythetic trap.

22.4 The categorical versus dimensional debate

Two ways to describe a patient: a box, or a set of sliders. The **categorical approach**, the one psychiatry actually uses, sorts patients into discrete named classes. The *dimensional* approach instead rates each patient on continuous scales of severity, as intelligence is rated by IQ rather than by "clever, average, dull". Neither is provably "right"; there is no statistical test that settles it, and the choice is pragmatic, decided by which is more useful. The strongest argument for a categorical system would be the demonstration of **zones of rarity**, natural gaps in the distribution between one disorder and the next, as Kendell put it; but attempts to find such gaps between related syndromes have largely failed, and the frequency with which clinicians reach for hybrid terms like "schizoaffective" is itself evidence that the categories shade into one another.

THE CATEGORICAL APPROACH FAVOURS	THE DIMENSIONAL APPROACH FAVOURS
Familiarity and ease of use, memory and communication	**More information: finer distinctions are preserved**
A ready prelude to action (diagnosis X implies treatment D)	**Flexibility, and easy conversion back to categories with a cut-off**
A prototype that captures the essence of a clinical concept	**No false boundaries imposed where none exist in reality**
Fits medical tradition and a conservative profession	**Handles boundary and mixed cases without distortion**

Categories versus dimensions. Categories win on usability and action; dimensions win on information and on not distorting patients who sit between classes.

The field's settled answer is a *hybrid*: retain categorical diagnoses for their usability while adding dimensional measures for severity and for cross-cutting symptoms. This is exactly the direction of both current manuals, and it is why the debate is not "which wins" but "how they combine".

TRAP **Treating the absence of zones of rarity as proof that a disorder is not real.** Continuity of symptoms across a boundary weakens the case for a natural category, but a concept can remain clinically useful (and worth keeping) even without a discoverable joint to carve at.

22.5 The two current systems: ICD-11 and DSM-5

One world classification, one American manual, deliberately harmonised. The ICD-11 chapter on mental, behavioural and neurodevelopmental disorders is the World Health Organization's global system, approved by the World Health Assembly and in effect since January 2022; DSM-5 (2013) is the American Psychiatric Association's manual. Their revisions were coordinated so that the two share a common organisation, the *metastructure*, that opens with neurodevelopmental disorders and orders the rest along developmental and internalising-externalising lines rather than the old organic-first hierarchy. Both abandoned the multiaxial system of DSM-IV (its five axes), folding contextual and disability information into the main diagnosis and a separate functioning measure. DSM-5 keeps three parts: an introductory section, the diagnostic criteria proper, and a Section III of emerging measures, the cross-cutting symptom scales, the cultural formulation interview and the alternative dimensional model of personality disorder.

The examinable difference is one of *style*. DSM-5 is strictly *operational*: it specifies exact symptom counts and durations. ICD-11 deliberately moved the other way, replacing rigid criteria with flexible *essential features*, the symptoms a clinician can reasonably expect in a typical case, applied as a prototype with room for clinical judgement and cultural variation. Field work showed clinicians overwhelmingly preferred this flexibility to a criteria-counting exercise. Both also moved toward dimensions where the evidence demanded it, most visibly in personality disorder, which ICD-11 now rates by severity (and optional trait domains) instead of the discrete personality types.

FEATURE	ICD-11	DSM-5
Owner and scope	WHO, global, all of medicine	**APA, United States, mental disorders**
In effect	Since 2022	**Since 2013**
Definitional style	Flexible "essential features", prototype-based	**Operational: explicit symptom counts and durations**
Guiding intent	Global, cross-cultural, clinical-judgement-friendly	**Reliability and research precision**
Structure	Chapter on mental, behavioural and neurodevelopmental disorders	Three sections; emerging measures in Section III
Multiaxial system	Never adopted a five-axis format	**DSM-IV five axes abandoned in DSM-5**
Personality disorder	Fully dimensional: severity plus trait domains	Categorical types; dimensional hybrid model in Section III
New entities	Gaming disorder, complex PTSD, prolonged grief disorder	Retains categorical syndromes with dimensional specifiers
Metastructure	**Shared, harmonised: developmental order, neurodevelopmental disorders first**	

ICD-11 against DSM-5. Same harmonised metastructure; the sharp discriminator is prototype-based essential features (ICD-11) versus operational criteria counts (DSM-5).

INDIA

India, as a World Health Organization member state, uses the *ICD*, not the DSM, as its official diagnostic and statistical classification; Indian teaching, examinations and clinical records are ICD-anchored, with the DSM used mainly for research. ICD-11's flexible essential-features approach, explicitly built to allow cultural variation and clinical judgement, suits India's multilingual, resource-varied settings and its cultural concepts of distress better than a rigid criteria count would (the wider transcultural frame is set out in the Consultation-liaison, geriatric and transcultural psychiatry notes). The classification also carries statutory weight: the Mental Healthcare Act 2017 directs that the determination of mental illness be made in accordance with nationally or internationally accepted medical standards, including the latest edition of the ICD, tying Indian clinical-legal practice to the WHO system (the full legislation is developed in the Mental health legislation and forensic psychiatry notes).

22.6 The diagnostic process: pattern, differential, hierarchy, formulation

How a clinician actually gets from a patient to a diagnosis. The **diagnostic process** has four moves, and naming them in order is a clean exam answer. First, *pattern recognition*: the clinician matches the history and mental state findings against the stored criteria set or prototype, generating a provisional diagnosis, often within minutes for a classical case. Second, the *differential diagnosis*: the alternatives that could produce the same pattern are listed and then tested, symptom by symptom, against the specific discriminators of each. Third, the *hierarchy rule*, the surviving clinical use of the diagnostic hierarchy: exclude the organic before resting on

the functional, because a physical or drug-induced cause overrides and redirects the whole assessment. Fourth, the diagnosis is set within a *formulation*, which does what a bare label cannot: it explains why this person developed this disorder at this time, integrating predisposing, precipitating and perpetuating factors into an individual account that guides management. The diagnosis says *what*; the formulation says *why*, and the two are complementary, not rivals.

WORKED EXAMPLE

A woman in her forties presents with two weeks of low mood, poor sleep and, for the first time, a conviction that her neighbours are poisoning her water. Pattern recognition offers a depressive episode with psychotic features. The differential then widens: is this a primary psychotic disorder, a bipolar mixed state, or an organic mood syndrome? The hierarchy rule fires first, so a cognitive screen, a physical examination and basic investigations are done to exclude a delirium, a space-occupying lesion or a thyroid or steroid effect before the functional diagnosis is accepted. Only once the organic is cleared, and the mood-congruence of the belief and its two-week arc against a low mood are weighed, is a depressive episode with psychotic symptoms settled on, and a formulation built around her recent bereavement and family history to guide treatment.

RULE **Exclude the organic first.** The one surviving clinical use of the diagnostic hierarchy is that a demonstrable organic or substance-induced cause pre-empts every functional diagnosis. Rule it out before you rest on a psychiatric label.

22.7 The reliability and validity of a diagnosis: the Robins and Guze validators

A diagnosis must be both consistent and true, and these are different demands. *Reliability* is the reproducibility of a diagnosis, whether two clinicians, or the same clinician twice, agree; it is quantified for categorical diagnoses by the kappa coefficient, and it is what operationalisation and structured interviews repaired. *Validity* is the harder and higher question of whether the category corresponds to a real, distinct entity in nature, and reliability does not guarantee it: clinicians can agree perfectly on a category that carves no real joint. The landmark answer to how validity is established is Robins and Guze's 1970 paper, which set out a **five**-phase programme, the diagnostic validators, that a category must pass. These validators were the template for the Feighner criteria, and an expanded set of them was applied in building the metastructure of both current manuals.

VALIDATOR	WHAT IT REQUIRES OF THE CATEGORY
Clinical description	**A distinctive cluster of co-varying symptoms and characteristic features**
Laboratory studies	Reliable biological, physiological or psychological markers
Delimitation from other disorders	**Clear exclusion criteria that mark it off from neighbouring diagnoses**
Follow-up study	A characteristic, predictable course and outcome
Family study	Raised rates of the same disorder among first-degree relatives

The five Robins and Guze diagnostic validators (1970). A category earns its validity by passing them; passing none of them, however reliably it is applied, is the mark of a doubtful entity.

MNEMONIC

Clinicians Look, Delimit, Follow, Family

The five Robins and Guze validators in order: **C**linical description, **L**aboratory studies, **D**elimitation from other disorders, **F**ollow-up study, **F**amily study. Reliability lets clinicians agree; these five decide whether what they agree on is real.

PEARL

Kappa is not a fixed property of a diagnosis. It rises and falls with the base rate and comorbidity of the sample it is measured in, which is why a criteria set can look reliable in a research clinic and shakier in a mixed general population. Reliability is a feature of the diagnosis *in a setting*; validity is the deeper claim about the category itself.

TRAP **Reading a reliable diagnosis as a valid one.** High inter-rater agreement (good kappa) shows only that clinicians apply the label the same way; it says nothing about whether the category is a genuine disease. A reliable diagnosis can still be an invalid one, which is precisely why the Robins and Guze validators exist.

GOOD TO REMEMBER

- **The principle:** psychiatric classification exists to serve communication, prediction, treatment selection, research and administration; modern systems (ICD-11 and DSM-5) are symptom-based, operationalised and largely categorical with dimensional additions, born of the operational turn that answered the mid-century reliability crisis.
- **The one discriminator:** reliability (do clinicians agree, measured by kappa) is not validity (is the category a real entity, established by the five Robins and Guze validators); operationalisation bought reliability but validity must be earned separately.
- **The one exam fact:** Kraepelin's 1899 dichotomy of dementia praecox versus manic-depressive insanity founded modern classification; the diagnostic process runs pattern recognition, differential diagnosis, the hierarchy rule (exclude the organic first) and formulation; and a category's validity rests on Robins and Guze's five validators (clinical description, laboratory studies, delimitation, follow-up study, family study).

HOLD THIS

Modern psychiatric classification is operationalised, symptom-based and largely categorical: Kraepelin's 1899 dichotomy founded it, the reliability crisis drove the operational turn of Feighner and DSM-III, and a diagnosis earns its validity through the five Robins and Guze validators, never through reliability alone.

23 · ICD-11 versus ICD-10

The examiner treats the classification chapters as a gift, because the changes between the two editions are finite, structural and easy to score if learned as a list of deltas rather than a re-reading of the whole nosology. ICD-11 was adopted by the 72nd World Health Assembly in 2019 and came into effect on 1 January 2022, with its clinical manual, the Clinical Descriptions and Diagnostic Requirements (CDDR), published in 2024; it is the classification India works to, so the shift from ICD-10 is not academic for the Indian trainee but the operating change in daily coding and in the exam. This page is built around the single question a paper on **icd-11 versus icd-10** actually asks: not "describe ICD-11" but "state, precisely and without error, what changed".

How to use this page. Fix the two framing moves first, the shift from fixed research rules to flexible **essential features**, and the shift from an almost purely categorical system to one carrying dimensional elements, because every specific change below is an instance of one or the other. Then learn the headline chapter-by-chapter deltas as discrete, examinable facts: the schizophrenia rebuild, the dimensional personality model, the batch of new entities, and the restructured and relocated groupings. A wrong change stated with confidence is worse than a gap, so the discipline here is accuracy over coverage. The deeper categorical-versus-dimensional debate and the descriptive-psychopathology vocabulary that populate these categories are developed in the Psychometry, Assessment and Descriptive Psychopathology notes; this page owns the concrete ICD-11 changes themselves.

23.1 From fixed rules to essential features: the CDDR replaces the ICD-10 dual system

ICD-11 abandons arbitrary symptom counts and precise durations for a flexible, prototype-based description. ICD-10 in fact ran two parallel documents: the clinical version, the *Clinical Descriptions and Diagnostic Guidelines* (CDDG), written as prose guidance for the practitioner, and a separate *Diagnostic Criteria for Research* (DCR) that was fully operationalised, with fixed symptom thresholds, exact counts and rigid duration cut-offs modelled closely on the DSM. ICD-11 collapses this into a single manual, the CDDR, and deliberately discards the operationalised straitjacket. Each disorder is now defined by its **essential (required) features**, the symptoms a clinician using reasonable judgement would expect to be present, stated without an arbitrary "five out of nine for two weeks" arithmetic. The stated rationale is that precise counts and durations produced false negatives that offered the clinician no useful guidance and travelled poorly across the world's cultures, and that a prototype description matched to clinical reality is both more usable and more globally applicable. Alongside the essential features, each category carries a standard set of headings: boundary with normality (the threshold), boundaries with other disorders (the differential), coded qualifiers and subtypes, course features, culture-related features, and developmental and sex- or gender-related presentations.

RULE **ICD-11 defines disorders by flexible essential features, not fixed counts.** The move from ICD-10's operationalised research criteria to the CDDR's prototype-based essential features is the master change; every specific delta is downstream of it, and it is designed for clinical judgement and cross-cultural use rather than symptom arithmetic.

23.2 Categorical to dimensional: the second organising shift

ICD-10 was almost purely categorical; ICD-11 keeps categories but adds dimensions in two ways. Under ICD-10 a diagnosis was, with very few exceptions, simply present or absent; the only concessions to gradation were the severity bands for mental retardation (mild, moderate, severe, profound) and for the depressive episode (mild, moderate, severe). Among the **icd-11 changes**, dimensionality enters through two distinct routes. First, more categories are now graded by *severity*: in addition to intellectual developmental disorder and the depressive episode, the CDDR sub-classifies bodily distress disorder, personality disorder and dementia as mild, moderate or severe. Second, several groupings now attach *cross-cutting symptom specifiers*, dimensional profiles that describe a presentation across a whole grouping rather than pinning it to one sub-diagnosis; the two examinable instances are the six symptom domains of the primary psychotic disorders and the trait domains of personality disorder. The point to hold is that ICD-11 did not become a dimensional system; it remained categorical at its base and grafted dimensional detail onto specific groupings where the evidence supported it.

PEARL

When an examiner asks "is ICD-11 dimensional?", the marks are in the qualification: it is a categorical classification that incorporates dimensional elements in two places, severity gradations for a handful of disorders and cross-cutting symptom or trait specifiers for a few groupings. Calling it "a dimensional system" overstates the change and loses the mark.

23.3 Schizophrenia rebuilt: the removal of subtypes, and catatonia set free

The classic subtypes are gone, replaced by symptom-domain and course specifiers. The single most quoted delta is the **removal of subtypes** of schizophrenia. ICD-10's familiar divisions, paranoid, hebephrenic, catatonic, undifferentiated, residual and simple, are abolished, on the evidence that they were unstable over time, poorly reliable and of little prognostic or treatment value. In their place ICD-11 describes the current presentation with two kinds of specifier. The first is a set of **6** *symptom-domain specifiers* that cut across the whole primary-psychotic grouping (positive symptoms, negative symptoms, depressive mood symptoms, manic mood symptoms, psychomotor symptoms and cognitive symptoms), each rated as not present, mild, moderate or severe for the past week. The second is a *course specifier* recording whether this is a first episode, multiple episodes or a continuous illness, and whether the person is currently symptomatic, in partial remission or in full remission. The diagnosis of schizophrenia itself, its core symptom set and duration, is developed with the PANSS and BPRS in clinical use in the Schizophrenia: clinical features and phenomenology notes; here the examinable fact is the swap of static subtypes for a dynamic symptom-and-course profile.

The old catatonic subtype does not simply disappear. ICD-11 recognises catatonia as a standalone grouping in its own right, an arousal-and-psychomotor syndrome that can arise with a mental disorder (6A40), be induced by substances or medications (6A41) or be secondary to another medical condition (6E69). Treating **catatonia as a syndrome** that spans diagnoses, rather than as a variety of schizophrenia, is the conceptual correction: catatonia occurs across mood disorders, psychotic disorders and general medical conditions, and tying it to schizophrenia obscured that.

TRAP **Saying the subtypes were "replaced by course specifiers alone", or that catatonia is now a schizophrenia specifier.** The subtypes were replaced by six cross-cutting symptom-domain specifiers *and* a course specifier; and catatonia was lifted out of schizophrenia entirely to become its own grouping applicable across disorders, not folded in as a psychotic specifier.

23.4 The dimensional personality model: severity plus trait domains

Every categorical personality type is abolished; one diagnosis, graded and profiled, takes their place. This is the boldest single change in the classification. ICD-10's menu of discrete types, paranoid, schizoid, dissocial, emotionally unstable (with its impulsive and borderline variants), histrionic, anankastic, anxious (avoidant) and dependent, is deleted wholesale. In its place stands a single **dimensional personality** disorder diagnosis, built in two steps. The clinician first establishes that a personality disturbance is present and rates its *severity* as mild, moderate or severe (the severity turning on the degree of dysfunction in the sense of self and in interpersonal functioning, and on the associated risk and harm), because severity, not type, is what predicts outcome and guides management. The clinician may then, optionally, record one or more prominent *trait domain* specifiers that describe the flavour of the difficulty: **5** domains are offered, negative affectivity, detachment, dissociality, disinhibition and anankastia. A single vestigial pattern qualifier, the *borderline pattern*, is retained as a pragmatic concession, so that the large evidence base and treatment pathways attached to borderline personality disorder are not orphaned by the reform. The dialectical behaviour therapy and schema therapy that this borderline pattern indicates are developed in the Personality disorders notes.

RULE **Severity first, traits second.** ICD-11 personality disorder is diagnosed by grading severity (mild, moderate, severe), then optionally attaching trait-domain specifiers; the categorical types are gone, and the only surviving named pattern is the borderline pattern qualifier.

23.5 The new entities: five arrivals and a consolidated somatic category

ICD-11 introduces several disorders that had no home in ICD-10. The high-yield newcomers cluster naturally. Two sit in the stress grouping: **complex PTSD** (6B41), which adds to the three core PTSD clusters (re-experiencing, avoidance and a sense of current threat) a further three "disturbances in self-organisation", namely affect dysregulation, a persistently negative self-concept and difficulties sustaining relationships, and captures the sequelae of prolonged or repeated trauma; and **prolonged grief** disorder (6B42), a grief response persisting for an abnormally long period (at least six months, and clearly exceeding the person's social, cultural or religious norm) with intense longing or preoccupation and marked impairment. Two are

behavioural: gaming disorder (6C51), placed in the new grouping of disorders due to addictive behaviours alongside gambling disorder, marked by impaired control over gaming, escalating priority given to it, and continuation despite harm, normally evident over at least twelve months; and compulsive sexual behaviour disorder (6C72), a persistent failure to control intense, repetitive sexual impulses classified among the impulse-control disorders (notably *not* as an addiction). The fifth is body integrity dysphoria (6C21), a rare and enduring desire for a major physical disability (typically amputation of a healthy limb) arising from a mismatch between the felt and the actual body. Separately, ICD-11 consolidates ICD-10's scattered somatoform disorders and neurasthenia into a single graded bodily distress disorder (6C20), defined by distressing bodily symptoms and excessive attention to them rather than by whether the symptoms are "medically explained".

MNEMONIC

Two traumas, two behaviours, one body

The five new entities in two pairs and a single: **two** in the stress grouping (**complex PTSD**, **prolonged grief** disorder); **two** behavioural (**gaming disorder**, an addiction; **compulsive sexual behaviour disorder**, an impulse-control disorder, deliberately not an addiction); and **one** body-focused (**body integrity dysphoria**). Bodily distress disorder is a consolidation, not a true newcomer.

WORKED EXAMPLE

A woman is referred fourteen months after her husband's death, unable to accept the loss, spending hours with his belongings, socially withdrawn and functionally impaired, with no pervasive anhedonia or worthlessness. Under ICD-10 there was no clean category; she would have been coded as an adjustment disorder or a depressive episode, both ill-fitting. Under ICD-11 this is prolonged grief disorder: the response has persisted well beyond the six-month floor and clearly beyond her cultural norm, it centres on longing and preoccupation with the deceased rather than on a depressive syndrome, and naming it correctly changes the therapeutic target from mood to grief.

23.6 Restructured groupings and the disorders moved out of the chapter

ICD-11 re-draws the map, both by creating new groupings and by exporting conditions to other chapters. Within the mental-disorders chapter, obsessive-compulsive disorder is pulled out of the old neurotic bracket into a dedicated *obsessive-compulsive and related disorders* (OCRD) grouping that now gathers hoarding disorder, body dysmorphic disorder, olfactory reference disorder, hypochondriasis (health anxiety) and the body-focused repetitive behaviours; the exposure and response prevention that treats this grouping is developed in the Anxiety, OCD and trauma-related disorders notes. A parallel *disorders specifically associated with stress* grouping brings PTSD, complex PTSD, prolonged grief disorder, adjustment disorder and reactive attachment disorders together under the shared requirement of an identifiable stressor, and in the same reform acute stress reaction is reclassified out of the mental disorders as a normal reaction (coded among factors influencing health status). Beyond the chapter, four ICD-10

subgroupings are exported entirely: nonorganic sleep disorders go to a new sleep-wake disorders chapter, tic disorders join diseases of the nervous system (as Tourette syndrome), and the "organic"/"nonorganic" split of sexual dysfunctions is dissolved by moving them, together with gender-related conditions, to a new chapter on conditions related to sexual health. It is here that **gender incongruence moved** out of the mental-disorders chapter altogether: reframed as a sexual-health condition on field-study evidence that the distress of transgender people is predicted by stigma and victimisation rather than being intrinsic, this depsychopathologisation is one of the most examined single facts in the whole comparison.

AREA	ICD-10	ICD-11 CHANGE
Manual and format	Two documents: clinical Guidelines (CDDG) plus operationalised Research Criteria (DCR) with fixed counts and durations	**Single CDDR with flexible, prototype-based essential features; no arbitrary counts**
Overall approach	Almost entirely categorical (present or absent)	**Categorical base with dimensional elements: severity gradings and cross-cutting specifiers**
Schizophrenia	Classic subtypes (paranoid, hebephrenic, catatonic, undifferentiated, residual, simple)	**Subtypes removed; six symptom-domain specifiers plus a course specifier**
Catatonia	A subtype of schizophrenia	**Standalone grouping applicable across disorders (catatonia as a syndrome)**
Personality disorder	Discrete categorical types (paranoid, schizoid, dissocial, emotionally unstable and the rest)	**Single diagnosis by severity (mild, moderate, severe) plus five trait domains; borderline pattern qualifier retained**
Stress-related	Reaction to severe stress and adjustment disorders (F43)	**New "disorders specifically associated with stress" grouping; adds complex PTSD and prolonged grief; acute stress reaction reclassified as a normal reaction**
Obsessive-compulsive	OCD within the neurotic and anxiety disorders	**New OCRD grouping (adds hoarding, body dysmorphic, olfactory reference, hypochondriasis, skin-picking, hair-pulling)**
Somatoform	Multiple somatoform disorders and neurasthenia	**Consolidated into a single graded bodily distress disorder**
Behavioural addictions	No grouping; pathological gambling coded among habit and impulse disorders	**New "disorders due to addictive behaviours": gambling disorder and gaming disorder**

AREA	ICD-10	ICD-11 CHANGE
Gender	Gender identity disorders within mental disorders (F64)	**Gender incongruence moved to the conditions related to sexual health chapter (depsychopathologised)**
Sleep and tics	Nonorganic sleep disorders (F51) and tic disorders inside the mental chapter	**Sleep-wake disorders and tic disorders (Tourette) exported to their own chapters**
Intellectual disability	Mental retardation, graded on IQ	**Disorders of intellectual development, on adaptive behaviour and intellectual functioning**

The master comparison of the ICD-11 changes against ICD-10, area by area. The highlighted cell in each row is the delta the examiner wants stated exactly; the recurring theme is a move from fixed categories toward flexible, dimensional and aetiologically cleaner groupings.

INDIA

ICD, not DSM, is the classification of record in India, which makes this comparison a working exam and clinical concern rather than a curiosity. The Mental Healthcare Act 2017 anchors the point in statute: it directs that mental illness be determined "in accordance with such nationally or internationally accepted medical standards (including the latest edition of the International Classification of Diseases of the World Health Organisation) as may be notified by the Central Government", so Indian psychiatric diagnosis is tied by law to the ICD, and the migration to ICD-11 flows through to certification, admission and the courts; the fuller legislative and forensic detail sits in the Mental health legislation and forensic psychiatry notes. Indian centres, including NIMHANS, took part in the WHO international field studies that tested the CDDR format, and the flexible, culturally sensitive essential-features approach, with its explicit culture-related features heading, suits the Indian idioms of distress and locally variable bereavement norms better than a rigid symptom-count system; the wider transcultural frame is in the Consultation-liaison, geriatric and transcultural psychiatry notes.

2022
YEAR ICD-11 CAME INTO EFFECT (ADOPTED 2019, CDDR PUBLISHED 2024)

6
SYMPTOM-DOMAIN SPECIFIERS REPLACING THE SCHIZOPHRENIA SUBTYPES

5
PERSONALITY-DISORDER TRAIT DOMAINS UNDER THE DIMENSIONAL MODEL

3
PERSONALITY-DISORDER SEVERITY LEVELS: MILD, MODERATE, SEVERE

GOOD TO REMEMBER

- **The principle:** the two master shifts from ICD-10 to ICD-11 are format (a single CDDR with flexible, prototype-based essential features replacing ICD-10's operationalised research criteria) and structure (a categorical base that now carries dimensional severity gradings and cross-cutting specifiers).
- **The one discriminator:** schizophrenia loses its subtypes and is described instead by six symptom-domain specifiers and a course specifier, while personality disorder loses its categorical types and is described by severity plus trait domains, so in both flagship areas fixed categories give way to a dimensional profile.
- **The one exam fact:** ICD-11 adds complex PTSD, prolonged grief disorder, gaming disorder, compulsive sexual behaviour disorder and body integrity dysphoria; makes catatonia a standalone syndrome; consolidates somatoform illness into bodily distress disorder; and moves gender incongruence out of the mental-disorders chapter to a sexual-health condition.

HOLD THIS

ICD-11 replaces ICD-10's fixed research criteria with flexible essential features and adds dimensions to a categorical base: schizophrenia subtypes give way to six symptom-domain specifiers plus a course specifier, categorical personality types give way to severity plus five trait domains, catatonia becomes a standalone syndrome, complex PTSD, prolonged grief, gaming disorder, compulsive sexual behaviour disorder and body integrity dysphoria are new, and gender incongruence moves out of the mental-disorders chapter to a sexual-health condition.

24 · ICD-11 versus DSM-5

Two classification systems govern the diagnosis of mental disorders, and the examiner expects the candidate to place them side by side and say precisely how they differ. The comparison of **ICD-11 versus DSM-5** is a favourite because it tests understanding rather than recall: the two books cover much the same disorders and were deliberately harmonised, yet they were built by different bodies, for different purposes, on different philosophies, and it is those **conceptual differences** and **structural differences** that carry the marks. The single line to hold above all others is the format contrast: ICD-11 describes each disorder through prose **essential features** and leaves the diagnostic decision to clinical judgement, whereas DSM-5-TR lays out operationalised criteria with explicit symptom counts and durations.

How to use this page. Fix the ownership and orientation first, because almost every downstream difference follows from who built each system and for whom. The World Health Organization built the ICD for every member state and for all of health; the American Psychiatric Association built the DSM for mental disorders and for a research-and-specialist readership. Then learn the format contrast (the classic discriminator), the architecture of each book, the selected content and placement differences, and the personality-disorder models, which are where the two diverge most sharply. Finally take the practical point that matters in this country: in India, as across most of the world, the ICD is the official system, and the DSM is used chiefly in research. The accompanying figure lays the two systems out as a crossmap so the equivalences and the divergences can be read at a glance.

The axis	ICD-11	DSM-5-TR
Diagnostic format the classic discriminator	clinical descriptions and diagnostic requirements: essential features, NO operationalised symptom counts	polythetic OPERATIONALISED criteria: specified symptom counts and durations
How a diagnosis is reached	clinical judgement matched against the prototype	count the criteria met against a stated threshold
Owner and orientation	WHO; global health, multilingual, primary-care inclusive	APA; research and specialist, of North American origin
Coverage and coding	part of a single classification of all health conditions	mental disorders only
Personality disorders	fully DIMENSIONAL: a severity grade plus trait domains	categorical types, with a dimensional alternative model in Section III
Use in India	the official diagnostic system	common in research and teaching

The classic exam discriminator (highlighted): ICD-11 states essential features and asks for clinical judgement, whereas DSM-5-TR sets operationalised criteria to be counted against a threshold.

Fig 19.15 ICD-11 and DSM-5-TR: the structural crossmap. The two systems classify the same disorders but differ in how they do it. The examinable difference is the diagnostic format: ICD-11 gives clinical descriptions and diagnostic requirements built around essential features and asks the clinician to judge the fit against a prototype, with no fixed symptom counts, whereas DSM-5-TR sets polythetic operationalised criteria with specified symptom counts and durations to be met against a threshold. Beneath that sit differences of ownership and purpose (the WHO's global-health, multilingual, primary-care-inclusive system versus the APA's research-and-specialist manual), of coverage (ICD-11 is part of a classification of all of health; the DSM covers mental disorders), and of the personality-disorder model. In India, ICD is the official diagnostic system.

24.1 Two classifications, two owners, two purposes

The orientation and ownership of each system explains the rest. The ICD-11 (the eleventh International Classification of Diseases) is a product of the World Health Organization, adopted by the World Health Assembly in 2019 and in effect from 2022. It is a global-health instrument: multilingual, free to use, designed for every member state from the primary-care health worker to the specialist, and built to generate the world's official morbidity and mortality statistics. Mental disorders are only one chapter of it. The DSM-5-TR (the Diagnostic and Statistical Manual, fifth edition, text revision, 2022) is a product of the American Psychiatric Association, a single national professional body. It covers mental disorders alone, is written for a research-and-specialist audience, is sold commercially, and is oriented to North American practice. This difference in purpose, a whole-of-health public-health classification against a specialist mental-disorders manual, is the root from which the coverage, the coding and the format differences all grow.

ICD-11

WHO's classification of all diseases and health conditions; mental disorders are Chapter 06 of a whole-health system. Global, multilingual, free, primary-care to specialist. The official statistical and reporting standard.

DSM-5-TR

The American Psychiatric Association's manual of mental disorders only. Specialist and research oriented, commercial, North American in origin and primary use.

Coverage

ICD-11 covers all of health; the DSM covers mental disorders exclusively.

Coding

ICD-11 supplies the official alphanumeric codes (for example 6A20 for schizophrenia); the DSM carries no independent code set and maps its disorders onto ICD codes.

RULE **The ICD is the world's official classification; the DSM is a specialist manual.** WHO's ICD-11 codes all of health for every member state and generates official statistics; the APA's DSM-5-TR covers mental disorders alone for a research-and-specialist readership and borrows ICD codes.

24.2 The format contrast: essential features versus operationalised criteria

This is the classic discriminator, and the one line the examiner is listening for. The ICD-11 clinical guideline for mental disorders, its Clinical Descriptions and Diagnostic Requirements (the CDDR, the successor to the ICD-10 "blue book"), sets out for each disorder a prose account of its **essential features**, meaning those features a clinician would reasonably expect to find in all cases, and then as a rule dispenses with rigid thresholds. It gives **no operationalised counts**: it generally avoids fixed symptom tallies and precise duration cutoffs, and leaves it to the diagnosing clinician to weigh whether each feature is present, considering the whole clinical context, culture and course. The design was deliberate, meant to match how clinicians actually diagnose and to raise clinical utility across the world's very different health systems. The **DSM-5 operationalised criteria** take the opposite approach: each disorder carries a numbered, polythetic criteria set with an explicit count and duration, the familiar "at least five of the following nine symptoms, for at least two weeks" template. The strength of the DSM style is reliability and reproducibility, especially for research; the strength of the ICD style is flexibility and fidelity to real clinical reasoning.

DIMENSION	ICD-11 (CDDR)	DSM-5-TR
Diagnostic format	**Prose essential features; clinical judgement**	Numbered polythetic operationalised criteria
Symptom counts	**As a rule none (no operationalised counts)**	Explicit ("at least five of the following")
Duration thresholds	Guideline durations, flexibly applied	Fixed cutoffs (for example two weeks, six months)
Design priority	**Clinical utility and global flexibility**	Reliability and research reproducibility
Culture and context	Culture-related features built into each entry	Cultural formulation and concepts placed in Section III and an appendix

The format contrast in one grid: ICD-11 describes essential features and trusts clinical judgement; DSM-5-TR operationalises the same territory into counted, time-bound criteria.

WORKED EXAMPLE

Take schizophrenia. The DSM-5 operationalised criteria require at least two of the five characteristic symptoms, present for a one-month active phase (with at least one being a core symptom such as delusions, hallucinations or disorganised speech), *and* continuous signs of the disturbance for at least six months in total. ICD-11 requires at least two of a comparable symptom set, at least one from its core list, persisting for at least one month, and it drops the six-month total-illness requirement altogether, presenting the whole as essential features to be weighed rather than a tally to be counted. Same disorder, two formats: the DSM candidate counts symptoms and clocks six months; the ICD candidate recognises the essential clinical picture at one month. The six-month total-duration requirement is a genuine, high-yield difference, present in the DSM and absent from the ICD.

24.3 The architecture of each book

The structural differences are visible before a single disorder is read. The DSM-5-TR is built in three sections. Section I is the basics and the guidance on use; Section II holds the diagnostic criteria and codes, the working chapters arranged on a developmental-and-lifespan metastructure that places neurodevelopmental disorders first and clusters internalising and externalising groupings together; and Section III, "Emerging Measures and Models", houses the assessment measures, the cultural formulation, the alternative dimensional model of personality disorder and the conditions for further study. ICD-11's mental disorders sit as **Chapter 06**, "mental, behavioural and neurodevelopmental disorders", one chapter within the whole classification of health. It has two paired products: the short brief descriptions in the main statistical volume (the MMS), used for coding and statistics, and the fuller Clinical Descriptions and Diagnostic Requirements for clinical, educational and service use. ICD-11 also adopted a lifespan structure, ending the old separation of childhood-onset disorders into their own block, and the two systems were harmonised through a joint WHO and APA working effort so that their groupings largely correspond even where the format differs.

PEARL

The DSM's dimensional experiment is quarantined in Section III precisely because it is "emerging": the alternative personality model and the cross-cutting symptom measures were judged not yet ready to govern routine diagnosis, so Section II still runs on the familiar categorical criteria. When an examiner asks "where does the DSM put its dimensional model?", the answer is Section III, not the main diagnostic text.

24.4 Selected content differences: new entities and where things sit

Beyond format, the two systems differ in what they include and where they place it. Several entities are the ICD-11's own, or sit differently across the two books, and these are the details the paper likes to probe. Complex post-traumatic stress disorder, a distinct diagnosis added in ICD-11 (PTSD plus disturbances in self-organisation), has no separate place in the DSM. Gaming disorder is a recognised diagnosis in ICD-11, whereas the DSM lists internet gaming disorder only as a condition for further study in its Section III. Catatonia is raised in ICD-11 to an

independent grouping rather than being tethered to schizophrenia and mood disorders. Gender incongruence was moved out of the mental disorders chapter entirely in ICD-11, into a new chapter on conditions related to sexual health, a deliberate de-psychopathologisation with no DSM parallel (the DSM retains gender dysphoria among its disorders). Convergence has also occurred: prolonged grief disorder now appears in both, added to ICD-11 and written into the DSM at its 2022 text revision.

ENTITY	ICD-11	DSM-5-TR
Complex PTSD	**Separate diagnosis**	Not a separate diagnosis
Gaming disorder	**Recognised diagnosis**	Section III, for further study only
Prolonged grief disorder	Included	Added at the 2022 text revision
Catatonia	**Independent grouping**	Specifier or associated with other disorders
Gender incongruence	**Moved out of mental disorders (sexual-health chapter)**	Gender dysphoria retained as a disorder
Bipolar type II	Named category	Named category
Personality disorder	**Single diagnosis, dimensional (severity plus traits)**	Ten categorical types (Section II); dimensional model in Section III

Selected content and placement differences. The shaded cells mark the distinctively ICD-11 positions; prolonged grief disorder is the notable convergence, now in both systems.

24.5 The personality-disorder models: the sharpest divergence

Nowhere do the two systems part company more completely than on personality disorder. ICD-11 abolished the traditional named types outright. There is no longer a paranoid, schizoid or histrionic personality disorder; instead there is a single diagnosis, **personality disorder**, graded by severity into one of three levels (mild, moderate or severe), to which the clinician may then add trait-domain qualifiers. There are five such trait domains in ICD-11 (negative affectivity, detachment, dissociality, disinhibition and anankastia), plus a separate borderline pattern qualifier retained for its treatment relevance. DSM-5-TR, by contrast, kept the older architecture in its main text: ten categorical personality-disorder types arranged in three clusters (A, the odd-eccentric; B, the dramatic-erratic; C, the anxious-fearful), diagnosed by operationalised criteria like any other DSM disorder. The DSM's own dimensional answer, the Alternative Model of Personality Disorders, lives only in Section III and rates a level of personality functioning against five pathological trait domains (negative affectivity, detachment, antagonism, disinhibition and psychoticism). So both offer a five-domain dimensional scheme, but ICD-11 has made it the official diagnosis while the DSM keeps it in reserve behind its categorical types. The deeper clinical use of these models for the personality disorders themselves is developed in the Personality disorders notes.

FEATURE	ICD-11	DSM-5-TR (SECTION II)
Structure	**One diagnosis, dimensional**	Ten categorical types
Severity	**Graded: mild, moderate, severe**	Not graded (present or absent)
Trait domains	Five, plus a borderline pattern qualifier	Five, but only in the Section III alternative model
Named types	**Abolished**	Retained in three clusters (A, B, C)

The personality-disorder models. ICD-11 replaced the categorical types with a severity-plus-traits dimensional diagnosis; DSM-5-TR keeps the ten categorical types up front and files its five-domain dimensional model in Section III.

TRAP **Saying ICD-11 kept the categorical personality types.** It did not: ICD-11 abolished the named types (paranoid, schizoid and the rest) and replaced them with a single personality-disorder diagnosis graded by severity with trait qualifiers. It is the DSM-5-TR main text that still runs the ten categorical types; the DSM's dimensional model is the one sitting in reserve, in Section III.

24.6 The Indian and global implication

For most of the world, including India, the ICD is the official system. India is a WHO member state, so the ICD is the classification used for the country's official health statistics and reporting, and Indian psychiatric training, clinical documentation and postgraduate examinations are ICD-based; the DSM is read and used chiefly in research and in the literature. This is not an incidental point but the reason ICD-11's design choices matter here. Its global-health orientation, its intended use from the primary-care worker upward, its multilingual availability and its built-in attention to cultural presentations all fit a country with a vast primary-care burden, many languages and diverse idioms of distress far better than a single-nation specialist manual would. The candidate should therefore treat ICD-11 as the working home system and the DSM-5-TR as the harmonised research reference to be cross-mapped, which is exactly how this chapter, and the accompanying figure, present them. The wider transcultural frame of the cultural concepts of distress is developed in the Consultation-liaison, geriatric and transcultural psychiatry notes.

INDIA

Because ICD is the notified reporting standard and the training classification in India, a candidate who has drilled only DSM criteria is answering in the wrong dialect. The examinable move is to diagnose forward in ICD-11, using its essential features and clinical judgement, and to bring in the DSM's operationalised criteria only to cross-check or to cite a research finding. ICD-11's inclusion of culture-related features in each disorder entry, and its primary-care and multilingual reach, also sit closer to Indian practice, where presentation, language and explanatory model vary widely and a rigid imported symptom count can mislead.

06
ICD-11 CHAPTER FOR MENTAL, BEHAVIOURAL AND NEURODEVELOPMENTAL DISORDERS

3
SECTIONS OF DSM-5-TR (BASICS; CRITERIA AND CODES; EMERGING MEASURES AND MODELS)

5
ICD-11 PERSONALITY TRAIT DOMAINS, PLUS A BORDERLINE PATTERN QUALIFIER

2022
ICD-11 CAME INTO EFFECT; DSM-5-TR ALSO PUBLISHED

GOOD TO REMEMBER

- **The principle:** ICD-11 (WHO, all of health, global, Chapter 06) and DSM-5-TR (APA, mental disorders only, specialist and research) classify the same disorders but were built by different bodies for different purposes, harmonised in content yet opposed in format.
- **The one discriminator:** ICD-11 gives prose essential features with no operationalised counts and trusts clinical judgement; DSM-5 uses operationalised criteria with explicit symptom counts and durations.
- **The one exam fact:** ICD-11 abolished the categorical personality-disorder types for a single severity-graded, five-trait-domain dimensional diagnosis, while DSM-5-TR keeps the ten categorical types in its main text and confines its dimensional model to Section III; in India the ICD is the official system.

HOLD THIS

The dividing line is format: ICD-11 sets out essential features with no operationalised counts and leaves the call to clinical judgement, whereas DSM-5 uses operationalised criteria with fixed symptom counts and durations; and in India, as across most of the world, the ICD is the official classification.

25 · The categorical-versus-dimensional debate

Every diagnostic manual must answer one prior question before it names a single disorder: does psychopathology come in **kinds** or in **degrees**? This is the categorical versus dimensional debate, and settling it is the **nosology call** that shapes the entire architecture of a classification. A categorical system sorts patients into discrete named boxes, present or absent; a dimensional system rates each patient along continuous scales of severity and trait, as intelligence is rated by an IQ score rather than by "clever, average, dull". The examiner tests this as understanding rather than recall, so the marks go to the candidate who can state what each model buys, why neither is provably correct, and how the modern systems have quietly moved to a hybrid.

Why the debate is live. The categorical model has held the clinic for a century because it is usable, but its cracks (arbitrary thresholds, heterogeneous categories, rampant comorbidity, and the not-otherwise-specified overflow) drove the field toward dimensions. The settled answer in both manuals is a hybrid, most visibly in the personality disorders; beyond the manuals sit two research programmes that abandon categories altogether, HiTOP and RDoC. The accompanying figure sets the box against the sliders. This page takes the core contrast first, then each model and its limits in turn, the hybrid the manuals have settled on, and finally the two fully dimensional research frameworks.

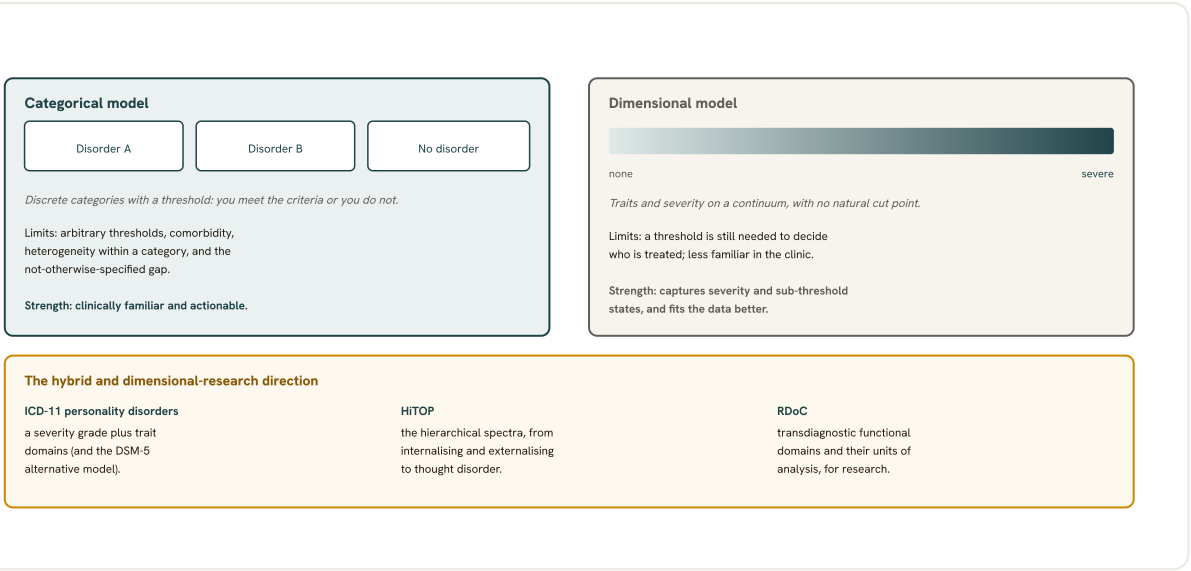


Fig 19.16 Categorical versus dimensional classification. The categorical model, used by the working manuals, sorts presentations into discrete diagnostic categories separated by a threshold: clinically familiar and actionable, but forced to draw arbitrary lines, and answerable for the comorbidity, the heterogeneity within a category and the not-otherwise-specified cases it generates. The dimensional model places traits and severity on a continuum, which fits the data better and captures sub-threshold states, but still needs a cut point to decide who is treated and is less familiar at the bedside. The field is converging on hybrids: ICD-11 already grades personality-disorder severity with trait domains, and the research frameworks HiTOP (hierarchical spectra) and RDoC (transdiagnostic functional domains) push the dimensional programme further.

25.1 The two models: a box, or a set of sliders

Two ways to describe the same patient. The **categorical model**, the one psychiatry actually runs on, places a patient inside a discrete class: the criteria are met or they are not, and the diagnosis is a noun. The dimensional model instead scores the patient on one or more continua, as blood pressure or intelligence is scored, so the description is a set of positions rather than a box. Neither is provably right. There is no statistical test that decides between a kind and a degree; the choice is pragmatic, made on which is more useful for the task at hand. The strongest evidence that would justify a true category is a **zone of rarity**, a natural gap in the distribution between one syndrome and its neighbour, as Kendell and Jablensky framed it. Searches for such gaps between related disorders have largely failed, and the ease with which clinicians reach for hybrid labels such as schizoaffective disorder is itself a sign that the categories shade into one another along a **spectrum**.

RULE **Categories are for use; dimensions are for accuracy.** A category is easy to remember, to communicate and to act on; a dimension preserves information and imposes no false boundary. Because both claims are true, the field's answer is not to pick one but to combine them.

PEARL

The debate is older than psychiatry. The Platonic ideal of classification was an exhaustive set of mutually exclusive categories; the Aristotelian view saw overlapping entities separated from normality only by arbitrary thresholds, which is the dimensional intuition in embryo. Kraepelin's disease categories are the Platonic inheritance; the modern turn to severity and traits is the Aristotelian one returning.

25.2 The categorical model: its clinical utility and its four discontents

Why the clinic keeps the category, and where it breaks. The categorical model earns its place: a single term compresses a mass of clinical information into a word two clinicians can exchange, it fits medical tradition and a conservative profession, and it is a ready prelude to action, since a named diagnosis implies a treatment. But four well-rehearsed problems, each a stock exam point, expose its limits, and each is an argument the dimensional camp turns against it.

DISCONTENT	WHAT GOES WRONG
Arbitrary thresholds	**The symptom count or duration rule (any five features, a two-week or six-month floor) draws a line across a continuum where nature shows no step; a patient one symptom short is called well**
Within-category heterogeneity	Polythetic criteria let two patients share a diagnosis with few or no symptoms in common, so the category is internally mixed rather than a uniform kind
Comorbidity	**Once hierarchical exclusions were relaxed, patients routinely meet several categories at once, suggesting the boxes cut one underlying disturbance into artificial pieces**
The not-otherwise-specified overflow	The more precise and restrictive the criteria, the more real patients fall between them into vague residual codes; "depressive disorder NOS" was once the commonest diagnosis made by North American psychiatrists

The four discontents of the categorical model. Arbitrary thresholds and comorbidity are the two most examined; the NOS overflow is the everyday symptom of categories that do not fit real patients.

TRAP **Forcing a categorical label where a dimensional formulation fits.** A patient who sits between two categories, or one symptom short of a threshold, is not diagnosis-free; the mixed and subthreshold presentations are exactly where a severity-and-trait description carries more truth than a box.

25.3 The dimensional model: its strengths and its clinical-utility limits

More information, at a price the clinic has been slow to pay. The dimensional model's strengths are the mirror of the categorical faults. It preserves fine distinctions rather than discarding them at a threshold; it handles boundary and mixed cases without distortion; it imposes no false discontinuity where the data show none; and it converts back to a category whenever a decision demands one, simply by applying a cut-off. Its costs are equally real, and clinical, which is why the clinic has resisted a wholesale switch.

DIMENSIONAL STRENGTHS	DIMENSIONAL CLINICAL-UTILITY LIMITS
Retains information lost at a categorical threshold	**A profile of scores is harder to remember and communicate than a single name**
Handles boundary, mixed and sub-threshold cases without forcing	**Does not map cleanly onto the yes-or-no decisions medicine makes (admit, treat, certify)**
Imposes no false boundary; convertible to a category by a cut-off	Reimbursement, health statistics and the medico-legal record still demand a categorical code
Tracks change and severity over time on the same scale	Clinicians trained on prototypes find a slider array unfamiliar and slow at the bedside

The dimensional trade-off. Dimensions win on accuracy and on not distorting patients who sit between classes; categories win on usability and on fitting the binary decisions of clinical medicine.

The honest summary is that dimensions win on accuracy and categories win on usability, and a working classification needs both. That is why the debate is no longer "which wins" but "how they combine".

25.4 The hybrid direction in the manuals: personality disorder leads

Both current manuals keep the box and bolt on the sliders, and personality disorder is where they went furthest. The manuals retain categorical diagnoses for usability while adding dimensional measures for severity and cross-cutting symptoms; the sharpest example is the personality disorders, where the categorical types finally collapsed under their own heterogeneity and comorbidity. ICD-11 abolished the named personality types outright and replaced them with a single diagnosis, **personality disorder**, graded into one of three severity levels (mild, moderate or severe, with a sub-threshold "personality difficulty" below them), to which the clinician may add trait qualifiers. There are **five** ICD-11 trait domains, negative affectivity, detachment, dissociality, disinhibition and anankastia, plus a borderline pattern qualifier kept for its treatment value. DSM-5-TR took the cautious route: it kept the ten categorical types in its main text and filed its dimensional answer, the alternative model of personality disorders, in Section III. That model rates a level of personality functioning (Criterion A, covering self and interpersonal functioning) against **five** pathological trait domains (Criterion B: negative affectivity, detachment, antagonism, disinhibition and psychoticism), comprising twenty-five facets. Both, then, describe a five-domain dimensional scheme; ICD-11 has made it the official diagnosis, while the DSM keeps it in reserve behind the categorical types. The deeper clinical use of these models for the personality disorders themselves belongs to the Personality disorders notes.

FEATURE	ICD-11	DSM-5-TR
Categorical types	Abolished; single "personality disorder" diagnosis	**Retained: ten types in three clusters (main text)**
Severity grading	Mild, moderate, severe (plus "personality difficulty")	**Present or absent; level of functioning only in the alternative model**
Trait scheme	Five domains, the official diagnosis, plus borderline pattern	Five domains, in the Section III alternative model only
Status	Dimensional model is the working diagnosis	**Dimensional model held in reserve behind the categories**

The hybrid, seen at personality disorder. ICD-11 made the dimensional model its official diagnosis; DSM-5-TR keeps the ten categorical types up front and files its five-domain alternative model in Section III.

INDIA

India, as a World Health Organization member state, uses the ICD as its official diagnostic and statistical classification, so it is ICD-11's dimensional personality diagnosis, severity plus traits, that now carries clinical and statutory weight in Indian practice rather than the DSM's reserved model. The Mental Healthcare Act 2017 directs that a determination of mental illness be made in accordance with nationally or internationally accepted medical standards, including the latest edition of the ICD, tying the Indian clinical-legal frame to the WHO system (the full statute is developed in the Mental health legislation and forensic psychiatry notes). ICD-11's flexible, severity-based scheme also sits more easily with India's cultural concepts of distress and its multilingual, resource-varied settings than a rigid categorical count would (the wider frame is set out in the Consultation-liaison, geriatric and transcultural psychiatry notes).

25.5 HiTOP: the Hierarchical Taxonomy of Psychopathology

A classification built from the data up, not from the committee down. Where the manuals start with expert-defined categories, the HiTOP model, the Hierarchical Taxonomy of Psychopathology, codified by Kotov and colleagues in 2017, starts from the observed covariation of symptoms and lets the structure emerge. Symptoms that co-occur are grouped into syndromes, and correlated syndromes into **spectra**; comorbidity is not a nuisance here but the very signal used to build the higher levels. The result is a dimensional hierarchy. At the base sit individual signs, symptoms and maladaptive traits; above them components and syndromes (the old disorders); then subfactors; then the broad spectra; and at the apex a general factor of psychopathology, the p factor, capturing a person's overall liability to disorder. The principal spectra run from internalising, through thought disorder and detachment, to the externalising spectra, a continuum that replaces sharp diagnostic borders with graded position. HiTOP reorganises the very clinical material the DSM contains, agnostic to its categories, so a patient placed on these continua can be compared and followed without the arbitrary thresholds and comorbidity artefacts of the categorical system.

HITOP SPECTRUM	WHAT IT GATHERS
Internalising	**The distress and fear conditions: depression, the anxiety disorders, and related eating pathology**
Thought disorder	Psychoticism and reality-testing failure: the schizophrenia-spectrum and psychotic features
Detachment	Social withdrawal, anhedonia and interpersonal disengagement
Disinhibited externalising	**Substance use and impulse-control problems; failures of restraint**
Antagonistic externalising	Aggression, manipulation and antisocial conduct
Somatoform	Bodily-distress and somatic-symptom presentations (a provisional spectrum)

The principal HiTOP spectra, with a general factor of psychopathology (the p factor) above them. Internalising and externalising are the best-validated poles; the continuum, not the boundary, is the unit.

25.6 RDoC: the Research Domain Criteria

Not a diagnostic system at all, but a research framework that ignores diagnoses. The RDoC project, the Research Domain Criteria, launched by the United States National Institute of Mental Health under Cuthbert and Insel in 2009 (its influential seven-pillars statement following in 2013, the year DSM-5 appeared), is dimensional in a deeper sense than HiTOP: it abandons clinical categories entirely and starts from basic neuroscience, asking which brain-and-behaviour systems, studied across the whole range from normal to abnormal, underlie psychopathology across diagnoses. It is arranged as a matrix. The rows are functional *constructs* grouped into a small set of *domains*, originally five (negative valence systems, positive valence systems, cognitive systems, social processes, and arousal and regulatory systems), now six with the addition of sensorimotor systems. The columns are the **units of analysis**, the seven levels at which any construct can be measured, running genes, molecules, cells, circuits, physiology, behaviour and self-report, with a further paradigms column for the tasks used. The intent is transdiagnostic and mechanistic: study fear, or reward, or working memory, as each varies across the population and across these levels, rather than starting from a DSM label. RDoC is explicitly not intended for clinical diagnosis; it is a scaffold for the research that might one day rebuild the nosology on mechanisms rather than on described syndromes.

RDOC DOMAIN	THE SYSTEMS IT COVERS
Negative valence systems	**Responses to aversive situations: acute and potential threat (fear, anxiety), loss, frustrative non-reward**
Positive valence systems	Reward: approach, valuation, effort, learning and habit
Cognitive systems	Attention, perception, working memory, cognitive control and language
Social processes	Affiliation and attachment, social communication, perception of self and others
Arousal and regulatory systems	Arousal, circadian rhythms, sleep and wakefulness, homeostatic regulation
Sensorimotor systems	Control, execution and refinement of motor behaviour (the domain added most recently)

The RDoC domains (originally five; sensorimotor systems added later), each studied across seven units of analysis from genes to self-report. A research matrix, not a clinical classification.

TRAP **Treating HiTOP or RDoC as ready-made diagnostic systems.** Neither is a classification you can diagnose a patient with today. HiTOP is a research taxonomy of dimensions built from symptom covariation; RDoC is a neuroscience research framework that is explicitly not for clinical diagnosis. The clinic still runs on the categorical ICD-11 and DSM-5-TR, hybridised with dimensions.

3
ICD-11 PERSONALITY SEVERITY GRADES (MILD, MODERATE, SEVERE)

5
ICD-11 TRAIT DOMAINS, MATCHED BY FIVE DSM-5 ALTERNATIVE-MODEL DOMAINS

6
RDOC FUNCTIONAL DOMAINS (THE ORIGINAL FIVE PLUS SENSORIMOTOR)

7
RDOC UNITS OF ANALYSIS, GENES TO SELF-REPORT

GOOD TO REMEMBER

- **The principle:** the categorical model classifies by kind and wins on clinical usability; the dimensional model classifies by degree and wins on accuracy; no statistical test settles which is correct, so both current manuals are categorical-dimensional hybrids, most fully at personality disorder.
- **The one discriminator:** HiTOP versus RDoC. HiTOP is a descriptive taxonomy that reorganises symptoms bottom-up into spectra (internalising, thought disorder, externalising) from their covariation; RDoC starts top-down from neuroscience constructs measured across units of analysis and is explicitly not for clinical diagnosis. Both are research frameworks, not clinical systems.
- **The one exam fact:** ICD-11 abolished the categorical personality types for a single diagnosis graded into three severity levels plus five trait domains; DSM-5-TR keeps ten categorical types in its main text and its five-domain alternative model in Section III; HiTOP arranges psychopathology into spectra under a general p factor; RDoC into six domains across seven units of analysis.

HOLD THIS

No test proves psychopathology is kinds rather than degrees, so the categorical versus dimensional call is pragmatic: categories for clinical usability, dimensions for accuracy, hybrids in ICD-11 and DSM-5-TR (severity plus traits at personality disorder), with HiTOP and RDoC the fully dimensional research programmes waiting in the wings.

26 · Comorbidity and the boundary problem

Once psychiatry relaxed its old diagnostic hierarchy and let clinicians record every disorder a patient meets, **comorbidity** stopped being suppressed and started being counted, and the counts turned out to be enormous. This short topic teaches what those high numbers actually mean: how much of the co-occurrence is real and how much is an artefact of the way our manuals carve distress into categories, and how that question opens onto the deeper **boundary problem**, the difficulty of finding a clean edge between one disorder and the next, and between disorder and normality. The examiner uses this material to test whether a candidate can think about classification rather than merely apply it, so the marks go to whoever can separate *true* from *artefactual* co-occurrence and say why the boundaries stay blurred.

How to use this page. Fix three moves. First, the meaning of comorbidity and the true-versus-artefactual split. Second, the boundary problem itself, built from **diagnostic overlap**, the old **splitting versus lumping** tension, and the **heterogeneity** that polythetic criteria leave inside every category. Third, what all this implies for classification: the drift toward a hybrid categorical-dimensional system. This sits alongside the broader account of category, prototype and the reliability-validity distinction in the classification-principles material; here the focus is narrowed to the single fault line of comorbidity and boundaries.

26.1 How common comorbidity is, and what it means: true versus artefactual

Comorbidity is the co-occurrence of two or more diagnoses in one patient, and it is the rule, not the exception. Community surveys such as those of Kessler showed the pattern is pervasive: roughly half of all patients meeting criteria for major depressive disorder also meet criteria for an anxiety disorder, and a person who qualifies for one disorder is far more likely than chance to qualify for another. The important examinable step is not the number but the interpretation, because the term covers two quite different situations. **True comorbidity** is real co-occurrence: either two genuinely separate disorders arising together by chance (the causally unrelated case, such as a presenile dementia beginning in someone with long-standing panic disorder), or two distinct clinical pictures that share one underlying process but are diagnosed separately for want of knowledge or by convention. **Artefactual comorbidity**, by contrast, is not two diseases at all: it is a by-product of how the classification is written, arising either when one broad condition is split across several narrow categories that then appear to "co-occur", or when overlapping criteria let the same symptom count toward two diagnoses at once. It has been argued that a good deal of psychiatric comorbidity is exactly this artefact of diagnostic rules that permit, if not encourage, multiple diagnoses (Maj, 2005), and that a simpler system reducing it would be preferable (Goldberg, 2010).

READING OF A COMORBID PAIR	MECHANISM	WORKED INSTANCE
True (chance)	Two causally unrelated disorders happen to co-occur	**A presenile dementia arising in a person with long-standing panic disorder**
True (shared cause)	One underlying process, two manifestations diagnosed separately for want of knowledge	An anxious and a depressive syndrome expressing one common vulnerability
Artefactual (splitting)	The manual carves one condition into several narrow categories that then "co-occur"	**A broad internalising syndrome recorded as separate depressive and anxiety diagnoses**
Artefactual (overlap)	Shared symptoms are counted toward two criteria sets at once	**A single personality disorder whose features straddle two overlapping criteria sets**

The two readings of any comorbid pair. True comorbidity is real co-occurrence; artefactual comorbidity is a by-product of how the manual splits and overlaps its categories (Maj, 2005).

RULE **Comorbidity means both criteria sets are fully met.** The term applies only when a patient satisfies the criteria for two or more distinct diagnoses; a patient who falls between categories and meets none is not comorbid but sub-threshold, and calling that comorbidity is an error.

TRAP **Reading every comorbid pair as two real diseases.** Much apparent comorbidity is artefactual, the product of splitting one condition across overlapping criteria, so counting diagnoses is not the same as counting diseases; the clinician still asks whether one formulation explains the whole picture.

26.2 The boundary problem: diagnostic overlap, splitting versus lumping, heterogeneity

High comorbidity is a symptom of a deeper condition: the categories do not have clean edges. This is the **boundary problem**, and it operates at two frontiers at once, the boundary between one disorder and its neighbours, and the boundary between disorder and normality. The strongest test of whether a syndrome-defined category is real is whether it is separated from related syndromes, and from health, by a zone of rarity, a genuine gap in the distribution where intermediate cases become uncommon (Kendell and Jablensky, 2003). For most disorders that gap cannot be found: attempts to demonstrate zones of rarity between related syndromes, or between illness and health, have largely failed, and the frequency with which clinicians reach for intermediate labels such as schizoaffective is itself evidence that symptom patterns merge into one another rather than sitting in discrete clusters. The unsettling implication is that the *validity* of many categories remains unproven even where their clinical *utility* is not in doubt. Learn the boundary vocabulary as crisp definitions.

Diagnostic overlap

Two categories share symptoms, so the same clinical feature can satisfy criteria for more than one disorder; overlap manufactures artefactual comorbidity and blurs the line between the categories.

Splitting versus lumping

The perennial tension between the "splitter", who prefers many narrow, homogeneous categories, and the "lumper", who prefers few broad ones. More splitting buys finer distinctions but multiplies

apparent comorbidity; more lumping cuts comorbidity but hides real differences inside each category.

Heterogeneity
The variety of patients who share a single diagnosis. Because criteria sets are polythetic (any specified subset suffices), two people can hold the same label with almost no symptoms in common, so a category name conceals a mixed population.

Boundary with normality
The absence of a natural cut between the disordered and the well; where symptoms shade continuously into ordinary experience, any threshold for "caseness" is a pragmatic convention rather than a discovered line.

Splitting and lumping trade the two problems against each other and neither dissolves the boundary. A splitter reduces heterogeneity inside each category but drives comorbidity up, because a patient's features now spill across several narrow neighbours; a lumper suppresses comorbidity but pays for it with wider heterogeneity inside each broad class. Because there is no zone of rarity to arbitrate, no split is provably the right one, which is why the accompanying figure sets two related syndromes as overlapping distributions with no clean valley between them.

26.3 What it implies for classification

The way out is not a better boundary but a change of instrument. If related disorders shade into one another and into normality, a purely categorical system will always generate the tell-tale strains, and the current manuals name them plainly. The limitations the categorical approach runs into are a stock list: the failure to find zones of rarity, the recurring need for intermediate categories such as schizoaffective disorder, high rates of comorbidity, the frequent resort to "other" and "unspecified" diagnoses, the weak yield of unique validators, and the lack of treatment specificity across categories (DSM-5-TR). The agreed response is not to abandon categories, which remain indispensable for the yes-or-no decisions of clinical work, but to add a dimensional layer on top of them: severity ratings and cross-cutting symptom measures that capture the **heterogeneity** a single label hides, and that describe the patient who sits on a boundary without forcing a false choice. This hybrid, categorical diagnoses with dimensional additions, is the direction of both current systems, and it is the field's practical answer to a boundary problem it cannot solve outright.

PEARL

Comorbidity rates did not rise because patients got sicker; they rose because the classification changed. When DSM-III and its successors relaxed the old hierarchical exclusions that had forced one diagnosis per patient, the co-occurrences that the hierarchy used to suppress became recordable, and the numbers appeared to soar. High comorbidity is partly a measurement effect of a permissive counting rule, which is exactly why the artefactual share is worth naming.

50%	2	6
OF MAJOR DEPRESSIVE DISORDER PATIENTS ALSO MEET CRITERIA FOR AN ANXIETY DISORDER (KESSLER)	READINGS OF ANY COMORBID PAIR: TRUE CO-OCCURRENCE VERSUS ARTEFACTUAL	LIMITATIONS OF THE CATEGORICAL APPROACH LISTED BY DSM-5-TR

INDIA

India, as a World Health Organization member state, classifies with the *ICD*, and the Mental Healthcare Act 2017 ties the determination of mental illness to internationally accepted standards including the latest ICD, so the boundary and comorbidity questions here are asked in ICD terms. The comorbidity most examined in Indian practice is dual diagnosis, the co-occurrence of a substance use disorder with another mental illness, and the standard caution is a true-versus-artefactual one in clinical dress: a substance-induced psychiatric state is *secondary*, not true comorbidity, so it must be distinguished from an independent disorder that merely co-occurs (the fuller treatment sits in the Substance use disorders notes). ICD-11's flexible, prototype-based essential features, built to tolerate cultural variation and clinical judgement, also handle boundary and mixed cases more gracefully than a rigid criteria count.

GOOD TO REMEMBER

- **The principle:** comorbidity, the co-occurrence of two or more diagnoses in one patient, is common (about half of depressed patients also meet criteria for an anxiety disorder) and is partly a real phenomenon and partly an artefact of how the classification is written.
- **The one discriminator:** true comorbidity is real co-occurrence (two independent disorders by chance, or two manifestations of one shared process), whereas artefactual comorbidity is a by-product of splitting one condition across several categories or of overlapping criteria (Maj, 2005).
- **The one exam fact:** the boundary problem is the failure to find zones of rarity between related syndromes and between disorder and normality (Kendell and Jablensky, 2003), which leaves category validity unproven despite clinical utility and drives the field toward a hybrid categorical-dimensional classification.

HOLD THIS

Psychiatric comorbidity is partly true co-occurrence and partly artefactual, the artefact of splitting one condition across overlapping criteria; because no zone of rarity separates related syndromes or marks off normality, the boundary problem cannot be solved by a better line and is instead met with a hybrid categorical-dimensional system.

27 · Cultural concepts of distress and culture-bound syndromes

Distress is never expressed in a cultural vacuum: the words a patient reaches for, the cause they blame, and the very shape of their symptoms are all patterned by the culture they live in. This page teaches the modern framework for that fact, the DSM-5 shift from the old, exoticising language of **culture-bound syndromes** to the broader idea of **cultural concepts of distress**, together with the assessment tool built to elicit it, the **cultural formulation** and its Cultural Formulation Interview. The examiner tests three things: that you can name and separate the three *types* of cultural concept, that you can define the classic examples (with the Indian and Asian ones, **dhat** and **koro**, held tight), and that you can say why getting this right prevents misdiagnosis in either direction.

How to use this page. Fix the reframing first, because the whole topic turns on it: a culture-bound syndrome is a discrete exotic entity, whereas cultural concepts of distress is a wider, non-pejorative construct with three parts. Then learn the three types as crisp definitions, the eight

classic syndromes as a definitions list, and the cultural formulation and its interview as the clinical skill that operationalises all of it. Close on the clinical pay-off, avoiding both the false-positive (pathologising a culturally normative expression) and the false-negative (missing the disorder hidden behind a culturally-framed presentation). The wider transcultural frame of the cultural concepts of distress, its epidemiology, migration and acculturation, belongs to the Consultation-liaison, geriatric and transcultural psychiatry notes; here the treatment stays at the level of the concepts themselves and the formulation that captures them.

27.1 From culture-bound syndromes to cultural concepts of distress

The DSM-5 retired a term it judged both narrow and pejorative. The older phrase culture-bound syndromes, still the term ICD-10 uses, named a set of illnesses thought to be locked to particular cultures and geographical areas and not seen in the developed West: dhat, koro, latah, amok, piblokto, wihtigo and their kin. DSM-5 and DSM-5-TR replaced it with cultural concepts of distress for two reasons. First, the old label *exoticised* non-Western presentations while quietly pretending that Western diagnostic categories are culture-free, when in truth the DSM's own diagnoses are themselves evolving Western cultural syndromes. Second, "syndrome" captured only one of the ways culture shapes distress; culture also patterns how people *talk* about suffering and how they *explain* it. The new construct therefore has three components, and naming all three is the reliable opening to any answer here.

Cultural syndrome

A cluster of co-occurring symptoms recognisable to, and often named by, a particular cultural group (for example, ataque de nervios). It may or may not be treated locally as an illness.

Cultural idiom of distress

A shared way of *talking about* suffering, a linguistic or somatic vocabulary common in a cultural group (for example, "thinking too much," or "butterflies in the stomach").

Cultural explanation or perceived cause

A shared **explanatory model** of what is wrong and why, the culturally patterned attribution of a symptom to a cause (for example, semen loss, soul loss, or a chemical imbalance).

The three are functions, not fixed boxes: the same term routinely serves more than one at once, and a term can migrate between them over time. "Depression" names a syndrome in one mouth and works as a plain **idioms of distress** in another. This is the point the examiner wants: cultural concepts of distress is a broader, more honest and less pejorative construct than culture-bound syndromes, of which the classic syndromes are merely the syndrome-shaped subset.

RULE **Three types, not one.** Cultural concepts of distress subsume cultural *syndromes* (clusters of symptoms), cultural *idioms* of distress (ways of talking about suffering) and cultural *explanations* or perceived causes (explanatory models). The old "culture-bound syndrome" covered only the first.

27.2 The three types, and Kleinman's explanatory model

Separate the cluster, the vocabulary and the cause. The distinction earns its keep clinically because each type is elicited by a different question and each misleads in a different way. A

cultural *syndrome* gives you a recognisable pattern, but that pattern may map onto more than one biomedical diagnosis, or none. A cultural *idiom* gives you the patient's language, which is why a somatic idiom ("my body burns," "gas rises to my head") so often brings anxiety or depression to a physician's door dressed as a bodily complaint. A cultural *explanation* gives you the perceived cause, and this is where the single most examinable name in the topic sits: the explanatory model of illness, pioneered by Arthur Kleinman. Kleinman's insight was that the clinician's biomedical model and the patient's model of the same illness frequently differ, and that eliciting the patient's model, what they call the problem, what they believe causes it, how severe and how long they expect it to run, and what treatment they want, is essential to engagement, adherence and accurate diagnosis.

TYPE	WHAT IT IS	WORKED EXAMPLE
Cultural syndrome	A recognisable cluster of co-occurring symptoms	**Ataque de nervios; dhat syndrome**
Cultural idiom of distress	A shared vocabulary for expressing suffering	**"Thinking too much"; kufungisisa**
Cultural explanation / perceived cause	A shared explanatory model of the cause	**Semen loss (dhat); soul loss (susto)**

The three components of cultural concepts of distress. The same cultural term (for example dhat, or "thinking too much") can act as more than one type at once.

PEARL

The clean viva line: a cultural *syndrome* is a set of symptoms, a cultural *idiom* is a set of words, and a cultural *explanation* is a claimed cause. Kleinman's explanatory model belongs to the third: it is the patient's own theory of their illness, and eliciting it is the engine of the whole cultural assessment.

27.3 The classic examples

Learn each as a one-line definition anchored to its region. DSM-5-TR gives **ten** illustrative examples (ataque de nervios, dhat, hikikomori, khyal cap, kufungisisa, maladi dyab, nervios, shenjing shuairuo, susto and taijin kyofusho), but the classic examinable set blends these with the older culture-bound roster. Hold the two Indian and Asian entries hardest, because they are the ones most likely to walk into an Indian clinic.

Dhat syndrome (dhat)

Indian subcontinent. Anxious preoccupation with the passage of a whitish discharge in the urine, believed to be semen, with fatigue (asthenia) and multiple somatic symptoms, rooted in the traditional belief that semen is a precious vital fluid whose loss weakens the body.

Koro

Asia, including India. A sudden, intense fear that the penis (or, in women, the breasts or vulva) is shrinking or retracting into the body and that death will follow; characteristically occurs in epidemics that spread rapidly through a community.

Amok

South-East Asia, classically Malaysia. A sudden, unprovoked outburst of homicidal rage in which the person "runs amok," attacking or killing indiscriminately, typically followed by exhaustion and amnesia for the episode.

Latah

South-East Asia, classically Malaysia and Indonesia, chiefly in women. An exaggerated startle response to a sudden stimulus, followed by echolalia, echopraxia and automatic obedience; the Japanese analogue is imu.

Ataque de nervios

Latinx contexts. An episode of intense emotional upset with uncontrollable screaming or crying, trembling, heat rising in the chest into the head, aggression and, in some, seizure-like or dissociative features; the hallmark is a sense of being out of control, usually triggered by a family stressor.

Brain fag

West Africa, Nigeria (described by Raymond Prince). Mental fatigue, difficulty concentrating and remembering, and head or neck discomfort, attributed to the strain of study and seen classically in students.

Taijin kyofusho

Japan. An intense fear that one's own body, its parts, odour, gaze or facial expression, will offend, embarrass or displease other people; an other-focused counterpart to social anxiety disorder.

Susto

Latin American contexts. "Fright" or "soul loss," an illness attributed to a frightening event that causes the soul to leave the body, with sadness, disturbed sleep and appetite, low self-worth and somatic symptoms.

INDIA

The two syndromes an Indian examiner will press are dhat and koro. Dhat is the paradigmatic South Asian culture-bound syndrome, classically described in Indian descriptive psychiatry (N.N. Wig), and ICD-10 files it under the "other specified neurotic disorders." Its cultural logic is a genuine explanatory model: the belief that semen is a concentrated, precious essence means its perceived loss is expected to produce weakness, so the patient presents with fatigue, somatic symptoms and sexual worry rather than a complaint of "anxiety." Koro too is seen in India and across Asia and can erupt in local epidemics. Beyond these, the Indian literature also names *suchi-bai* (a purity or washing preoccupation), the ascetic syndrome, nuptial psychosis and jhinjhinia. The clinician's task is not to collect these as curios but to recognise the explanatory model behind them so the underlying, often treatable, anxiety or depression is addressed rather than dismissed.

COMMON TRAP

Do not automatically upgrade a culturally sanctioned concern to a psychotic symptom. A koro conviction held in an epidemic within a community that shares the belief is not, on its own, a delusion in the thought-content sense; a dhat patient's semen-loss attribution is a shared explanatory model, not hypochondriacal delusion. Whether a belief is delusional turns on whether it is idiosyncratic and outside the person's subculture, exactly the distinction developed in the Psychometry, Assessment and Descriptive Psychopathology notes.

27.4 The cultural formulation and the Cultural Formulation Interview

Culture is captured by a structured formulation, not a hunch. The tool is the **cultural formulation**, introduced as the Outline for Cultural Formulation (OCF) in DSM-IV and carried into DSM-5, which places the patient's own experience at the centre of the assessment across five domains. DSM-5 then added its operational companion, the Cultural Formulation Interview (CFI): a semistructured, person-centred set of questions that gathers the information the OCF needs. The core interview runs **16** questions grouped into **four** sections; a CFI-informant version gathers the same from a relative, and a set of **twelve** supplementary modules (explanatory model, level of functioning, social network, psychosocial stressors, spirituality, cultural identity, coping and help-seeking, patient-clinician relationship, children and adolescents, older adults, immigrants and refugees, and caregivers) extend it. The CFI is applicable to every patient, not only to those from a visibly different background.

OCF DOMAIN	WHAT IT ASSESSES
Cultural identity of the individual	**Ethnicity, language, religion, migration and other identities, self-ascribed and ascribed**
Cultural conceptualisations of distress	The syndromes, idioms and explanatory models the patient uses (this is where cultural concepts of distress live)
Psychosocial stressors and cultural features of vulnerability and resilience	**Stressors, supports, the role of family and religion, and culturally-defined functioning**
Cultural features of the clinician-patient relationship	Differences in language, culture and status that shape rapport and trust
Overall cultural assessment	**How the above bears on diagnosis and on a culturally-appropriate management plan**

The five domains of the Outline for Cultural Formulation. The Cultural Formulation Interview is the semistructured instrument that gathers the information each domain requires.

MNEMONIC

PROBLEM · PERCEPTIONS · PAST · PRESENT

The four sections of the core CFI, in order: the cultural **definition of the problem**; cultural **perceptions** of cause, context and support; cultural factors in self-coping and **past** help-seeking; and cultural factors in **present** (current) help-seeking and treatment expectations.

3	4	16	10
TYPES OF CULTURAL CONCEPT: SYNDROMES, IDIOMS, EXPLANATIONS	SECTIONS OF THE CULTURAL FORMULATION INTERVIEW	QUESTIONS IN THE CORE CFI	ILLUSTRATIVE EXAMPLES LISTED IN DSM-5-TR

27.5 Why it matters: avoiding misdiagnosis in both directions

The cultural formulation exists to stop two opposite errors. The *false-positive* error is pathologising a culturally normative expression: an ataque de nervios at a funeral, or grief expressed through vivid somatic and dissociative features, is not automatically a psychiatric disorder, and DSM-5-TR is explicit that some ataques are normative expressions of acute distress

without clinical sequelae. The *false-negative* error is the mirror image and, in practice, the commoner one: mistaking the cultural packaging for the whole story and missing the treatable disorder inside it, reading a dhat presentation as mere "cultural belief" when a major depressive or anxiety disorder sits underneath, or dismissing a somatic idiom of distress as having no psychiatric content at all. The corrective is the same in both cases: elicit the explanatory model, situate the presentation in the patient's subculture, and let the cultural formulation, rather than the surface label, guide the diagnosis and plan.

WORKED EXAMPLE

A young man attends a general clinic complaining that "dhat is leaking" in his urine, that he is weak, cannot concentrate, and fears his marriage will fail. Taken at face value the presentation is a "cultural belief"; taken as an explanatory model it is a doorway. The Cultural Formulation Interview elicits his conviction that lost semen is draining his vitality (his cultural explanation), his family's shared endorsement of that model (context and support), and, behind it, two months of low mood, anhedonia, initial insomnia and hopelessness. The formulation names a depressive episode expressed through a dhat idiom, and management pairs education about semen physiology with treatment of the depression, rather than either scolding the belief or missing the illness.

TRAP **Treating "it's cultural" as a diagnosis or a dismissal.** Labelling a presentation a culture-bound syndrome is not the end of assessment; cultural concepts of distress frequently coexist with, and conceal, standard psychiatric disorders. The error runs both ways: pathologising the normative, or normalising the pathological.

GOOD TO REMEMBER

- **The defining principle:** DSM-5 replaced the narrow, pejorative "culture-bound syndromes" with *cultural concepts of distress*, a broader construct with three parts, cultural syndromes, cultural idioms of distress and cultural explanations or perceived causes (Kleinman's explanatory model).
- **The one discriminator:** a cultural *syndrome* is a cluster of symptoms, a cultural *idiom* is a way of talking about distress, and a cultural *explanation* is a claimed cause; the same term can serve more than one function at once.
- **The one exam fact:** the cultural formulation has five OCF domains and is elicited by the Cultural Formulation Interview (a core interview of sixteen questions in four sections); the classic Indian and Asian examples are dhat (semen-loss concern) and koro (fear of genital retraction), and the whole apparatus exists to prevent misdiagnosis in either direction.

HOLD THIS

Cultural concepts of distress (DSM-5, replacing culture-bound syndromes) come in three types, syndromes, idioms and explanatory models; they are captured by the cultural formulation and its 16-question, four-section Cultural Formulation Interview, and their clinical purpose is to stop the clinician both from pathologising the culturally normal and from missing the treatable disorder behind a dhat, koro or ataque presentation.

28 · The forensic essentials

When a psychiatrist steps into a courtroom the questions change shape: the court does not want a diagnosis, it wants a legal opinion, and the two are not the same thing. These **forensic**

psychiatry essentials gather the small cluster of medico-legal questions that recur in every exam, three of which do almost all the work. Can the accused be tried at all (**fitness to stand trial**)? Was the accused answerable for the act (**criminal responsibility** and the insanity defence)? Can a person make a valid will (**testamentary capacity**)? Each rests on a capacity test with a named authority, and the marks go to the candidate who states the test, the case behind it and the Indian provision without blurring one into another.

How to use this page. Fix the three capacities and the one time-frame rule that separates them, learn the two limbs of the insanity test and their Indian mirror, and hold the four-limb will test with its case name. This is the compact treatment; the fuller forensic material, narcoanalysis and the detailed assessment procedure, the review board and the admission provisions, and the wider statutes, lives in the Mental health legislation and forensic psychiatry notes, and this page cross-refers there rather than repeating it.

Fitness to stand trial

The accused's *present* capacity to understand the charge and the court proceedings and to instruct counsel; a here-and-now assessment, not a comment on the offence.

Criminal responsibility

Whether, *at the time of the act*, the accused was so disordered as to be excused from the guilty mind (mens rea) the offence requires; the insanity defence answers this.

Diminished responsibility

A partial defence: an abnormality of mind that substantially impaired responsibility, reducing murder to manslaughter rather than acquitting.

Testamentary capacity

The capacity to make a valid will, judged task-specifically at the time the will is made, under the Banks v Goodfellow test.

28.1 Fitness to stand trial: understand the charge, follow the proceedings, instruct counsel

Fitness to stand trial is a present-state question about the accused's ability to take part in the trial, not about the offence. The accused must be able to understand the nature of the charge, follow the course of the proceedings, and instruct and assist counsel in the defence; in English practice these are the Pritchard criteria for fitness to plead, and in the United States the parallel is the Dusky standard, a rational and factual understanding of the proceedings together with the ability to consult a lawyer. The decisive feature for the exam is the time-frame: fitness is assessed *here and now*, so a person may be perfectly fit to be tried today yet have been insane at the moment of the crime, or unfit today yet have been fully responsible then. When an accused is found unfit, the trial is postponed and the person is dealt with under the mental-health provisions rather than convicted.

28.2 Criminal responsibility and the insanity defence: the McNaughten rules

The insanity defence asks whether disease of the mind, at the time of the act, deprived the accused of the knowledge that makes an act blameworthy. English law defines this by the McNaughten rules (also spelled McNaughton or M'Naghten), framed by the House of Lords after Daniel McNaughten in **1843** shot and killed Edward Drummond, secretary to the Prime

Minister Sir Robert Peel, under a persecutory delusional system; he was found not guilty by reason of insanity and admitted to Bethlem Hospital, and the public outcry produced the rules. The test requires proof that, at the time of committing the act, the accused was labouring under such a defect of reason, from disease of the mind, as (the first limb) not to know the nature and quality of the act, or (the second limb) if he did know it, not to know that what he was doing was wrong. These are the two limbs of a purely *cognitive* test, the classic right-wrong test: it turns on whether the accused could *know*, never on whether he could *control* his conduct, so an irresistible impulse in someone who knew the act was wrong falls outside it.

WORKED EXAMPLE

A man with schizophrenia, driven by command voices and a fixed belief that his neighbour is an assassin sent to kill him, attacks and kills the neighbour convinced he is defending his own life. At the material time he did not know the act was wrong, so he satisfies the second limb of the insanity test and the Indian provision below. Contrast a man who strangles his wife in a jealous rage, knows perfectly well it is wrong, but says he "could not stop himself": knowledge is intact, so neither the McNaughten rules nor the Indian section excuses him, because there is no volitional (loss-of-control) limb.

RULE **Insanity is a legal verdict, not a diagnosis.** The McNaughten test is cognitive, whether the accused could know the nature of the act or that it was wrong; a psychiatric diagnosis by itself never exculpates, and there is no arm for loss of control.

28.3 The Indian frame: unsoundness of mind under Section 84 of the Indian Penal Code

India codifies the same cognitive test as a general exception to criminal liability. Section **84** of the Indian Penal Code, headed the act of a person of **unsound mind**, states that nothing is an offence which is done by a person who, at the time of doing it, by reason of unsoundness of mind, is incapable of knowing the nature of the act, or that he is doing what is either wrong or contrary to law. Two examinable points sit on top of the McNaughten mirror. First, the section adds the arm "or contrary to law", so incapacity as to *either* moral wrong *or* legal wrong will do. Second, the section covers legal insanity, not medical insanity: a diagnosis, even of florid psychosis, does not by itself attract the benefit; what must be shown is the incapacity to know at the material moment. The crucial time is the instant the act was committed (settled in Rattan Lal versus State of Madhya Pradesh), and the burden of proving unsoundness lies on the accused, on the preponderance of probability, after which the onus shifts to the prosecution.

CAPACITY	THE QUESTION IT ANSWERS	TIME FRAME	GOVERNING STANDARD
Fitness to stand trial	Can the accused understand the charge, follow proceedings and instruct counsel?	**Present (here and now)**	Pritchard criteria (England); Dusky standard (USA); NIMHANS proforma (India)
Criminal responsibility (insanity)	Was the accused so disordered as not to know the act's nature, or that it was wrong?	**At the time of the act**	McNaughten rules; Section 84 of the Indian Penal Code
Diminished responsibility	Did an abnormality of mind substantially impair responsibility for the killing?	At the time of the act	**English partial defence (murder reduced to manslaughter)**
Testamentary capacity	Can the person make a valid will?	When the will is made	**Banks v Goodfellow; Indian Succession Act 1925 (sound disposing mind)**

The forensic capacities separated by their time-frame: fitness is a present-state test, responsibility looks back to the moment of the offence, testamentary capacity to the moment of the will.

TRAP **Collapsing fitness to stand trial into criminal responsibility.** They ask different questions at different times: fitness is the accused's capacity now to be tried; responsibility is his mental state then, at the offence. Currently fit does not mean he was sane at the act, and currently unfit does not mean he was insane.

28.4 Diminished responsibility, in brief

Where insanity fully acquits, diminished responsibility only softens the verdict. It is an English partial defence to murder: where an abnormality of mind (arising from a recognised condition) substantially impaired the accused's mental responsibility for the killing, the charge is reduced from murder to manslaughter, avoiding the mandatory life sentence rather than excusing the act. It is invoked far more often than the insanity defence, which critics find too narrow to fit most mentally ill offenders. India has no equivalent general partial defence; there the routes are the Section 84 exception and the separate law of grave and sudden provocation, so **diminished responsibility** is best learned as the English contrast to the all-or-nothing insanity verdict.

28.5 Testamentary capacity: the Banks v Goodfellow criteria

Capacity to make a will is task-specific: a person with serious mental illness may still make a valid will if the illness does not touch the disposition. The governing test comes from Banks v Goodfellow in **1870**, where John Banks, a testator with chronic delusional illness, was nonetheless held capable because his delusions did not affect how he left his estate, establishing that testamentary capacity is judged against the specific task, not the global mental state. The testator must satisfy four limbs: he must understand the nature of the act of making a will and its effects; know the nature and extent of the property he is disposing of; appreciate the persons who have a reasonable claim as beneficiaries; and be free of any disorder of mind or insane delusion that perverts the disposition. Indian law aligns through the Indian Succession Act 1925,

which requires a sound disposing mind, and treats capacity as both task-specific and time-specific, tied to the moment the will is made and instructed.

BANKS V GOODFELLOW LIMB	WHAT THE TESTATOR MUST SHOW
Nature of the act	Understands that he is making a will and what a will does (disposing of his estate after death)
Extent of the estate	Knows the nature and approximate extent of the property being disposed of
Claims of beneficiaries	Appreciates the persons who have a reasonable claim, the natural heirs he is including or excluding
Undeluded judgment	**Is free from any disorder of mind or insane delusion that perverts the disposition of the estate**

The four limbs of the Banks v Goodfellow test. The last limb is the discriminating one: the delusion must not be shaping who inherits.

MNEMONIC

WILL · WEALTH · WHO · (no) WARP

The four Banks v Goodfellow limbs: understands the **WILL** and its effect; knows the extent of his **WEALTH**; appreciates **WHO** has a claim; and no delusional **WARP** of the disposition.

PEARL

The word "wrong" is where India and the classic English rule diverge. The McNaughten second limb asks only whether the accused knew the act was wrong; Section 84 of the Indian Penal Code spells out "wrong *or* contrary to law", so incapacity as to moral wrong or legal wrong will each suffice. Either way, the test is knowledge at the material time, and a diagnosis without that incapacity does not exculpate: legal insanity is not medical insanity.

1843
THE MCNAUGHTEN CASE, FROM WHICH THE INSANITY RULES WERE FRAMED

84
THE INDIAN PENAL CODE SECTION FOR UNSOUNDNESS OF MIND

1870
BANKS V GOODFELLOW, THE TESTAMENTARY-CAPACITY TEST

4
LIMBS OF THE BANKS V GOODFELLOW TEST

INDIA

The NIMHANS fitness-to-stand-trial proforma structures the assessment into five sections: cognitive functions, understanding of the charges, knowledge of the court proceedings, understanding of one's own lawyer, and expected behaviour during the trial. Criminal responsibility runs through Section 84 of the Indian Penal Code, testamentary capacity through the Indian Succession Act 1925's "sound disposing mind", and the whole field now sits under the Mental Healthcare Act 2017. Note the recodification for current exams: the Indian Penal Code has been replaced by the Bharatiya Nyaya Sanhita 2023, whose unsoundness-of-mind provision (its Section 22) carries essentially the same wording as the old Section 84, so the capacity test is unchanged even as the numbering moves.

GOOD TO REMEMBER

- **The principle:** forensic assessment answers a legal question, not a clinical one; the psychiatrist informs the court, but the verdict, of responsibility, fitness or capacity, is the court's, and a diagnosis alone never decides it.
- **The one discriminator:** time-frame separates the capacities, criminal responsibility looks back to the moment of the act (McNaughten rules; Section 84 of the Indian Penal Code, incapacity to know the nature of the act or that it was wrong), whereas fitness to stand trial is a present-state test (understand the charge and proceedings, instruct counsel).
- **The one exam fact:** testamentary capacity is task-specific under Banks v Goodfellow (1870): understand the nature of the will, the extent of the estate and the claims of beneficiaries, free from any delusion that perverts the disposition.

HOLD THIS

Two questions, two time-frames: criminal responsibility asks whether, at the time of the act, disease or unsoundness of mind left the accused unable to know the nature of the act or that it was wrong (McNaughten; Section 84 of the Indian Penal Code), while fitness to stand trial asks whether, here and now, he can understand the charge and proceedings and instruct counsel.

29 · The Mental Healthcare Act 2017

Indian psychiatry now runs on a single statute, and the examiner treats it as compulsory: the **mental healthcare act 2017** is the law under which every admission, every certificate and every act of compulsory treatment in the country is made lawful. It replaced the custodial Mental Health Act 1987 and rebuilt the field on a **rights-based** foundation, enacted to bring Indian law into line with the United Nations Convention on the Rights of Persons with Disabilities, which India had ratified. Where the old law asked "how do we detain the insane", the new one asks "how do we protect the rights of a person with mental illness while they are treated". That inversion is the single idea from which every provision below descends, and it is what the marks reward.

How to hold the Act. It runs to **16** chapters and **126** sections, but only a spine is examinable: the definition of mental illness and the capacity test that gates it; the two instruments of self-determination, the **advance directive** and the **nominated representative**; the **admission categories**, independent and supported; the oversight bodies, the review board and the two authorities; the decriminalisation of attempted suicide; and the treatments the Act forbids or fences. This page teaches that spine as an exam skill; the full admission procedure, the forensic detail and the wider statutory landscape are developed in the Mental health legislation and forensic psychiatry notes.

29.1 The rights-based turn: from custody to capacity

A law built on capacity, not on custody. The Act received presidential assent in 2017 and came into force on the twenty-ninth of May 2018, repealing the Mental Health Act 1987, whose reception-order machinery had treated the patient as an object of custody rather than a holder of rights. Two definitions carry the whole rights architecture. First, **mental illness** is defined as a substantial disorder of thinking, mood, perception, orientation or memory that grossly impairs judgment, behaviour, the capacity to recognise reality or the ability to meet the ordinary

demands of life; the definition expressly takes in conditions arising from the abuse of alcohol and drugs, and expressly excludes **mental retardation** (intellectual disability), a condition of arrested or incomplete development of mind. The determination of mental illness must be made in accordance with nationally or internationally accepted medical standards, such as the latest edition of the ICD, and never on the basis of political, economic or social status, caste, religion, or mere non-conformity with a community's moral, social or cultural norms.

Capacity is the concept the whole Act turns on. Every adult is presumed to have the **capacity** to make their own mental-healthcare decisions unless the contrary is shown, and capacity is decision-specific: the ability to understand the information relevant to the decision, to appreciate the reasonably foreseeable consequences of taking it or not taking it, and to communicate that decision by any means. This is the gate that sorts the patient. A person who retains capacity is admitted and treated only on their own informed consent; a person who has lost it is *supported* to decide rather than simply overruled. On that footing the Act guarantees a suite of rights: access to affordable, good-quality, geographically reachable, community-based care from government services; the right to live with dignity and to be free from cruelty, neglect and degrading treatment; equality and non-discrimination in care; the right to information about one's illness and treatment; confidentiality of records; free legal aid; and the right to complain to the establishment, the review board or the state authority.

RULE **Capacity is the gateway, and it is presumed.** Retained capacity routes a patient to independent admission on their own consent; lost capacity routes them to supported admission, where the nominated representative and the advance directive step in. Establish capacity first; everything else follows from it.

INDIA

The Act is India's instrument for honouring the Convention on the Rights of Persons with Disabilities, and it borrows that Convention's language of supported, not substituted, decision-making. It ties Indian clinical practice to the WHO classification by naming the ICD as the standard for determining mental illness, so the diagnostic frame that carries statutory weight here is the ICD rather than the DSM (the wider transcultural frame is set out in the Consultation-liaison, geriatric and transcultural psychiatry notes). Two Indian realities temper the text on paper: the Act routes the patient's right to free legal aid through the Legal Services Authorities (the NALSA framework), giving a person facing supported admission a route to counsel; and implementation lags the statute, since many states were slow to constitute their review boards and authorities, so the safeguards are only as real as the bodies that deliver them.

29.2 The advance directive: the right to state how one wishes to be treated

The Act's flagship innovation lets a patient bind their future care. An advance directive is a written document in which a person states the way they wish to be cared for and treated for a mental illness, the way they wish *not* to be treated, and the individuals they appoint as nominated representative in order of precedence. Any adult with capacity may make one; a legal guardian may make it for a minor. Its defining feature, and the classic exam point, is that it lies dormant

while the person has capacity and comes into force only when they cease to have the capacity to make mental-healthcare decisions, remaining in effect until capacity returns. It may be revised or revoked any number of times while the person is capacitous, and it is void from the outset if it is made contrary to any law. The directive is registered on an online register maintained by the review board, and it is the duty of the treating psychiatrist and the establishment to give treatment in accordance with a valid advance directive.

The directive is not absolute. A mental health professional, relative or carer who does not wish to follow an advance directive may apply to the **review board**, which then tests whether it was made of the person's own free will and free of coercion, whether it was intended to cover the present circumstances, whether the person was sufficiently informed and had capacity when they made it, and whether its content offends any other law. The board may then uphold, modify or cancel it. A clinician is protected from liability for following a valid advance directive, and equally is not penalised for failing to follow one they were never given a copy of.

> **PEARL**
>
> An advance directive that refuses all treatment is not automatically binding: it is precisely the case a treating team can escalate to the review board, which weighs the refusal against the four validity tests. The Act gives the patient a powerful voice in advance; it does not hand them an unreviewable veto over life-saving care.

29.3 The nominated representative: the patient's chosen decision-partner

A named person who supports, rather than supplants, the patient's choices. The nominated representative is the individual a person appoints, in writing on plain paper with their signature or thumb impression, to support them in mental-healthcare decisions. The role reflects the Act's shift from the old proxy or substituted consent of guardianship to *supported* decision-making: the representative helps the patient reach and voice a decision rather than deciding over their head. Any adult may be appointed, provided they consent in writing and are competent to discharge the duties; a person may revoke or change the appointment at any time. Where a patient has made no nomination, the Act sets an order of precedence (a relative, then a carer, and so on), and where none is available the review board itself appoints a representative. For a minor, the legal guardian is the nominated representative unless the board orders otherwise.

The representative's duties track the whole care pathway: to consider the person's wishes and least-restrictive care, to apply for admission and for discharge, to have access to the person's advance directive and clinical information, to be informed of any use of restraint, and to give or withhold consent to research on the person's behalf. In a supported admission, it is the representative, not the clinician alone, who applies for and consents to admission, which is the structural safeguard against unilateral detention.

29.4 The admission categories: independent and supported admission

Two doors, sorted by capacity. Chapter twelve rebuilt admission around consent. Independent admission is the default and the aspiration: a capacitous adult who understands the nature and purpose of admission, is likely to benefit, and makes the request of their own free will is admitted

on their own application under Section 86, and may not be treated without their informed consent. Such a patient may discharge themselves on request under Section 88, though the establishment may hold them for a maximum of twenty-four hours to assess whether the criteria for supported admission have arisen. Supported admission (the Act's deliberate replacement for the old term "involuntary") is the exception, used only where capacity is lost and a defined risk is present, and it is hedged with time limits, two-professional certification and mandatory reporting to the review board.

CATEGORY	SECTION	WHO AND WHEN	SAFEGUARD AND EXIT
Independent admission (adult with capacity)	Section 86	**Capacity intact; understands nature and purpose; likely to benefit; requests admission of their own free will. No treatment without informed consent**	Self-discharge on request (Section 88); may be held up to twenty-four hours to assess for supported admission; converts to Section 89 if capacity is lost and risk arises
Admission of a minor	Section 87	**On the nominated representative's application; opinion of two independent professionals; least-restrictive option; separate child ward; a female attendant for a minor girl**	Discharged when the representative withdraws support; converts to Section 86 on attaining majority; ECT only with prior board approval
Supported admission, up to thirty days	Section 89	**Representative's application; person lacks capacity *and* meets a harm-to-self, harm-to-others or inability-to-self-care limb; certified by one psychiatrist and one mental health professional or medical practitioner**	Capacity reviewed weekly; reported to the board within seven days, and within three days for a woman or minor; on regaining capacity, moved to Section 86 or discharged
Supported admission, beyond thirty days	Section 90	Continued incapacity with continuing risk; independent evaluation by two psychiatrists	Capacity reviewed every fourteen days; extended in defined steps (up to ninety, then to one hundred and eighty days) under board oversight

The admission categories of the Act. The examinable discriminator is Section 89 against Section 90: the professional and the clock both change at the thirty-day line.

MNEMONIC

Eighty-six ask for yourself; eighty-nine supported to thirty; ninety beyond

Section 86 is the capacitous patient asking for their own admission; Section 89 is the supported admission capped at thirty days on one psychiatrist plus one other professional; Section 90 carries a supported admission beyond thirty days and demands two psychiatrists. Section 87 sits between them for the minor.

WORKED EXAMPLE

A man in his thirties with schizophrenia is brought in acutely psychotic, threatening his family and unable to grasp why admission is proposed. He plainly lacks capacity and meets a risk limb, so he cannot be an independent patient. His nominated representative applies, one psychiatrist and one medical practitioner independently certify the criteria, and he is admitted under Section 89 with the board informed within seven days. His capacity is checked weekly; a fortnight in he improves, understands his situation and consents to stay, so his admission is transferred to Section 86 as an independent patient. Had he still lacked capacity beyond thirty days, two psychiatrists would have had to evaluate him afresh to continue under Section 90.

TRAP **Confusing Section 89 with Section 90.** Section 89 is supported admission up to thirty days, certified by one psychiatrist plus one mental health professional or medical practitioner, with weekly capacity review; Section 90 is the extension beyond thirty days, demanding two psychiatrists and a fortnightly review. Naming the wrong professional or the wrong clock is a stock way to lose the mark.

29.5 The oversight architecture: the review board and the two authorities

A quasi-judicial guardian at the bedside, and two administrative regulators above it. The Act separates the body that protects the individual patient from the bodies that regulate the system. The definitions worth memorising are these four institutions.

Mental Health Review Board

The Mental Health Review Board is the quasi-judicial body, constituted by the state authority, that protects the individual patient. It registers, reviews and can cancel advance directives; appoints nominated representatives; and receives and decides applications against admission decisions under Sections 87, 89 and 90. It is chaired by a district judge and includes a district-administration representative, one psychiatrist and one medical practitioner, and members drawn from persons with mental illness, carers or non-governmental organisations.

Central Mental Health Authority

The Central Mental Health Authority registers and supervises central-government establishments, develops service norms, maintains the national register of clinical psychologists, mental health nurses and psychiatric social workers, and advises the central government.

State Mental Health Authority

The State Mental Health Authority mirrors that role within the state: it registers and supervises establishments in the state, keeps the state register of mental health professionals, sets minimum standards and receives complaints about deficient services.

Mental health establishment
Any facility, public or private and including AYUSH facilities, offering care for mental illness; it must register with the relevant authority and conform to prescribed standards. A family home where a person lives with relatives is not an establishment.

The division of labour is the point: the review board adjudicates the rights of a named patient, functioning as an accessible tribunal; the central and state authorities license and inspect the establishments and hold the registers of professionals. Every supported admission must be reported to the board, which is the mechanism that keeps compulsory care under continuing external scrutiny rather than clinician discretion alone.

29.6 The decriminalisation of attempted suicide

The provision that changed emergency practice overnight. Section 115 delivers the **decriminalisation of attempted suicide**. Its words are the ones to keep: notwithstanding anything contained in Section 309 of the Indian Penal Code, any person who attempts to commit suicide shall be presumed, unless proved otherwise, to have severe stress, and shall not be tried and punished under that Code. The presumption is the engine of the clause: the burden inverts, so the person who has attempted suicide is taken to have been under severe stress rather than treated as an offender. The section pairs this immunity with a positive duty on the appropriate government to provide care, treatment and rehabilitation to a person under such severe stress, to reduce the risk of a further attempt. The practical effect is that a survivor of self-harm now reaches a clinician, not a police station, and can be assessed and treated without the shadow of prosecution. The clinical assessment that follows, the suicide risk evaluation and the C-SSRS as used inside the mental state examination, is developed in the Somatic-symptom, sexual, impulse-control disorders and suicide notes.

> **COMMON TRAP**
> Section 115 does not repeal Section 309 of the Penal Code; the older offence remains on the statute book. What the Act does is raise a rebuttable presumption of severe stress that *overrides* Section 309 in almost every case, so the attempt is not tried or punished. Say "presumption of severe stress, overriding Section 309", not "Section 309 has been deleted".

29.7 Prohibited and safeguarded treatments

The Act draws a hard line around the interventions most open to abuse. Section 95 flatly prohibits a short, high-yield list, and each item answers a documented historical harm: electroconvulsive therapy without the use of muscle relaxants and anaesthesia (unmodified ECT is banned outright); electroconvulsive therapy for minors, except with the prior approval of the review board and the guardian's consent; sterilisation of men or women when it is intended as a treatment for mental illness; and chaining a person in any manner or form whatsoever. Around this core the Act fences other interventions with consent and oversight rather than banning them.

PROVISION	SECTION	THE SAFEGUARD
Prohibited treatments	Section 95	**Unmodified ECT, ECT for minors, sterilisation as treatment for mental illness, and chaining are forbidden**
Psychosurgery	Section 96	Permitted only with the informed consent of the person and the prior approval of the review board
Seclusion and restraint	Section 97	**Seclusion and solitary confinement banned; physical restraint only as the least means to prevent imminent harm, psychiatrist-authorised, recorded, and never a punishment**
Emergency treatment	Section 94	Any needed treatment permitted to prevent death, serious self-harm or harm to others, capped at seventy-two hours or until assessment at an establishment

The Act's treatment safeguards. The four Section 95 prohibitions are the most examined line; emergency treatment under Section 94 has a firm seventy-two-hour ceiling.

16
CHAPTERS IN THE ACT, SPANNING 126 SECTIONS

2018
CAME INTO FORCE, ON 29 MAY, REPEALING THE 1987 ACT

30
DAYS, THE SECTION 89 SUPPORTED-ADMISSION CEILING BEFORE SECTION 90

72
HOURS, THE SECTION 94 EMERGENCY-TREATMENT CEILING

GOOD TO REMEMBER

- **The principle:** the mental healthcare act 2017 replaced the custodial 1987 Act with a rights-based, capacity-centred law that honours the UN Convention on the Rights of Persons with Disabilities; capacity is presumed and decision-specific, and it decides whether a patient is admitted independently on their own consent or supported when consent is lost.
- **The one discriminator:** independent admission (Section 86, capacitous, self-requested, self-dischargeable) versus supported admission (Section 89 up to thirty days on one psychiatrist plus one other professional; Section 90 beyond thirty days on two psychiatrists), each reported to the mental health review board.
- **The one exam fact:** Section 115 presumes severe stress, unless proved otherwise, in anyone who attempts suicide and bars trial and punishment under Section 309 of the Penal Code; the advance directive and nominated representative give a patient a binding voice in future care; and Section 95 forbids unmodified ECT, ECT for minors, sterilisation as treatment, and chaining.

HOLD THIS

The Mental Healthcare Act 2017 is a rights-based, capacity-gated statute: capacity is presumed and sorts patients into independent (Section 86) or supported (Sections 89 and 90) admission, the advance directive and nominated representative carry the patient's voice, the review board and the two authorities police the system, Section 115 presumes severe stress and decriminalises attempted suicide, and Section 95 bans unmodified ECT, ECT for minors, sterilisation and chaining.

30 · Capacity, consent and confidentiality

Three ideas govern the ethics and the law of every clinical encounter, and psychiatry tests all three harder than the rest of medicine because the illnesses it treats can themselves erode a patient's judgement. **Capacity** asks whether this patient can make this decision; **consent** is the permission a patient with capacity gives to be treated; and **confidentiality** is the duty to hold what the patient tells you in confidence. They form a chain: capacity underwrites valid consent, and consent is what makes it lawful to treat and, later, one of the things that can lift the duty of confidentiality. The examiner rewards the candidate who can define each cleanly, state its limits and its exceptions, and, in an Indian answer, tie it to the Mental Healthcare Act, 2017.



Fig 19.17 Decision-making capacity requires understanding relevant information, appreciating consequences, reasoning between options and communicating a choice. Valid consent is informed and voluntary; confidentiality is preserved except for defined safety or legal grounds.

How to use this page. Fix **decisional capacity** first, because valid consent is impossible without it, and learn the four **elements of capacity** as a functional test the clinician performs. Then take **informed consent** as three conditions (adequate disclosure, capacity and voluntariness) with a short, carefully-bounded list of exceptions. Then take confidentiality and its recognised limits, and name the Tarasoff principle. Finally read all three through the Indian statute. Throughout, hold apart the two words examiners try to conflate: *capacity* is a clinical judgement a doctor makes, *competence* is the legal status a court confers.

30.1 Decisional capacity: the four elements

Capacity is the ability to make a particular decision, tested by four abilities. Capacity is the patient's ability to understand and use information well enough to reach and express a treatment decision. It is assessed functionally, by what the patient can actually do with the relevant information, not by their diagnosis and not by whether their choice pleases the clinician. The examinable test has four **elements of capacity**, and a patient must satisfy all four to have

capacity to consent to (or refuse) the decision in front of them: they must **understand** the information relevant to the decision, **retain** it long enough to use it, **use and weigh** it as part of the process of deciding, and **communicate** their choice by any means. Fail any one element and capacity for that decision is absent.

ELEMENT	WHAT THE PATIENT MUST BE ABLE TO DO	WHERE IT TYPICALLY FAILS
Understand	Take in the nature of the condition, the proposed treatment, its risks, benefits and alternatives	**Intellectual disability, dementia, acute confusion, low attention**
Retain	Hold the information long enough to use it in the decision (not necessarily for long)	Amnestic syndromes, delirium, severe dementia
Use and weigh	Reason with the information, balancing risks against benefits in line with the patient's own values	**Psychosis, severe depression, delirium, a delusion that overrides the facts**
Communicate	Express a stable choice by speech, writing, gesture or any other means	Coma, catatonic mutism, a fixedly non-communicating patient

The four elements of decisional capacity. All four are required; the "use and weigh" element is the one most often lost in psychosis and severe depression, where the patient can repeat the facts yet cannot reason with them.

This four-element functional test (understand, retain, use and weigh, communicate) is the one adopted in modern mental-capacity law and in Indian teaching. The closely-related clinical model of Appelbaum and Grisso, widely quoted in the American literature, names four parallel abilities: to *communicate a choice*, to *understand* the relevant information, to *appreciate* the situation and its consequences (apply the facts to oneself), and to *reason* about the options. "Appreciation" and "using and weighing" cover the same clinical ground: the patient who says "the tablets treat infection but my body does not need them because I am already dead" understands the facts but cannot appreciate or weigh them, and so lacks capacity.

RULE **Capacity is clinical and functional; competence is legal.** A clinician assesses *capacity* for a specific decision at the bedside; a court determines *competence* as a legal status. Assess capacity, do not pronounce competence.

30.2 The three principles that govern any capacity assessment

Presumption, specificity and process, not outcome. Three principles frame every assessment and each is a stock exam line. First, the **presumption of capacity**: every adult is presumed to have capacity unless the opposite is shown, and the burden falls on the person who alleges incapacity. Crucially, a psychiatric diagnosis, even a severe one, does *not* by itself remove capacity. Second, capacity is **decision-specific and time-specific**: it is judged for one decision at one moment, so a patient may have capacity to consent to a blood test yet lack it for a complex operation, and capacity lost in an acute relapse may return with recovery. Third, the test is of the

process of decision-making, not its *outcome*: a capacitous patient is entitled to make what others regard as an unwise choice.

Presumption of capacity

Every adult is assumed to have capacity until incapacity is demonstrated; mental illness does not equal incapacity.

Decision-specific

Capacity is assessed for the particular decision, not globally; it can be present for one choice and absent for another.

Time-specific

Capacity can fluctuate; it is judged at the moment the decision must be made and re-assessed as the clinical state changes.

Process over outcome

Capacity turns on how the patient reaches the decision, not on whether the decision is sensible; an unwise choice is not, by itself, evidence of incapacity.

COMMON TRAP

Reading a refusal, or an unwise choice, as proof of incapacity. A patient who declines a life-saving blood transfusion on settled religious grounds understands and weighs the facts and retains capacity; a starving patient with anorexia nervosa who refuses food because they cannot accept anything is wrong may lack it, because the illness blocks the "use and weigh" element. The test is the reasoning, not the answer, and the equally common error runs the other way: assuming a patient with schizophrenia automatically cannot consent.

TRAP **Confusing capacity with the diagnosis.** Incapacity must be shown for the specific decision through the four elements; it is never inferred from the mere presence of a mental disorder. The presumption of capacity survives the diagnosis.

30.3 Informed consent: disclosure, capacity and voluntariness

Valid consent stands on three legs. Informed consent is the patient's voluntary agreement, given with capacity and adequate information, to a proposed intervention; it is a continuing process, not a signature on a form. For a **consent** to be valid, three conditions must all hold. There must be adequate **disclosure** of information; the patient must have the **capacity to consent**; and the decision must be **voluntary**, free of coercion, duress or undue influence. Remove any one and the consent is invalid, so a signed form from a patient who was not told the risks, or who lacked capacity, or who was pressured, is worthless.

Disclosure

The patient is given the information a reasonable person in their position would want: the diagnosis, the nature and purpose of the proposed treatment, its material risks and benefits, the alternatives (including no treatment), and the likely outcome of each.

Capacity

The patient meets the four-element test for this decision (the subject of the preceding sections); without capacity there can be no valid personal consent, and a substitute route is needed.

Voluntariness

The choice is the patient's own, free of coercion, threat, undue influence or manipulation, whether from clinicians, family or institution.

How much must be disclosed is set by a legal standard. The older *professional (reasonable-doctor) standard* asked what a responsible body of clinicians would disclose; the modern, patient-centred position is the *reasonable-person (materiality) standard*, which asks what a reasonable patient in this position would want to know, supplemented by the *subjective standard* of what *this* patient would want. The shift is toward the patient's informational needs, not the profession's custom.

RULE **Consent is not a form, it is three conditions.** Disclosure, capacity and voluntariness must all be present; a signature without any one of them is not informed consent.

30.4 When treatment may proceed without the patient's consent

Three carefully-bounded exceptions. The default is that no adult is touched or treated without their informed consent. The recognised exceptions are narrow and each must be documented. In an **emergency**, immediately necessary treatment may be given to save life or prevent serious harm to a patient who cannot consent, limited to what the emergency requires. For the **incapacitous patient** (one who fails the capacity test and is not in an emergency), treatment proceeds not by overriding consent but by a substitute route: a decision in the patient's best interests, a valid advance directive, or a legally-recognised substitute decision-maker. **Therapeutic privilege** is the narrowest and most easily abused: it is the clinician's right to withhold a specific piece of information from a patient who does have capacity, where full disclosure would itself cause the patient serious, foreseeable harm. It is not a licence to keep a patient in the dark for convenience, must be invoked for the individual patient and rarely, and must be recorded with reasons.

EXCEPTION	WHAT IT PERMITS, AND ITS LIMIT
Emergency	**Immediately necessary, life- or harm-preventing treatment for a patient who cannot consent; confined to what the emergency demands**
The incapacitous patient	Treatment via best interests, a valid advance directive or a substitute decision-maker, not by ignoring consent
Therapeutic privilege	**Withholding a specific disclosure that would itself gravely harm a capacitous patient; narrow, individual, documented, not routine paternalism**

The exceptions to informed consent. Emergency and incapacity dispense with personal consent by law; therapeutic privilege trims disclosure only, and is the one an examiner expects you to state with caution.

PEARL

Therapeutic privilege and the emergency exception are limits on *consent*, not on *capacity*: the therapeutic-privilege patient still has capacity, and the emergency patient is treated *because* the emergency prevents a valid consent from being obtained in time. Keep the two axes separate in the viva and you will not tangle them.

30.5 Confidentiality and its limits: patient consent, the duty to protect, statute and the court

A strong duty, but not an absolute one. The duty of confidentiality, owed since the Hippocratic oath and codified by professional bodies, holds that information a patient shares in the clinical relationship is theirs and is not disclosed without their leave. In psychiatry the duty is unusually weighty, because disclosure of a psychiatric contact still carries stigma. It is nonetheless a duty that can be outweighed, and the examinable task is to name the situations in which a **breach of confidentiality** is justified. There are four the candidate must give: the patient's own **consent** to disclosure; the **duty to warn or protect** an identifiable third party at serious risk; a **statutory reporting** obligation; and a **court order** compelling disclosure. In every case the disclosure is kept to the minimum necessary for the purpose.

JUSTIFIED DISCLOSURE	TRIGGER
Patient consent	**The patient authorises release, for example to a family member, insurer or another treating clinician**
Duty to warn or protect	A serious, credible threat of harm to an identifiable third party (the Tarasoff situation)
Statutory reporting	**A legal reporting duty, for example child or elder abuse, certain notifiable conditions, unfitness to drive**
Court order	A judge compels production of records or testimony; also risk of harm to self

The recognised limits of confidentiality. Patient consent is the routine lifting of the duty; the other three lift it against the patient's wishes, and each must be justified and minimised.

The Tarasoff principle. The duty to warn and protect was crystallised by the American case of Tarasoff v. Regents of the University of California. A student, Prosenjit Poddar, in psychotherapy at a university clinic, told his therapist he intended to kill a young woman, Tatiana Tarasoff, who had rebuffed him. The therapist alerted his supervisor and the campus police, who briefly detained and then released Poddar, but no one warned Tarasoff herself; Poddar later killed her, and her parents sued. The Supreme Court of California held (an initial 1974 ruling framed a duty to warn, and the landmark **1976** ruling a broader duty to protect) that when a therapist determines a patient poses a serious danger of violence to an identifiable other, the therapist incurs a duty to take reasonable steps to protect the foreseeable victim, and that this duty can override confidentiality. In the court's phrase, the protective privilege ends where the public peril begins. Tarasoff binds only California and is not a precedent elsewhere, but it has shaped professional and legal attitudes internationally, including in India.

WORKED EXAMPLE

A man in outpatient care names a specific former colleague he intends to kill, describes a plan and has the means. The clinician weighs the duty of confidentiality against the risk: the threat is serious, the victim is identifiable, and the danger is credible. Following the Tarasoff logic, the clinician takes reasonable protective steps (which may include warning the potential victim and informing the police), disclosing only what the risk requires and documenting the reasoning. Had the patient voiced only a vague, non-specific hostility with no identifiable target, the threshold for a protective breach of confidentiality would not be met, and the duty of confidentiality would hold.

RULE **Confidentiality is strong but not absolute.** It yields to the patient's own consent, to a duty to protect an identifiable third party at serious risk, to a statutory reporting duty and to a court order, and never more than the minimum the purpose demands.

30.6 The Indian statutory frame: the Mental Healthcare Act, 2017

In India these three principles are not only ethical, they are law. The Mental Healthcare Act, 2017 writes capacity, consent and confidentiality into statute and re-centres the Indian system on the rights and will of the person with mental illness. Its capacity test (Section 4) mirrors the elements taught above: a person has capacity to make mental-healthcare decisions if able to understand the information relevant to the decision, to appreciate the reasonably foreseeable consequences of deciding or not deciding, and to communicate the decision by speech, expression, gesture or any other means. It states the presumption of capacity, and provides (Section 4(3)) that a decision others regard as wrong does not by itself show incapacity, the process-over-outcome principle in statutory form.

INDIA

The Act supplies India's substitute-decision architecture and its confidentiality rule. Where capacity is lost, a person may plan ahead through an advance directive (Section 5), stating how they wish, and wish not, to be treated, and may appoint a nominated representative (Section 14) as substitute decision-maker; the treating clinician has a duty to check for an advance directive. The right to confidentiality is explicit in Section 23: a person with mental illness has the right to confidentiality in respect of their mental health, mental healthcare, treatment and physical healthcare, extending to records in electronic form, and Section 24 restricts release of a patient's photograph or information to the media without consent. The Act's confidentiality exceptions echo the general ones, disclosure being permitted to protect life, to prevent harm to others, on a court order or in the interests of public safety. The Act also decriminalised attempted suicide (Section 115), presuming severe stress. The full admission procedure, the Mental Health Review Board and the wider forensic machinery are developed in the Mental health legislation and forensic psychiatry notes.

Two Indian nuances are worth carrying into an answer. The reach of confidentiality is partly cultural: in the Indian family-centred setting a degree of information-sharing with a co-resident nominated representative or caregiver is often expected and, within the statute, appropriate, whereas a purely individualist reading of confidentiality would refuse it; the wider transcultural

frame is set out in the Consultation-liaison, geriatric and transcultural psychiatry notes. And the Act ties clinical practice to accepted diagnostic standards, so that capacity, consent and confidentiality operate on top of an ICD-anchored diagnostic system rather than in a vacuum.

4	3	1976	2017
ELEMENTS OF DECISIONAL CAPACITY: UNDERSTAND, RETAIN, USE AND WEIGH, COMMUNICATE	CONDITIONS FOR VALID INFORMED CONSENT: DISCLOSURE, CAPACITY, VOLUNTARINESS	TARASOFF: THE SUPREME COURT OF CALIFORNIA DUTY-TO-PROTECT RULING	MENTAL HEALTHCARE ACT, INDIA'S GOVERNING MENTAL-HEALTH STATUTE

GOOD TO REMEMBER

- **The principle:** capacity underwrites consent, and consent is one of the things that lifts confidentiality; capacity has four elements (understand, retain, use and weigh, communicate), is presumed, and is decision- and time-specific; valid consent needs disclosure, capacity and voluntariness; and confidentiality is strong but not absolute.
- **The one discriminator:** capacity is the clinician's functional bedside judgement about a specific decision, competence is the court's legal status; and confidentiality is tested on the *process* of decision-making, never on whether the patient's choice is wise.
- **The one exam fact:** the Tarasoff ruling (Supreme Court of California, 1976) established the duty to warn and protect an identifiable third party as a justified breach of confidentiality, and in India the Mental Healthcare Act, 2017 codifies the capacity test (Section 4), the presumption of capacity, the advance directive (Section 5) and the right to confidentiality (Section 23).

HOLD THIS

Capacity (four elements, presumed, decision-specific) makes consent valid; consent needs disclosure, capacity and voluntariness; confidentiality is strong but yields to the patient's consent, a Tarasoff duty to protect a named third party, statutory reporting and a court order, and in India all three are law under the Mental Healthcare Act, 2017.

Apply and consolidate

31 · Worked cases

This is the arc-closer for the whole psychotherapies, assessment and nosology chapter, and it is deliberately a set of **worked cases** rather than more theory, because the paper does not test whether you can recite a modality or list the mental-state domains; it tests whether you can *do* the five jobs the chapter teaches on a patient put in front of you. Each of the five subtopics below takes one short **vignette** and reasons it through end to end: a therapy-selection call, a mental-state write-up, a biopsychosocial formulation, a categorical-versus-dimensional argument, and a scale-selection decision. Read each as a rehearsal of the viva move it stands for.

How to use this page. For every case the discipline is the same: name the diagnosis first, then do the specific job the question asks, and justify each step out loud. Nothing here is new content; it is the chapter's machinery applied. Where a named therapy closes a case it ends with an indication-anchored recall box (the model, the lead indication, the one technique); where an assessment or nosology skill closes a case it ends with a rule-anchored recall box (the principle, the discriminator, the one exam fact).

31.1 A therapy-selection case: the ambivalent drinker

Match the disorder to its evidence base, then match the intervention to the patient's readiness. Here is the case: a 41-year-old self-employed man is referred after his wife raises concern about his drinking. He drinks daily, scores 18 out of a possible 40 on the AUDIT (the harmful range), and has no history of withdrawal seizures or features demanding urgent detoxification, and no comorbid severe depression. Crucially, he is *ambivalent*: he half-wants to cut down and half-minimises ("I can stop any time I like"). The formulation of this presentation is not a skills deficit but low readiness to change, and reading that correctly is the whole of the selection reasoning. His diagnosis is alcohol use disorder in the harmful range; the maintaining problem is that he sits in the contemplation stage of the stages of change, of which there are **five** (precontemplation, contemplation, preparation, action and maintenance; Prochaska and DiClemente).

The matched first-line therapy is motivational enhancement therapy, its brief structured four-session form, delivered in the motivational interviewing style of Miller and Rollnick; this is first-line for alcohol use disorder (IPS 2014 grade A; VA/DoD 2021). The reasoning is stage-matching: you do not hand a contemplator an abstinence contract, you evoke his own change talk and roll with his resistance, developing the discrepancy between his stated values and his drinking until he moves himself toward an action plan. Motivational interviewing as used across the addictions is developed in the Substance use disorders notes; this worked example only makes the selection call.

RULE **Read the stage before you choose the plan.** The disorder's evidence base sets the default therapy; the patient's stage of change sets how it is delivered. For an ambivalent drinker the answer is motivational enhancement therapy in a motivational-interviewing style, not action-stage abstinence work.

TRAP **Pushing an action-stage plan onto a contemplator.** Prescribing abstinence, disulfiram supervision or relapse-prevention homework to a patient who has not resolved his ambivalence is the classic mismatch; it raises resistance and predicts drop-out. Meet the stage first.

INDIA

The Indian answer adds a family limb the guideline formalises. The Indian Psychiatric Society's alcohol-use guidance endorses family-based treatment using a co-resident relative as the recovery monitor and the supervisor of supervised disulfiram (IPS 2014, grade B), a culturally specific adaptation to Indian family structures. So the fuller selection here is motivational enhancement therapy for the man, plus enlistment of a willing co-resident relative as the treatment ally once he reaches the action stage, rather than an individual-only Western template.

GOOD TO REMEMBER

- **The model:** motivational interviewing (Miller and Rollnick) is a collaborative, person-centred and directive style that resolves ambivalence and evokes change talk across the five stages of change; motivational enhancement therapy is its brief, structured four-session form.
- **The lead indication:** substance use, first-line for alcohol use disorder (IPS 2014 grade A; VA/DoD 2021), and stage-matched to the patient's readiness.
- **The one technique:** evoke change talk and roll with resistance (developing discrepancy), never an action-stage abstinence plan imposed on a contemplator.

31.2 An MSE write-up case: describing a manic presentation, domain by domain

The examined skill is to write the here-and-now in observational language, in the fixed order, without slipping into diagnosis. Here is the case: a 27-year-old man is brought by his family after three weeks of reduced sleep, overactivity, overspending and grandiose plans. The task is not to label him but to write the mental state examination, and the whole of the mark lies in running the seven domains in their order (appearance and behaviour; speech; mood and affect; thought form and content; perception; cognition; insight and judgement) and describing signs, not conclusions. The table below turns the vignette into a domain-by-domain write-up; note that every entry is an observation, that absences are recorded explicitly, and that nowhere does the word "mania" or "bipolar" appear.

MSE DOMAIN (IN ORDER)	THE WRITE-UP FROM THIS VIGNETTE
Appearance and behaviour	Flamboyantly dressed in bright, mismatched clothing; restless, pacing, intrusive and over-familiar; psychomotor activity markedly increased; fleeting, over-intense eye contact; no abnormal involuntary movements
Speech	**Rapid, pressured and loud, increased in quantity, difficult to interrupt**
Mood and affect	Subjectively "on top of the world"; objectively affect elevated and expansive, becoming irritable when thwarted, labile but reactive and congruent with the elevated mood
Thought form	**Flight of ideas, with rhyming and clang associations and marked distractibility; the links between ideas remain followable**
Thought content	Grandiose ideas of a special mission and inflated abilities; no delusions of control; no suicidal or homicidal ideation elicited
Perception	No hallucinations elicited in any modality; no illusions reported
Cognition	Alert and oriented; attention impaired by distractibility; no gross memory deficit, though formal cognitive testing is limited by his cooperation

MSE DOMAIN (IN ORDER)	THE WRITE-UP FROM THIS VIGNETTE
Insight and judgement	**Insight impaired (denies being unwell, Grade I to II); judgement impaired, evidenced by uncontrolled spending and unrealistic plans**

The manic vignette written up domain by domain in the fixed MSE order. Every line is an observed sign or a recorded absence; no diagnostic label is admitted into the examination.

WORKED EXAMPLE

Rendered as continuous notes, the same MSE reads: "A flamboyantly dressed young man, restless and over-familiar, with markedly increased psychomotor activity. Speech rapid, pressured and hard to interrupt. Subjectively elevated ('on top of the world'); objectively expansive, irritable when crossed, labile but reactive. Thought form shows flight of ideas with clang associations; content includes grandiose ideas of a special mission, with no suicidal or homicidal ideation. No hallucinations in any modality. Alert, oriented, distractible. Insight impaired; judgement impaired." Note what this worked example is not: it is not a history (no past episodes, no reported symptoms over time) and it is not a diagnosis (no "mania"). It is a cross-sectional description that, set against the history, will later support one.

RULE **The MSE is a cross-sectional snapshot of signs, not the history and not a diagnosis.** Write what you observe and what the patient says, in the seven-domain order, and record absences explicitly; the label is reasoned later from the MSE plus the history, never written into the MSE itself.

GOOD TO REMEMBER

- **The principle:** the mental state examination is a here-and-now observational survey across seven domains in fixed order (appearance and behaviour; speech; mood and affect; thought form and content; perception; cognition; insight and judgement), and the descriptive vocabulary that populates it is developed in the Psychometry, Assessment and Descriptive Psychopathology notes.
- **The one discriminator:** record observed signs and the patient's own words, not interpretations; a manic patient's overactivity, pressured speech and flight of ideas are the signs, "mania" is the later conclusion.
- **The one exam fact:** state the absence of a phenomenon (no hallucinations, no suicidal ideation) as deliberately as its presence; an unrecorded domain reads as an incomplete examination.

31.3 A formulation case: first-episode psychosis on the 4-Ps grid

Name the diagnosis, then explain the individual by crossing the three domains with the four Ps. Here is the case: a 22-year-old engineering student presents with two months of social withdrawal, suspiciousness, auditory hallucinations and a decline in academic function; he uses cannabis regularly, has a paternal uncle with schizophrenia, was premorbidly shy and solitary, moved recently to a hostel in a new city, and has a critical, high-expressed-emotion father, though the family remains engaged and brought him in early. The diagnosis is a first-episode psychotic disorder. The formulation then places every factor onto the biopsychosocial four-Ps grid, so that the plan can attack the perpetuating column and mobilise the protective one.

DOMAIN	PREDISPOSING	PRECIPITATING	PERPETUATING	PROTECTIVE
Biological	Family history of schizophrenia (paternal uncle); genetic loading	Heavy cannabis use	**Continued cannabis use; likely medication non-adherence**	Young, first episode, no physical comorbidity, prospect of good treatment response
Psychological	Premorbid shy, solitary temperament; limited stress-coping	Perceived academic failure	**Poor insight; hopelessness about studies**	Good premorbid intelligence and function
Social	Academic pressure; few close ties	Migration to a hostel; isolation in a new city	**High expressed emotion at home; stigma; academic disruption**	Engaged, financially stable family who sought help early

The filled four-Ps grid for this first-episode-psychosis case. The perpetuating column (shaded) is what treatment attacks; the protective column carries the prognosis and the plan's allies.

The plan falls straight out of the grid, read down the rows and across the columns: an antipsychotic and active work on the cannabis use (biological), psychoeducation and cognitive behaviour therapy for psychosis as an adjunct (psychological), and a family intervention to lower expressed emotion (social), all aimed squarely at the perpetuating factors while enlisting the already-engaged family as the protective one. Notice the discipline: the diagnosis named the category, the formulation explained *this* young man, and the plan mirrored the grid.

GOOD TO REMEMBER

- **The principle:** a formulation crosses the three biopsychosocial domains with the four Ps (predisposing, precipitating, perpetuating, protective) to explain why this person is ill now; the diagnosis names the category, the formulation explains the individual, and it is a revisable hypothesis.
- **The one discriminator:** perpetuating factors (continued cannabis, non-adherence, high expressed emotion) are the treatment target; protective factors (an engaged family, a first episode) carry the prognosis.
- **The one exam fact:** name the diagnosis first and formulate second; the management plan is built biopsychosocially, attacking the perpetuating column and mobilising the protective column.

31.4 A categorical-versus-dimensional case: the borderline presentation argued both ways

A boundary presentation is best answered by arguing it categorically and dimensionally, then stating the pragmatic call. Here is the case: a 23-year-old woman has a five-year history of recurrent self-harm, chronic emptiness, intense and unstable relationships, impulsive spending and bingeing, identity disturbance, affective instability and transient stress-related suspiciousness. She is a genuinely "borderline" presentation in both senses of the word, and the higher-order question is not "what is the label?" but "how do the two nosological models describe her, and which is more useful here?".

READING	HOW THIS PATIENT IS DESCRIBED	ITS STRENGTH AND ITS LIMIT
Categorical (DSM-5-TR)	She meets at least five of the nine borderline personality disorder criteria, so the categorical label is "borderline personality disorder"; the ten types sit in the main text, the five-domain alternative model in Section III	**Strength: one communicable term with an immediate treatment implication (dialectical behaviour therapy). Limit: two patients can share the label with different symptom sets, and her affective features blur the mood-personality boundary**
Dimensional (ICD-11)	A single personality disorder diagnosis, graded moderate in severity, with trait qualifiers from the five domains (prominently negative affectivity and disinhibition) and the borderline pattern qualifier	**Strength: preserves severity and the trait profile and absorbs her mixed features without a second box. Limit: a profile of scores is harder to remember and to communicate than a single name**

The same patient described categorically and dimensionally. DSM-5-TR keeps the categorical types up front; ICD-11 abolished them for one severity-graded diagnosis plus five trait domains and a borderline pattern qualifier.

The pragmatic call is that both current manuals are hybrids, so you use both: name the categorical label because it communicates instantly and matches her to a therapy, and add the dimensional severity-and-trait description because it is truer to a boundary case that straddles the mood and personality territory. The matched therapy is dialectical behaviour therapy, delivered in its **four** modes (individual therapy, group skills training, telephone coaching and the therapist consultation team; Linehan), which is the lead therapy for borderline personality disorder where recurrent self-harm dominates (IPS 2023; NICE 2009); dialectical behaviour therapy and schema therapy for the personality disorders are developed in the Personality disorders notes.

TRAP **Forcing one label onto a boundary case.** A patient who straddles two categories, or sits one symptom short of a threshold, is not diagnosis-free and is not settled by a single box; the mixed and sub-threshold presentation is exactly where a severity-and-trait description carries more truth than a category, and the strong answer argues it both ways.

GOOD TO REMEMBER

- **The principle:** no statistical test proves psychopathology is kinds rather than degrees, so categories (usability) and dimensions (accuracy) are combined; both ICD-11 and DSM-5-TR are categorical-dimensional hybrids, most fully at personality disorder.
- **The one discriminator:** DSM-5-TR keeps the ten categorical types in its main text with its five-domain alternative model in Section III; ICD-11 abolished the types for one diagnosis graded into three severity levels plus five trait domains and a borderline pattern qualifier.
- **The one exam fact:** argue the boundary case both ways, categorical for communication and treatment matching, dimensional for severity and trait profile, then state the call.

31.5 A scale-selection case: measuring depression severity in two settings

Choose the instrument to fit the construct, the setting, the rater and the purpose; a screen is not an outcome measure and neither is a diagnosis. Here is the case: a liaison colleague asks

two questions about the same construct, depressive severity, in two different settings, and each setting selects a different scale. In a busy primary-care clinic he wants to screen and then monitor treatment; in a specialist depression service he wants to measure outcome precisely. The selection reasoning weighs four things: the construct, who administers the scale (self versus clinician), the purpose (screening versus severity or outcome), and whether the instrument tracks change.

SETTING AND PURPOSE	THE SCALE TO CHOOSE	RATER	READING IT
Primary-care screening and repeat monitoring	PHQ-9 (nine self-report items, out of a possible 27)	Patient self-completed	**Brief and sensitivity-tuned; she scores 16 out of a possible 27, in the moderately severe band, but a positive screen is not a diagnosis and must be confirmed clinically**
Specialist severity rating and outcome or trial use	MADRS (ten clinician-rated items, out of a possible 60)	Clinician-administered	**Sensitive to treatment-related change and less confounded by somatic overlap; the reference-standard interviewer-rated outcome measure**

Two scales for one construct, chosen by setting and purpose. A self-report screen (PHQ-9) rules out and monitors cheaply; a clinician-administered severity scale (MADRS) is the outcome and trial standard. The HAM-D, MADRS and YMRS in clinical use are developed in the Mood disorders: classification, depressive and bipolar syndromes, neurobiology notes.

The interpretive discipline is that a raw number means nothing until it is read against validated, locally-relevant norms and cut-offs. An imported cut-off is only valid in the population its norms were drawn from, which is why an instrument used in India should be translated, re-validated and re-normed rather than borrowed wholesale; the psychometric theory of standardisation and norms underneath this is developed in the Psychometry, Assessment and Descriptive Psychopathology notes.

7 MSE DOMAINS, APPEARANCE AND BEHAVIOUR TO INSIGHT AND JUDGEMENT	**4** THE FOUR PS OF THE FORMULATION GRID	**27** PHQ-9 MAXIMUM (OUT OF A POSSIBLE 27)	**40** AUDIT MAXIMUM (OUT OF A POSSIBLE 40)

GOOD TO REMEMBER

- **The principle:** a scale is chosen to fit the construct AND the setting AND the purpose; a screen (brief, self-report, high sensitivity) is not the same instrument as an outcome measure (clinician-rated, sensitive to change).
- **The one discriminator:** self-report screens (PHQ-9, out of a possible 27) rule out and monitor cheaply; clinician-administered severity scales (MADRS, out of a possible 60) are the outcome and trial standard; a screening score is never a diagnosis.
- **The one exam fact:** read a score against validated, locally-normed cut-offs, not raw; an imported cut-off is only valid in the population it was normed on.

HOLD THIS

Work every case the same way: name the diagnosis, then do the exact job asked, match the therapy to the disorder's evidence base and the patient's stage of change, write the MSE as cross-sectional signs in seven-domain order, formulate on the biopsychosocial four-Ps grid, argue a boundary case both categorically and dimensionally, and pick the scale that fits the construct, the setting and the rater.

32 · Consolidation

This is the closing topic of the chapter, and its job is not to teach anything new but to make the twenty-odd topics before it *retrievable* under examination pressure: the psychotherapies with their models, techniques and lead indications; the mental state examination and the bedside cognitive screens; the psychometric principles that decide whether a scale can be believed; and the two classifications with the debate that shapes them. The organising idea comes from the science of learning rather than from psychiatry: you keep what you have *pulled out* of memory, not what you have looked at again, so this page is built as **active recall** and **retrieval practice**, not as a summary to skim.

How to use this page. First collect the master **mnemonic** paid off from the opening classification and common factors topic, then work the answer-free prompt bank aloud, then walk the two branches of the **synthesis map**, the therapy branch and the assessment-and-nosology branch, testing each count and discriminator against what you can produce cold rather than what you can recognise on the page. Finish by covering the accompanying figure and trying to **redraw from memory**; the branch that stalls is the branch to revise tonight.

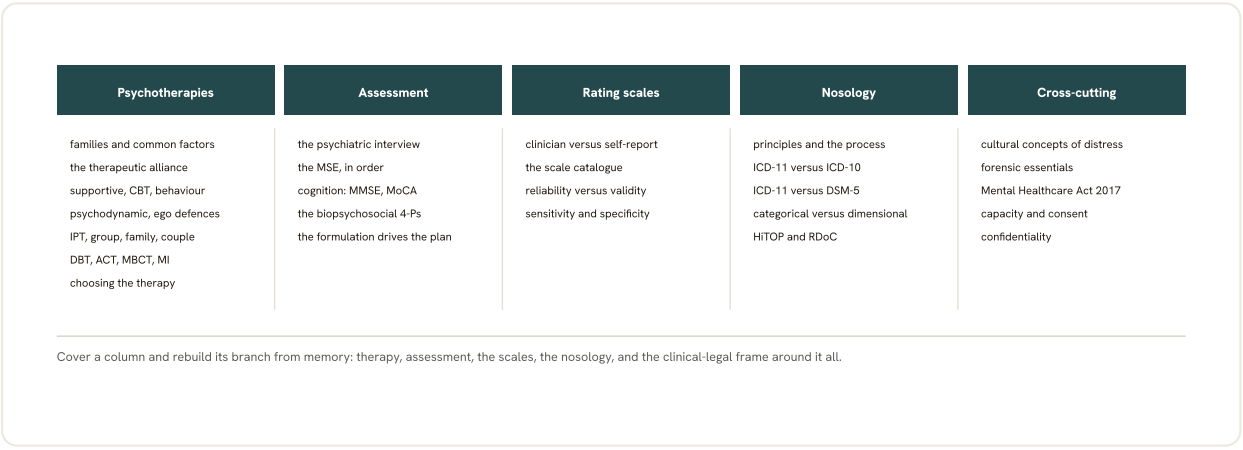


Fig 19.18 Chapter synthesis map. The chapter reduces to five branches: the psychotherapies (their families, the common factors and the alliance, the specific modalities, and how to choose one for a presentation); clinical assessment (the interview, the mental state examination in order, the cognitive screen, and the biopsychosocial formulation that drives the plan); the rating scales (clinician-rated versus self-report, the catalogue, and reliability versus validity); nosology (the principles of classification, ICD-11 against ICD-10 and against DSM-5, and the categorical-versus-dimensional debate with HiTOP and RDoC); and the cross-cutting clinical issues (the cultural concepts of distress, the forensic essentials, the Mental Healthcare Act 2017, and capacity, consent and confidentiality). Cover each column and rebuild its branch from memory.

32.1 Consolidation is retrieval practice, not re-reading

You keep what you pull out of memory, not what you look at again. The single most robust finding in the psychology of learning is the testing effect: actively retrieving a fact strengthens

the memory far more than re-reading it, and the effort of retrieval is itself the mechanism, which is why fluent, comfortable re-reading is a poor guide to what you will produce in the hall. Consolidation therefore means self-testing, not re-highlighting. The efficient way through this chapter is to turn every heading into a question, answer it aloud or on paper without looking, and only then check, spending the revision time on the branches you could not produce rather than the ones you could. The master **mnemonic** below is the trunk of the whole map: seeded deliberately at the opening classification topic and paid off here, it holds the six schools that every specific modality hangs from, and the phrase itself carries the common-factors message that most of the healing is shared, not branded.

RULE **Retrieve, do not re-read.** Recognising a familiar page feels like learning but is not; only pulling the answer from memory before you check it builds the recall the examination actually tests.

MNEMONIC

PLEASE BRING CARE, HOPE, SUPPORT, TRUST

The chapter's master mnemonic for the six **schools of psychotherapy**, seeded at the opening classification topic and paid off here as the trunk of the synthesis map: **P**sychodynamic, **B**ehavioural, **C**ognitive (and cognitive-behavioural), **H**umanistic (and experiential), **S**ystemic (and family), **T**hird-wave. Every named therapy hangs off one of these six trunks, and the phrase's meaning, care, hope, support and trust, is itself the common-factors payload, the shared ingredients that carry more of the outcome than any single technique.

32.2 The active-recall prompt bank: the therapy families and the common factors

Cover the rest of this page and answer each aloud before you read on. This list is deliberately answer-free, because supplying the answer defeats the point: the whole value is in the retrieval attempt. Work down it, and any prompt you cannot complete cleanly marks the topic to reopen. The prompts run across the psychotherapy families and the common factors first, then the assessment and nosology skills that the synthesis map below expands.

1. Name the six schools of the psychotherapy-family tree from the master mnemonic, and say why supportive belongs on the depth axis, not the school axis.
2. Give Frank's four common ingredients shared by every bona fide psychotherapy, and state which single common factor is the best-evidenced predictor of outcome.
3. Recite Bordin's three components of the therapeutic alliance, and say what you do when one of them ruptures.
4. List the five stages of change, and name the intervention error of handing an action plan to a precontemplator.
5. Draw the CBT cognitive model as a causal chain, and name the three views of Beck's cognitive triad.
6. Distinguish systematic desensitisation from flooding by whether a graded hierarchy is used, and place behavioural activation against both.

7. Rank the four levels of Vaillant's defence hierarchy, and place suppression and splitting on the correct levels.
8. List Yalom's therapeutic factors, give the exact count, and name the central one.
9. Name the four modes of standard DBT and the distinct function each delivers.
10. Recite the seven mental state examination domains in their conventional order, and say why the examination is a cross-sectional snapshot and not a diagnosis.
11. Separate reliability from validity in one line, and state which is necessary for the other.
12. Give the MMSE and the MoCA cut-offs out of a possible 30, and say which screen catches mild cognitive impairment and why.
13. State the one-line ICD-11 versus DSM-5 format discriminator, and name the official system used in India.
14. Say why no statistical test settles the categorical versus dimensional debate, and name the disorder where both manuals went most dimensional.

TRAP **Mistaking recognition for recall.** Reading the synthesis map and nodding along is recognition, which feels fluent and predicts almost nothing about performance; only covering it and producing the branch unaided is the retrieval practice that consolidates. If it felt easy, you probably read rather than retrieved.

32.3 The synthesis map, therapy branch: models, techniques and the counts to reproduce cold

Each widely-practised therapy compresses to a model, a signature technique and a lead indication. This is the therapy branch of the map, and the exam-ready form of every modality is exactly these three cells, the one-line mechanism, the one procedure that names it, and the one condition it is first choice for (the chapter's therapy topics and the guideline evidence). Cover the right-hand columns and produce them from the therapy name alone; the niche modalities (brief and crisis work, relaxation and biofeedback, and the projective tests) stay compact and are recalled by their one distinguishing feature rather than by this full grid.

THERAPY (SCHOOL)	MODEL IN ONE LINE	SIGNATURE TECHNIQUE	LEAD INDICATION
Supportive (depth axis)	Bolsters existing adaptive defences, self-esteem and coping without probing the unconscious	Reassurance, ventilation, reinforcing healthy defences	**The seriously or chronically ill and those in crisis; SSCM is first-line for anorexia nervosa**
Cognitive behaviour therapy	Interpretation, not the event, drives the emotional, physiological and behavioural response	Cognitive restructuring via the thought record, within collaborative empiricism	**Depression and the anxiety disorders; the best-evidenced therapy, first-line across the widest range**

THERAPY (SCHOOL)	MODEL IN ONE LINE	SIGNATURE TECHNIQUE	LEAD INDICATION
Behaviour therapy	Maladaptive behaviour is learned and can be unlearned by conditioning principles	Graded exposure and systematic desensitisation; behavioural activation; exposure and response prevention	Specific phobia and OCD (exposure); depression (behavioural activation)
Psychodynamic (STPP)	Unconscious conflict, transference and defence worked through to insight	Interpretation of transference and defence	A second-line or alternative option for depression and somatisation; MBT for borderline personality disorder
Interpersonal therapy	Symptoms are linked to one of four current interpersonal problem areas (grief, role transitions, role disputes, deficits)	Working the identified interpersonal problem area	**Depression, first-line, and particularly the perinatal period**
Group	The group is a social microcosm healing through Yalom's eleven therapeutic factors, cohesiveness central	Here-and-now process illumination and peer feedback	Interpersonal and relational problems; group CBT inherits CBT's evidence (first-line for gambling disorder)
Family and couple (systemic)	The family or couple, not the individual, is the unit of treatment	Restructuring communication, roles and expressed emotion	**Adolescent anorexia (FT-AN, first-line) and relapse prevention in schizophrenia**
Dialectical behaviour therapy (third wave)	Linehan's biosocial theory: emotional vulnerability meeting an invalidating environment, balancing acceptance and change	The four modes delivering the four skills modules	**Borderline personality disorder, especially where self-harm must be reduced**
Motivational interviewing / MET	Collaborative, person-centred, directive resolution of ambivalence across the stages of change	Evoking change talk; MET is its brief structured form	The substance use disorders (first-line); MET runs to four structured sessions

The therapy branch of the synthesis map: cover the last three columns and produce the model, the technique and the lead indication from the therapy name alone (the chapter's therapy topics; the guideline evidence).

The counts an examiner asks for cold, and the defence ladder underneath the dynamic therapies. Several numbers on this branch must be reproduced exactly, because a wrong count is itself a marked error. Beck's cognitive triad has exactly **3** views (self, world, future); the transtheoretical model has **5** stages of change (precontemplation, contemplation, preparation, action, maintenance); Yalom's therapeutic factors number exactly **11**, with cohesiveness the central one; and standard DBT from Linehan has exactly **4** modes (individual therapy, skills-training group, telephone coaching and the therapist consultation team) delivering the four skills

modules (mindfulness, distress tolerance, emotion regulation, interpersonal effectiveness). Beneath the psychodynamic and supportive therapies sits Vaillant's maturity hierarchy of the ego defences, ranked into 4 levels, and it is the predominant level, not any single defence, that locates a patient's personality organisation.

Mature defences

Sublimation, altruism, humour, suppression, anticipation. The hallmark of healthy adult functioning; suppression is the only partly conscious member.

Neurotic defences

Repression, reaction formation, displacement, intellectualisation, isolation of affect, undoing, rationalisation. Repression-based; undoing underlies obsessional rituals.

Immature defences

Projection, acting out, splitting, passive aggression, somatisation, regression, idealisation and devaluation. A predominance of splitting marks borderline personality organisation.

Psychotic defences

Denial (of an obvious external reality), distortion, delusional projection. They abolish reality itself and are normal only in early childhood and in dreams.

11	4	5	3
YALOM'S THERAPEUTIC FACTORS (COHESIVENESS CENTRAL)	MODES OF STANDARD DBT (LINEHAN)	STAGES OF CHANGE (TRANSTHEORETICAL MODEL)	VIEWS IN BECK'S COGNITIVE TRIAD (SELF, WORLD, FUTURE)

32.4 The synthesis map, assessment-and-nosology branch, and how to redraw it from memory

The assessment and nosology topics compress to a principle, a discriminator and a single exam fact. This is the other branch of the map, and it is examined as understanding rather than recall, so the retrieval target is the governing rule, the one contrast that separates a right answer from a wrong one, and the fact the paper reaches for. The mental state examination anchors the branch: it is a cross-sectional, here-and-now examination of the seven domains in their conventional order, *appearance and behaviour; speech; mood and affect; thought (form and content); perception; cognition; insight and judgement* (the mnemonic ALL SANE MEN THINK PRECISELY CONSIDERING INSIGHT), and it is neither the history nor a diagnosis but a snapshot that a diagnosis is later built upon.

TOPIC	THE PRINCIPLE	THE ONE DISCRIMINATOR OR EXAM FACT
Mental state examination	A cross-sectional here-and-now examination of seven domains in a fixed order	**It is not the history and not a diagnosis; a snapshot, not a summary of the illness over time**
The cognitive examination	A hierarchy tested attention first, then orientation, memory, language and praxis, then executive function	**Fluctuating inattention, not amnesia, is the hallmark of delirium and it invalidates every tier below it**

TOPIC	THE PRINCIPLE	THE ONE DISCRIMINATOR OR EXAM FACT
MMSE and MoCA	Bedside cognitive screens, each bundling the same items and scored out of a possible 30	**MMSE cut-off 24 (no executive items, misses mild impairment); MoCA cut-off 26, plus one point for twelve years or fewer of schooling, the more sensitive to mild cognitive impairment**
Reliability and validity	Reliability is consistency; validity is accuracy	**A scale can be reliable without being valid, but never valid without being reliable (reliability is necessary but not sufficient)**
ICD-11 versus DSM-5	Two harmonised classifications built by different bodies for different purposes	**ICD-11 gives prose essential features with no operationalised counts (clinical judgement); DSM-5 uses operationalised criteria with explicit counts and durations; the ICD is India's official system**
Categorical versus dimensional	Psychopathology as kinds versus degrees; no statistical test settles it, so both manuals are hybrids	**Categories win on usability, dimensions on accuracy; the manuals went most dimensional at personality disorder (ICD-11 severity plus five trait domains)**

The assessment-and-nosology branch of the synthesis map: cover the last two columns and produce the discriminator and the exam fact for each topic (the chapter's assessment and nosology topics; ICD-11 CDDR; DSM-5-TR).

Now cover the branches and redraw the chapter from memory. The accompanying figure draws the whole chapter as a single branching tree: the trunk is the master mnemonic's six schools, the leaves are the named modalities, and a second main branch carries the assessment skills (the mental state and cognitive examinations, the psychometric principles) and the nosology (the two classifications and the categorical-versus-dimensional debate). The retrieval drill is to hide it and rebuild it: speak, for each therapy leaf, its model, technique and lead indication, and for each assessment or nosology node, its principle, discriminator and one exam fact. Wherever the redraw stalls is the exact branch to reopen; wherever it flows, the consolidation has taken.

PEARL

Do the cover-the-branches redraw against the clock. In a viva you have seconds, not minutes, so practise producing a whole branch (the six schools, or the seven mental-state domains, or the four DBT modes) as a single fluent run rather than hunting item by item. Speed of retrieval, not mere possession of the fact, is what separates a confident answer from a hesitant one.

INDIA

The Indian MD and DNB psychiatry examinations are heavily viva-based and drill exactly this branch structure: the ego-defence grid, the mental state examination and the eponym counts are perennial theory-paper and viva questions taken straight from Kaplan and Sadock, so the counts are examined here, not treated as a Western aside. Two anchors are genuinely Indian and worth holding. The classification you diagnose forward in is the ICD-11, because India as a World Health Organization member state uses the ICD as its official statistical and training system and the Mental Healthcare Act 2017 ties the determination of mental illness to nationally or internationally accepted standards including the latest ICD. And the cognitive screens travel poorly across the country's languages and literacy levels, which is why the Hindi Mental State Examination and the vernacular adaptations from the NIMHANS and AIIMS assessment tradition exist, and why an imported cut-off is re-standardised rather than borrowed.

GOOD TO REMEMBER

- **The principle:** consolidation is retrieval practice, not re-reading; turn every heading into a question, answer it from memory, and spend the revision time on the branches you could not produce, because the effort of retrieval is what builds the recall the examination tests.
- **The one discriminator:** the synthesis map has two branches, the therapy branch (each modality compresses to a model, a signature technique and a lead indication) and the assessment-and-nosology branch (each topic compresses to a principle, a discriminator and one exam fact); learn each leaf as its three cells.
- **The one exam fact:** the master mnemonic (PLEASE BRING CARE, HOPE, SUPPORT, TRUST) holds the six schools; the counts to reproduce cold are Yalom's eleven factors, DBT's four modes, the five stages of change and Beck's three-view triad; and the cut-offs are the MMSE at 24 and the MoCA at 26, each out of a possible 30.

HOLD THIS

Consolidate by retrieval, not re-reading: cover the accompanying synthesis map and redraw it from memory, producing for every therapy leaf its model, technique and lead indication (the six schools of PLEASE BRING CARE, HOPE, SUPPORT, TRUST, with Yalom's eleven factors, DBT's four modes, the five stages of change and Beck's three-view triad as the counts to reproduce cold), and for every assessment-and-nosology node its principle, discriminator and one exam fact (the seven-domain MSE is a snapshot not a diagnosis; reliability is consistency and validity is accuracy; the MMSE cut-off is 24 and the MoCA 26 out of a possible 30; ICD-11 gives essential features while DSM-5 operationalises; and the categorical-versus-dimensional call is a pragmatic hybrid).

Previously asked

This chapter is examined as skills rather than syndromes, and it rewards precise, structured answers. The reliable pattern is that the specific psychotherapies recur as short notes (each wanting its model, its technique, its evidence and its one indication), that the defence mechanisms and transference come as their own essay and note, that the mental state examination, the projective tests and the rating scales are asked as assessment notes, and that the culture-bound syndromes and testamentary capacity are the recurring cross-cutting questions.

The long essays reward a named structure (a hierarchy of defences, the domains of the examination in order, an enumerated list of culture-bound syndromes), so the scheme and its exact count must be exam-ready. The genuine questions on record are grouped by band below.

HOW THIS TERRITORY IS ACTUALLY TESTED

- **The specific psychotherapies, as short notes.** Each named modality has come as a 10-mark note: "CBT (Cognitive Behaviour Therapy)" and "Cognitive Behaviour therapy", "Dialectical Behaviour Therapy (DBT)", "Interpersonal therapy", "Family therapy", "Biofeedback", "Meditation as a relaxation technique", and "Describe the principles, process and uses of Rational Emotive Behaviour Therapy (REBT)"; "Basic principles and application of behaviour therapy" has come as a full 25-mark essay. Prepare each modality to be described the same way, its model, its core technique, its evidence base and its one lead indication, and be able to place it on the psychotherapy-family tree. essay and short note, recurring

- **The defence mechanisms and the transference, the psychodynamic essay and note.** "Discuss defence mechanisms and their relevance in mental illness" has come as a 25-mark essay across more than one sitting, and "Transference and counter-transference" recurs as a 10-mark note. Prepare the defence-mechanism maturity hierarchy (mature, neurotic, immature, psychotic) with a clinical example for each, and the clinical meaning of transference, counter-transference and resistance. essay and short note, recurring

- **The projective tests, the mental state examination and the rating scales, as assessment notes.** "Rorschach's test" recurs as a 10-mark note across several sittings, with "Indications of the various psychiatric disorders on the Rorschach test" as a later note; "MMSE" and the frontal-lobe screen have come as notes; and "Rating scales in psychiatry" and the "need, clinical implications and problems of psychiatric rating scales" recur. Prepare the projective hypothesis and the main instruments, the mental state examination domain by domain, the bedside cognitive screen and the MMSE and MoCA cut-offs, and the rating scales as a catalogue with reliability versus validity. short note, recurring

- **The culture-bound syndromes, the recurring cross-cutting essay.** "Discuss the culture-bound syndromes" has come as a 25-mark essay across several sittings, and "Enumerate the culture-bound syndromes and describe Dhat syndrome in detail" as a 10-mark note. Prepare the reframing to cultural concepts of distress (syndromes, idioms, explanations), the enumerated examples, and the cultural formulation; the deep treatment of Dhat as an Indian culture-bound presentation is developed in the Somatic-symptom, sexual, impulse-control disorders and suicide notes. essay and short note, recurring

- **Testamentary capacity and the forensic essentials, as notes.** "Testamentary capacity" and "Assessment of testamentary capacity" recur as 10 to 25-mark answers, and the medico-legal and forensic-science angle has come as an essay. Prepare the Banks versus Goodfellow criteria for a valid will, fitness to stand trial, and criminal responsibility under the McNaughten rules and the Indian frame; the fuller legislation and forensic procedure are developed in the Mental health legislation and forensic psychiatry notes. short note and essay, recurring

- **Classification and the nosological shifts, as essays.** The classification questions come attached to a disorder, for example "Discuss the nosological shift of OCD in DSM-5 and its spectrum" or "Classification of personality disorders". Prepare the principles of classification and the diagnostic process, the ICD-11 changes against ICD-10 and the ICD-11-versus-DSM-5 discriminator, and the categorical-versus-dimensional debate here; the disorder-specific nosological shifts are developed in the disorder chapters they belong to. essay, disorder-attached

Prepare this material to be applied, not just recited: each therapy ready to be chosen for a presentation, the mental state examination ready to be performed and written up, the rating scales ready to be selected and interpreted, and the nosology ready to place a case in the current classification. The disorder-specific therapy protocols (exposure and response prevention,

trauma-focused CBT, dialectical behaviour therapy for borderline personality disorder, interpersonal therapy for depression) and the disorder-specific rating scales are developed in their disorder chapters; the deep psychometric theory and the descriptive psychopathology are developed in the Psychometry, Assessment and Descriptive Psychopathology notes; and the fuller mental-health legislation is developed in the Mental health legislation and forensic psychiatry notes.

Quick review

THE PSYCHOTHERAPIES: CLASSIFICATION, THE COMMON FACTORS, AND CHOOSING	
CLASSIFICATION	By **depth** (supportive to reconstructive), by **school** (psychodynamic, behavioural, cognitive and cognitive-behavioural, humanistic, systemic and family, third-wave), by **duration** (brief to long-term) and by **format** (individual, group, family).
COMMON FACTORS	Much of the outcome is carried not by the technique but by factors common to all therapies: above all the **therapeutic alliance** (Bordin: the bond, plus agreement on goals and tasks), and alongside it expectancy and hope, the therapist's empathy and warmth, and the patient's own resources. Frank's shared credible rationale. The technique is one contributor, not the whole effect.
STAGES OF CHANGE	**Precontemplation, contemplation, preparation, action, maintenance** (five core; relapse recycles to an earlier stage). Match the intervention to the stage; this is the frame motivational interviewing works within.
CHOOSING THE THERAPY	Match the presentation and the formulation to the evidence-based modality (depression to CBT or IPT; borderline personality to DBT; substance use to MI and CBT; a family problem to family therapy; psychosis to family psychoeducation and CBTp alongside medication). The disorder-specific protocols are developed in their disorder chapters.
THE SPECIFIC THERAPIES: MODEL, TECHNIQUE AND LEAD INDICATION	
SUPPORTIVE	Ego-supportive (not exploratory); reassurance, ventilation, guidance, environmental manipulation, ego-strengthening. The most widely used therapy; for acute crisis, chronic and severe illness, and low ego-strength. Not a stand-alone guideline first-line specific treatment.
CBT (CORE)	The Beckian **cognitive model**: situation to automatic thought to emotion, body and behaviour; the levels (automatic thoughts, intermediate and core beliefs); the **cognitive triad** (self, world, future); the distortions. Cognitive restructuring plus behavioural experiments and activation. The most-evidenced therapy; first-line for depression and the anxiety disorders (ERP for OCD, cross-ref).
BEHAVIOUR THERAPY	Learning theory. **Systematic desensitisation** = a graded hierarchy plus relaxation (reciprocal inhibition, Wolpe); **flooding** = maximal exposure with NO hierarchy. Token economy (operant, Ayllon and Azrin). Trap: confusing flooding with desensitisation.

THE SPECIFIC THERAPIES: MODEL, TECHNIQUE AND LEAD INDICATION	
PSYCHODYNAMIC	Topographic and structural models; **transference**, counter-transference and resistance; free association, interpretation, working through. From classical analysis to brief dynamic therapy. The defences run **mature to neurotic to immature to psychotic**.
INTERPERSONAL (IPT)	Four problem areas: **grief, role dispute, role transition, interpersonal deficits**. Time-limited, present-focused; first-line for depression.
GROUP	**Yalom's eleven therapeutic factors** (universality, instillation of hope, imparting information, altruism, corrective recapitulation, socialising techniques, imitative behaviour, interpersonal learning, cohesiveness, catharsis, existential factors).
FAMILY AND COUPLE	Systemic (the system, not the individual, is treated); **structural** (Minuchin), **strategic** (Haley, Milan); the genogram; expressed emotion.
THIRD-WAVE	**DBT** (Linehan): biosocial theory, the **four modes** (individual, skills group, phone coaching, consultation team) and four skills modules; for borderline personality disorder. **ACT** (psychological flexibility, the hexaflex). **MBCT** for depressive relapse prevention.
MOTIVATIONAL INTERVIEWING	The spirit (partnership, acceptance, compassion, evocation); work with **ambivalence** and elicit **change talk**; OARS. For substance use and behaviour change.

CLINICAL ASSESSMENT: THE INTERVIEW, THE MSE, COGNITION AND FORMULATION	
THE HISTORY	Presenting complaint and history of the present illness, past psychiatric and medical history, drug and family history, personal and developmental history, premorbid personality, and the collateral history.
THE MSE, IN ORDER	**Appearance and behaviour; speech; mood and affect; thought (form and content); perception; cognition; insight and judgement.** A cross-sectional here-and-now examination: it is NOT the history, and it is NOT a diagnosis. Mood is subjective, affect is observed.
THE COGNITIVE EXAMINATION	Attention, orientation, memory, language and praxis, and the frontal-executive tests. **MMSE**: out of a possible 30, impairment at or below 23, read against age and education, ceilings in the educated. **MoCA**: out of a possible 30, normal at or above 26, add one point if twelve years or fewer of education; more sensitive to mild and executive impairment. India: the HMSE and the NIMHANS battery.
THE FORMULATION	The biopsychosocial model and the **4-Ps** (predisposing, precipitating, perpetuating, protective) across the biological, psychological and social levels. The formulation, not the diagnosis, drives the plan.

RELIABILITY, VALIDITY AND THE RATING SCALES	
RELIABILITY VERSUS VALIDITY	**Reliability** = **consistency** (test-retest, inter-rater, internal consistency and Cronbach's alpha); **validity** = **accuracy** (content, criterion, construct). A test can be reliable without being valid, but not valid without being reliable. Sensitivity rules a condition out (SnNout), specificity rules it in (SpPin).
THE CLINICIAN-RATED VERSUS SELF-REPORT SPLIT	Clinician-rated (HAM-D, MADRS, YMRS, PANSS, BPRS, HAM-A, Y-BOCS): captures signs, resists faking, needs training. Self-report (GAD-7, PHQ-9, the Beck inventories): fast, the patient's view, limited by insight and candour.
THE CRUNCH CUT-OFFS	**MMSE** impaired at or below 23 and **MoCA** normal at or above 26 (each out of a possible 30) are the two to hold. **MADRS** remission at or below 10 and **YMRS** at or below 12 (each out of a possible 60); **HAM-D** remission at or below 7; **GAD-7** screen-positive at or above 10 (out of a possible 21); **Y-BOCS** symptomatic at or above 16 (out of a possible 40); **PANSS** floored at 30 (up to a possible 210, never zero); **AUDIT** at or above 8 (out of a possible 40).

NOSOLOGY: THE PRINCIPLES, THE SYSTEMS AND THE DEBATE	
PRINCIPLES AND THE PROCESS	The Kraepelinian dichotomy; the reliability crisis that drove the operationalised turn (Feighner, DSM-III); the purposes of classification; the diagnostic process (prototype and criteria, the hierarchy, the formulation); the Robins and Guze validators.
ICD-11 VERSUS ICD-10	The schizophrenia **subtypes removed** (symptom and course specifiers instead); a **dimensional** personality-disorder model (severity plus trait domains); new entities (complex PTSD, prolonged grief disorder, gaming disorder, compulsive sexual behaviour disorder); **catatonia** a standalone grouping; **gender incongruence moved out** of the mental-disorders chapter; the clinical-descriptions-and-diagnostic-requirements format.
ICD-11 VERSUS DSM-5	The discriminator: ICD-11 states **essential features** with NO operationalised counts (clinical judgement against a prototype); DSM-5-TR sets **polythetic operationalised criteria** with symptom counts and durations. WHO global-health versus APA research orientation. ICD is India's official system.
CATEGORICAL VERSUS DIMENSIONAL	Categorical: discrete, familiar and actionable, but arbitrary thresholds, comorbidity and heterogeneity. Dimensional: a continuum, fits the data and captures sub-threshold states, but still needs a cut point. Hybrids: ICD-11 personality severity plus traits, the DSM-5 alternative model; the research frameworks **HiTOP** (spectra) and **RDoC** (functional domains).

THE CROSS-CUTTING CLINICAL ISSUES	
CULTURAL CONCEPTS OF DISTRESS	The reframing from culture-bound syndromes to cultural **syndromes, idioms and explanations**; the cultural formulation interview; the examples (Dhat and koro in the Indian and Asian context, amok, ataque de nervios). Deep treatment of Dhat is in the somatic and suicide notes.
FORENSIC ESSENTIALS	**Fitness to stand trial** (understand the proceedings, instruct counsel); **criminal responsibility** (the McNaughten rules; India: unsoundness of mind, IPC Section 84); **testamentary capacity** (Banks versus Goodfellow). The fuller statute and procedure are in the legislation and forensic notes.
MENTAL HEALTHCARE ACT 2017	**Independent** (capacitous, consenting) versus **supported** admission (with safeguards and time limits); the **advance directive**; the **nominated representative**; the Mental Health Review Board; the decriminalisation of attempted suicide (the presumption of severe stress, Section 115).
CAPACITY, CONSENT, CONFIDENTIALITY	**Capacity** (understand, retain, use and weigh, communicate; decision-specific and time-specific; presumed); informed consent and its exceptions; confidentiality and its limits (the duty to warn or protect, the Tarasoff principle).
THE TRAPS	Confusing flooding with systematic desensitisation; confusing reliability (consistency) with validity (accuracy); calling the MSE a history or a diagnosis; misplacing a defence on the maturity hierarchy; quoting the PANSS floor as zero; and forcing a categorical label where a dimensional formulation fits.

The rating scales in full

This appendix gathers the rating instruments used across the whole series into one place. The licence-cleared forms are reproduced as their actual instruments and the permission-required ones are typeset from their published structure; every cut-off here is verified against a primary source and stated out of its possible total. These reproductions are cleared for the free, non-commercial resident edition only, never a paid product.

Cognition

MMSE (TYPESET, NOT REPRODUCED)	VERIFIED STRUCTURE AND CUT-OFF
Instrument	Mini-Mental State Examination, the standard bedside cognitive screen (Folstein, Folstein and McHugh, 1975)
Domains	orientation to time and place (10), registration (3), attention and calculation (5), recall (3), language covering naming, repetition, a three-stage command, reading and writing (8), and construction by copying interlocking pentagons (1)
Total	sum of all items, out of a possible 30
Cut-off	**a score below 24 out of a possible 30 is the common threshold for cognitive impairment, adjusted for age and education; a rough severity reading is 24 to 30 no or questionable impairment, 18 to 23 mild and below 18 more marked (bands vary by source)**

A.1 The Mini-Mental State Examination (MMSE). The standard bedside cognitive screen across orientation, registration, attention and calculation, recall, language and construction, summing to a total out of a possible 30, with a score below 24 the common cut-off for cognitive impairment (adjusted for age and education). The instrument is copyright (PAR Inc, from 2001) and permission-required, so its structure is typeset from the published instrument rather than reproduced (Folstein MF, Folstein SE, McHugh PR. J Psychiatr Res. 1975).

MOCA (TYPESET, NOT REPRODUCED)	VERIFIED STRUCTURE AND CUT-OFF
Instrument	Montreal Cognitive Assessment, a screen more sensitive than the MMSE to mild cognitive impairment (Nasreddine et al., 2005)
Domains	visuospatial and executive (5), naming (3), attention (6), language (3), abstraction (2), delayed recall (5) and orientation (6)
Total	out of a possible 30, with one point added if the person has 12 or fewer years of formal education
Cut-off	**a score below 26 out of a possible 30 suggests cognitive impairment**

A.2 The Montreal Cognitive Assessment (MoCA). A cognitive screen more sensitive than the MMSE to mild cognitive impairment, spanning visuospatial and executive function, naming, attention, language, abstraction, delayed recall and orientation, out of a possible 30, with one point added for 12 or fewer years of education; a score below 26 suggests impairment. Copyright and permission-required (registration is needed to use it), so typeset from the published structure rather than reproduced (Nasreddine ZS, et al. J Am Geriatr Soc. 2005).

Mood

HAM-D (TYPESET)	VERIFIED STRUCTURE AND BANDS
Instrument	Hamilton Depression Rating Scale, 17-item version, the reference clinician-rated severity measure for depression (Hamilton, 1960)
Items	17 items, nine scored 0 to 4 and eight scored 0 to 2
Total	out of a possible 52
Severity bands	**0 to 7 none or remission, 8 to 16 mild, 17 to 23 moderate, 24 or more severe**

A.3 The Hamilton Depression Rating Scale (HAM-D, 17-item). The reference clinician-rated depression severity measure: 17 items, nine scored 0 to 4 and eight scored 0 to 2, summing to a total out of a possible 52, with 0 to 7 normal or remission, 8 to 16 mild, 17 to 23 moderate and 24 or more severe. The HAM-D is in the public domain; its structure is typeset here for the consolidated appendix (Hamilton M. J Neurol Neurosurg Psychiatry. 1960).

MADRS (TYPESET, NOT REPRODUCED)	VERIFIED STRUCTURE AND BANDS
Instrument	Montgomery-Asberg Depression Rating Scale, clinician-rated and designed to be sensitive to change (Montgomery and Asberg, 1979)
Items	10 anchored items, each scored 0 to 6
Total	out of a possible 60
Severity bands	**0 to 6 normal, 7 to 19 mild, 20 to 34 moderate, 35 to 60 severe**

A.4 The Montgomery-Asberg Depression Rating Scale (MADRS). A clinician-rated depression severity measure designed to be sensitive to change: ten anchored items each scored 0 to 6, out of a possible 60, with 0 to 6 normal, 7 to 19 mild, 20 to 34 moderate and 35 to 60 severe. Copyright and permission-required, so typeset from the published structure rather than reproduced (Montgomery SA, Asberg M. Br J Psychiatry. 1979).

YMRS (TYPESET, NOT REPRODUCED)	VERIFIED STRUCTURE AND THRESHOLDS
Instrument	Young Mania Rating Scale, the reference clinician-rated measure of manic severity (Young, Biggs, Ziegler and Meyer, 1978)
Items	11 items; four core items weighted 0 to 8 and seven items scored 0 to 4
Total	out of a possible 60
Interpretation	**dimensional, with no official diagnostic cut-off; a total near 12 out of a possible 60 is the most widely used remission threshold and near 20 the common acute-mania trial entry level**

A.5 The Young Mania Rating Scale (YMRS). The reference clinician-rated measure of manic severity: 11 items, four core items weighted 0 to 8 and seven scored 0 to 4, out of a possible 60. It is dimensional with no official diagnostic cut-off; a total near 12 is the common remission threshold and near 20 the usual acute-mania trial entry level. Copyright and permission-required, so typeset from the published structure rather than reproduced (Young RC, Biggs JT, Ziegler VE, Meyer DA. Br J Psychiatry. 1978).

Psychosis

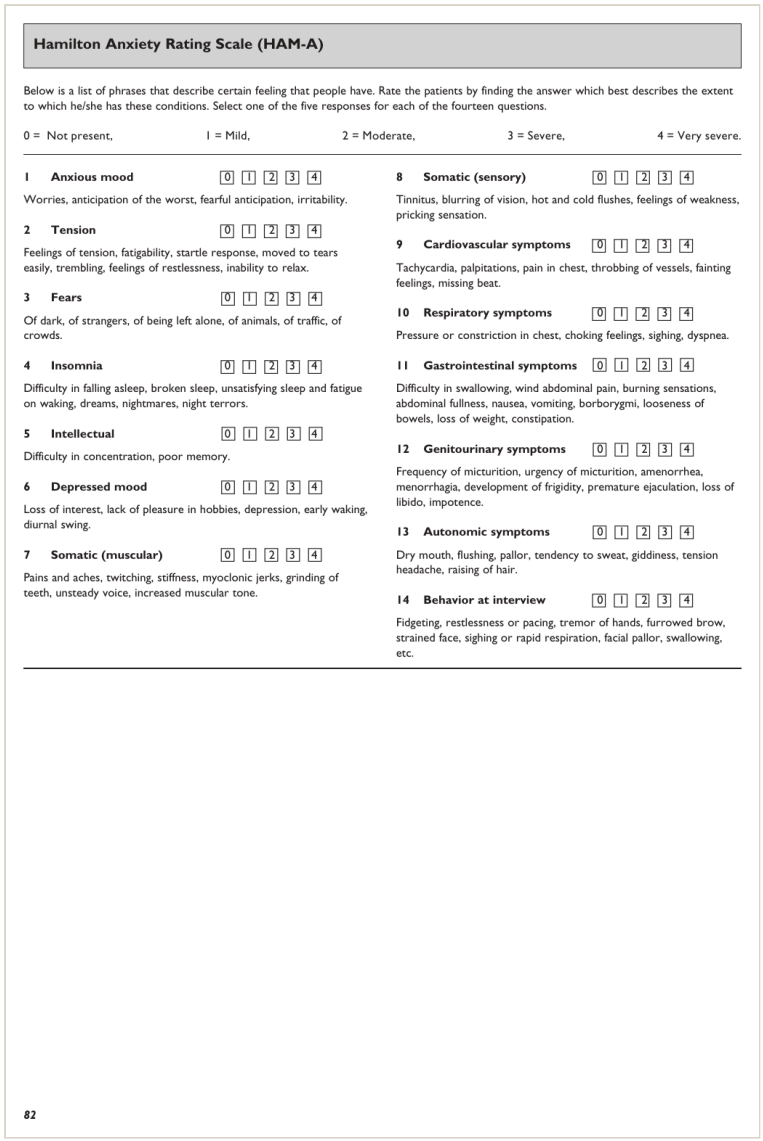
PANSS (TYPESET, NOT REPRODUCED)	VERIFIED STRUCTURE
Instrument	Positive and Negative Syndrome Scale, the interview-based severity measure for schizophrenia (Kay, Fiszbein and Opler, 1987)
Subscales	30 items each rated 1 to 7: Positive P1 to P7 (7 to 49), Negative N1 to N7 (7 to 49), General Psychopathology G1 to G16 (16 to 112)
Total	out of a possible 210; the floor is 30 because the lowest rating on each item is 1
Interpretation	**dimensional, with no official cut-off; any CGI-anchored severity mapping is approximate**

A.6 The Positive and Negative Syndrome Scale (PANSS). The interview-based severity measure for schizophrenia: 30 items each rated 1 to 7, split into Positive (seven items), Negative (seven items) and General Psychopathology (sixteen items), for a total out of a possible 210 (the floor is 30 because the lowest rating is 1). It is dimensional with no official cut-off. Copyright and permission-required, so typeset from the published structure rather than reproduced (Kay SR, Fiszbein A, Opler LA. Schizophr Bull. 1987).

BPRS (TYPESET)	VERIFIED STRUCTURE
Instrument	Brief Psychiatric Rating Scale, a broad clinician-rated symptom-severity measure (Overall and Gorham, 1962); the widely used expanded version has 18 items
Items	18 items, each rated 1 (not present) to 7 (extremely severe)
Total	range 18 to 126, out of a possible 126
Interpretation	**dimensional severity, with no official cut-off**

A.7 The Brief Psychiatric Rating Scale (BPRS). A broad clinician-rated measure of psychiatric symptom severity, most often the 18-item expanded version, each item rated 1 (not present) to 7 (extremely severe), for a total out of a possible 126 (range 18 to 126). It is dimensional with no official cut-off. Typeset here as structure only for the consolidated appendix (Overall JE, Gorham DR. Psychol Rep. 1962).

Anxiety and OCD



Hamilton Anxiety Rating Scale (HAM-A)

Below is a list of phrases that describe certain feeling that people have. Rate the patients by finding the answer which best describes the extent to which he/she has these conditions. Select one of the five responses for each of the fourteen questions.

0 = Not present, 1 = Mild, 2 = Moderate, 3 = Severe, 4 = Very severe.

1 Anxious mood [0] [1] [2] [3] [4]
Worries, anticipation of the worst, fearful anticipation, irritability.

2 Tension [0] [1] [2] [3] [4]
Feelings of tension, fatigability, startle response, moved to tears easily, trembling, feelings of restlessness, inability to relax.

3 Fears [0] [1] [2] [3] [4]
Of dark, of strangers, of being left alone, of animals, of traffic, of crowds.

4 Insomnia [0] [1] [2] [3] [4]
Difficulty in falling asleep, broken sleep, unsatisfying sleep and fatigue on waking, dreams, nightmares, night terrors.

5 Intellectual [0] [1] [2] [3] [4]
Difficulty in concentration, poor memory.

6 Depressed mood [0] [1] [2] [3] [4]
Loss of interest, lack of pleasure in hobbies, depression, early waking, diurnal swing.

7 Somatic (muscular) [0] [1] [2] [3] [4]
Pains and aches, twitching, stiffness, myoclonic jerks, grinding of teeth, unsteady voice, increased muscular tone.

8 Somatic (sensory) [0] [1] [2] [3] [4]
Tinnitus, blurring of vision, hot and cold flushes, feelings of weakness, pricking sensation.

9 Cardiovascular symptoms [0] [1] [2] [3] [4]
Tachycardia, palpitations, pain in chest, throbbing of vessels, fainting feelings, missing beat.

10 Respiratory symptoms [0] [1] [2] [3] [4]
Pressure or constriction in chest, choking feelings, sighing, dyspnea.

11 Gastrointestinal symptoms [0] [1] [2] [3] [4]
Difficulty in swallowing, wind abdominal pain, burning sensations, abdominal fullness, nausea, vomiting, borborygmi, looseness of bowels, loss of weight, constipation.

12 Genitourinary symptoms [0] [1] [2] [3] [4]
Frequency of micturition, urgency of micturition, amenorrhea, menorrhagia, development of frigidity, premature ejaculation, loss of libido, impotence.

13 Autonomic symptoms [0] [1] [2] [3] [4]
Dry mouth, flushing, pallor, tendency to sweat, giddiness, tension headache, raising of hair.

14 Behavior at interview [0] [1] [2] [3] [4]
Fidgeting, restlessness or pacing, tremor of hands, furrowed brow, strained face, sighing or rapid respiration, facial pallor, swallowing, etc.

82

A.8 The Hamilton Anxiety Rating Scale (HAM-A). The clinician-rated severity measure for anxiety: 14 items spanning psychic and somatic anxiety, each scored 0 to 4, for a total out of a possible 56; the reproduced form's bands read below 17 mild, 18 to 24 mild to moderate and 25 to 30 moderate to severe (bands vary by source). Reproduced as its actual form; the HAM-A is in the public domain (Hamilton M. Br J Med Psychol. 1959).

GENERALIZED ANXIETY DISORDER 7-ITEM SCALE (GAD-7)

Spitzer RL, Kroenke K, Williams JBW, Lowe B, 2006

Over the **last 2 weeks**, how often have you been bothered by the following problems? *(Use the scale to the right to indicate your answer.)*

Question	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious, or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid, as if something awful might happen	0	1	2	3

Add columns (total): Column totals summed give a total score of 0 to 21.

Score interpretation: 0-4 minimal anxiety; 5-9 mild anxiety; 10-14 moderate anxiety; 15-21 severe anxiety.

Clinical threshold: A score of 10 or greater is the common cut-off for probable generalized anxiety disorder (a cut-off of 8 or greater maximizes sensitivity and specificity).

If you checked off any problems, how **difficult** have these made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all □ Somewhat difficult □ Very difficult □ Extremely difficult □

Source: Spitzer RL, Kroenke K, Williams JBW, Lowe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med. 2006;166(10):1092-1097.

Copyright / permission: Developed by Drs. Robert L. Spitzer, Janet B.W. Williams, Kurt Kroenke and colleagues, with an educational grant from Pfizer Inc. Copyright Pfizer Inc. No permission required to reproduce, translate, display or distribute. Reproduced here for free, non-commercial educational use.

A.9 The GAD-7 (Generalised Anxiety Disorder 7-item scale). The brief self-report screen for generalised anxiety: seven items each scored 0 to 3 over the last two weeks, for a total out of a possible 21, with 0 to 4 minimal, 5 to 9 mild, 10 to 14 moderate and 15 to 21 severe, and a score of 10 or more the common cut-off for probable generalised anxiety disorder. Reproduced as its actual open form (Spitzer, Kroenke, Williams and Lowe, 2006; developed with an educational grant from Pfizer, no permission required to reproduce).

Y-BOCS (TYPESET, NOT REPRODUCED)	VERIFIED STRUCTURE AND BANDS
Instrument	Yale-Brown Obsessive Compulsive Scale, the reference clinician-rated severity measure for OCD (Goodman, Price, Rasmussen and colleagues, 1989)
Items	10 items: 5 rate the obsessions and 5 rate the compulsions, each across time occupied, interference, distress, resistance and control; each item scored 0 to 4 (obsession subscale 0 to 20, compulsion subscale 0 to 20)
Total	out of a possible 40
Severity bands	**0 to 7 subclinical, 8 to 15 mild, 16 to 23 moderate, 24 to 31 severe, 32 to 40 extreme**

A.10 The Yale-Brown Obsessive Compulsive Scale (Y-BOCS). The reference clinician-rated severity measure for OCD: ten items, five for obsessions and five for compulsions, each rating time occupied, interference, distress, resistance and control on a 0 to 4 scale, for a total out of a possible 40, with 0 to 7 subclinical, 8 to 15 mild, 16 to 23 moderate, 24 to 31 severe and 32 to 40 extreme. Copyright and permission-required, so typeset from the published structure rather than reproduced (Goodman WK, Price LH, Rasmussen SA, et al. Arch Gen Psychiatry. 1989).

Trauma and somatic

PCL-5

Instructions: Below is a list of problems that people sometimes have in response to a very stressful experience. Keeping your worst event in mind, please read each problem carefully and then select one of the numbers to the right to indicate how much you have been bothered by that problem in the past month.

Your worst event: _____

In the past month, how much were you bothered by:	Not at all	A little bit	Moderately	Quite a bit	Extremely
1. Repeated, disturbing, and unwanted memories of the stressful experience?	0 ○	1 ○	2 ○	3 ○	4 ○
2. Repeated, disturbing dreams of the stressful experience?	0 ○	1 ○	2 ○	3 ○	4 ○
3. Suddenly feeling or acting as if the stressful experience were actually happening again (as if you were actually back there reliving it)?	0 ○	1 ○	2 ○	3 ○	4 ○
4. Feeling very upset when something reminded you of the stressful experience?	0 ○	1 ○	2 ○	3 ○	4 ○
5. Having strong physical reactions when something reminded you of the stressful experience (for example, heart pounding, trouble breathing, sweating)?	0 ○	1 ○	2 ○	3 ○	4 ○
6. Avoiding memories, thoughts, or feelings related to the stressful experience?	0 ○	1 ○	2 ○	3 ○	4 ○
7. Avoiding external reminders of the stressful experience (for example, people, places, conversations, activities, objects, or situations)?	0 ○	1 ○	2 ○	3 ○	4 ○
8. Trouble remembering important parts of the stressful experience?	0 ○	1 ○	2 ○	3 ○	4 ○
9. Having strong negative beliefs about yourself, other people, or the world (for example, having thoughts such as: I am bad, there is something seriously wrong with me, no one can be trusted, the world is completely dangerous)?	0 ○	1 ○	2 ○	3 ○	4 ○
10. Blaming yourself or someone else for the stressful experience or what happened after it?	0 ○	1 ○	2 ○	3 ○	4 ○
11. Having strong negative feelings such as fear, horror, anger, guilt, or shame?	0 ○	1 ○	2 ○	3 ○	4 ○
12. Loss of interest in activities that you used to enjoy?	0 ○	1 ○	2 ○	3 ○	4 ○
13. Feeling distant or cut off from other people?	0 ○	1 ○	2 ○	3 ○	4 ○
14. Trouble experiencing positive feelings (for example, being unable to feel happiness or have loving feelings for people close to you)?	0 ○	1 ○	2 ○	3 ○	4 ○
15. Irritable behavior, angry outbursts, or acting aggressively?	0 ○	1 ○	2 ○	3 ○	4 ○
16. Taking too many risks or doing things that could cause you harm?	0 ○	1 ○	2 ○	3 ○	4 ○
17. Being "superalert" or watchful or on guard?	0 ○	1 ○	2 ○	3 ○	4 ○
18. Feeling jumpy or easily startled?	0 ○	1 ○	2 ○	3 ○	4 ○
19. Having difficulty concentrating?	0 ○	1 ○	2 ○	3 ○	4 ○
20. Trouble falling or staying asleep?	0 ○	1 ○	2 ○	3 ○	4 ○

PCL-5 (18 August 2023) National Center for PTSD Page 3 of 3

A.11 The PTSD Checklist for DSM-5 (PCL-5). The 20-item self-report measure of the DSM-5 PTSD symptoms, each scored 0 to 4 over the past month, for a total out of a possible 80; a provisional cut-off of 31 to 33 flags probable PTSD, which the National Center for PTSD frames as provisional and under review. Reproduced as its actual form; the PCL-5 is in the public domain (Weathers, Litz, Keane, Palmieri, Marx and Schnurr, 2013; National Center for PTSD, US Department of Veterans Affairs).

Patient Health Questionnaire-15: Physical Symptoms

During the last 4 weeks, how much have you have been bothered by any of the following problems? Please place a check mark in the box to indicate your answer.

		Not bothered	Bothered a little	Bothered a lot
		0	1	2
1.	Stomach pain	☐	☐	☐
2.	Back pain	☐	☐	☐
3.	Pain in your arms, legs, or joints (knees, hips, etc)	☐	☐	☐
4.	Menstrual cramps or other problems with your periods [women only]	☐	☐	☐
5.	Headaches	☐	☐	☐
6.	Chest pain	☐	☐	☐
7.	Dizziness	☐	☐	☐
8.	Fainting spells	☐	☐	☐
9.	Feeling your heart pound or race	☐	☐	☐
10.	Shortness of breath	☐	☐	☐
11.	Pain or problems during sexual intercourse	☐	☐	☐
12.	Constipation, loose bowels, or diarrhea	☐	☐	☐
13.	Nausea, gas, or indigestion	☐	☐	☐
14.	Feeling tired or having low energy	☐	☐	☐
15.	Trouble sleeping	☐	☐	☐
TOTAL SCORE =				

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Source instrument available at http://www.phqscreeners.com/
Consortium version 12May2013. Available at http://www.rdc-tmdinternational.org/

A.12 The PHQ-15 (Patient Health Questionnaire, physical symptoms). The 15-item somatic-symptom severity scale, each item scored 0 to 2, for a total out of a possible 30, with 0 to 4 minimal, 5 to 9 low, 10 to 14 medium and 15 to 30 high somatic-symptom burden. Reproduced as its actual open form (Kroenke, Spitzer and Williams; copyright Pfizer Inc, no permission required to reproduce).

Substance use and dependence

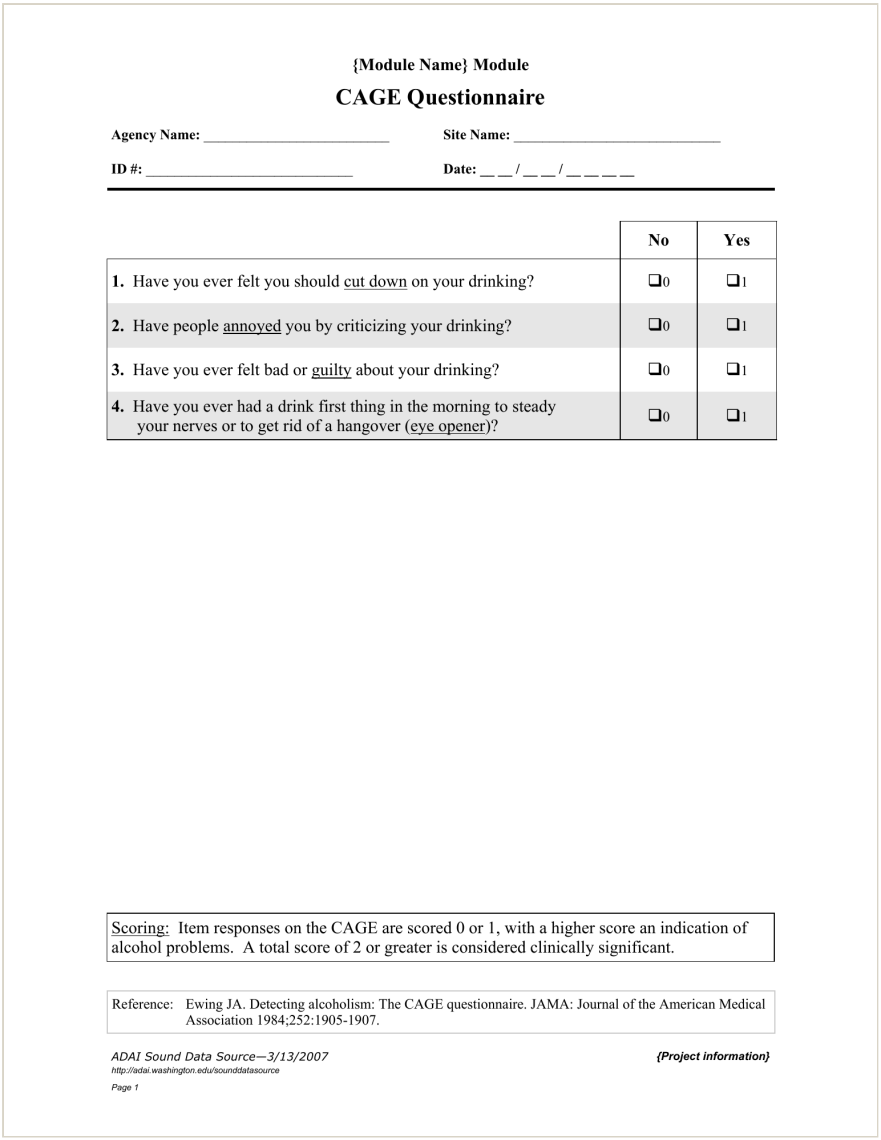
Box 10

The Alcohol Use Disorders Identification Test: Self-Report Version

PATIENT: Because alcohol use can affect your health and can interfere with certain medications and treatments, it is important that we ask some questions about your use of alcohol. Your answers will remain confidential so please be honest.
Place an X in one box that best describes your answer to each question.

Questions	0	1	2	3	4	
1. How often do you have a drink containing alcohol?	Never	Monthly or less	2-4 times a month	2-3 times a week	4 or more times a week	
2. How many drinks containing alcohol do you have on a typical day when you are drinking?	1 or 2	3 or 4	5 or 6	7 to 9	10 or more	
3. How often do you have six or more drinks on one occasion?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
4. How often during the last year have you found that you were not able to stop drinking once you had started?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
5. How often during the last year have you failed to do what was normally expected of you because of drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
7. How often during the last year have you had a feeling of guilt or remorse after drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
8. How often during the last year have you been unable to remember what happened the night before because of your drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
9. Have you or someone else been injured because of your drinking?	No		Yes, but not in the last year		Yes, during the last year	
10. Has a relative, friend, doctor, or other health care worker been concerned about your drinking or suggested you cut down?	No		Yes, but not in the last year		Yes, during the last year	
					Total	

A.13 The AUDIT (Alcohol Use Disorders Identification Test). The WHO 10-item screen for hazardous and harmful drinking, each item scored 0 to 4, for a total out of a possible 40, with a score of 8 or more indicating hazardous or harmful use and possible dependence (a lower cut-off of 7 is recommended for women and adults over 65). Reproduced from the WHO manual, free for non-commercial reproduction under the WHO copyright grant (Babor, Higgins-Biddle, Saunders and Monteiro, WHO, 2001).



{Module Name} Module

CAGE Questionnaire

Agency Name: _____ Site Name: _____

ID #: _____ Date: __ __ / __ __ / __ __ __ __

	No	Yes
1. Have you ever felt you should cut down on your drinking?	❑0	❑1
2. Have people annoyed you by criticizing your drinking?	❑0	❑1
3. Have you ever felt bad or guilty about your drinking?	❑0	❑1
4. Have you ever had a drink first thing in the morning to steady your nerves or to get rid of a hangover (eye opener)?	❑0	❑1

Scoring: Item responses on the CAGE are scored 0 or 1, with a higher score an indication of alcohol problems. A total score of 2 or greater is considered clinically significant.

Reference: Ewing JA. Detecting alcoholism: The CAGE questionnaire. JAMA: Journal of the American Medical Association 1984;252:1905-1907.

ADAI Sound Data Source—3/13/2007
http://adai.washington.edu/sounddatasource
Page 1

{Project information}

A.14 The CAGE questionnaire. The four-item screen for alcohol misuse (Cut down, Annoyed, Guilty, Eye-opener), each item scored 0 or 1, for a total out of a possible 4, with a score of 2 or more clinically significant and warranting fuller assessment. Reproduced with acknowledgement for non-commercial use per the Bowles Center permission (Ewing JA. JAMA. 1984).

Clinical Institute Withdrawal Assessment of Alcohol Scale, Revised (CIWA-Ar)

Patient:_____ Date: _____ Time: _____ (24 hour clock, midnight = 00:00)

Pulse or heart rate, taken for one minute:_____ Blood pressure:_____

NAUSEA AND VOMITING -- Ask "Do you feel sick to your stomach? Have you vomited?" Observation.
0 no nausea and no vomiting
1 mild nausea with no vomiting
2
3
4 intermittent nausea with dry heaves
5
6
7 constant nausea, frequent dry heaves and vomiting

TACTILE DISTURBANCES -- Ask "Have you any itching, pins and needles sensations, any burning, any numbness, or do you feel bugs crawling on or under your skin?" Observation.
0 none
1 very mild itching, pins and needles, burning or numbness
2 mild itching, pins and needles, burning or numbness
3 moderate itching, pins and needles, burning or numbness
4 moderately severe hallucinations
5 severe hallucinations
6 extremely severe hallucinations
7 continuous hallucinations

TREMOR -- Arms extended and fingers spread apart. Observation.
0 no tremor
1 not visible, but can be felt fingertip to fingertip
2
3
4 moderate, with patient's arms extended
5
6
7 severe, even with arms not extended

AUDITORY DISTURBANCES -- Ask "Are you more aware of sounds around you? Are they harsh? Do they frighten you? Are you hearing anything that is disturbing to you? Are you hearing things you know are not there?" Observation.
0 not present
1 very mild harshness or ability to frighten
2 mild harshness or ability to frighten
3 moderate harshness or ability to frighten
4 moderately severe hallucinations
5 severe hallucinations
6 extremely severe hallucinations
7 continuous hallucinations

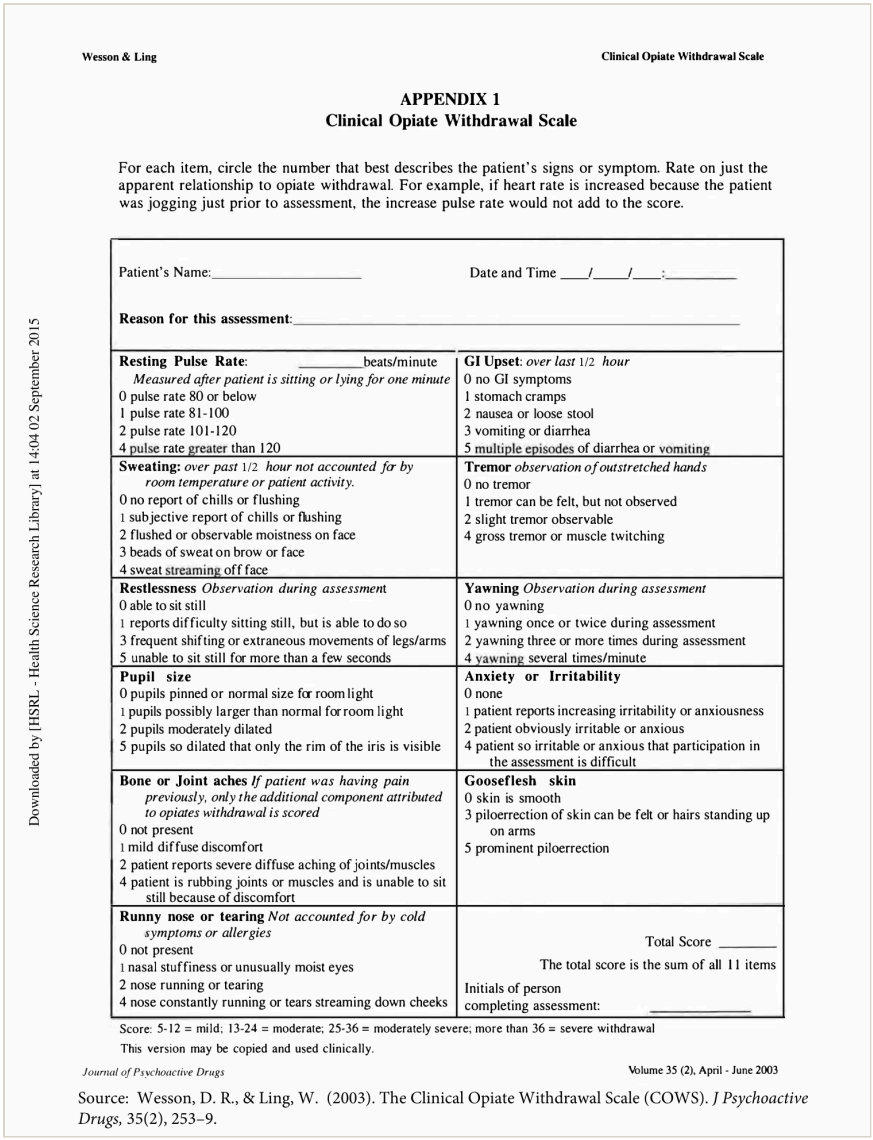
PAROXYSMAL SWEATS -- Observation.
0 no sweat visible
1 barely perceptible sweating, palms moist
2
3
4 beads of sweat obvious on forehead
5
6
7 drenching sweats

VISUAL DISTURBANCES -- Ask "Does the light appear to be too bright? Is its color different? Does it hurt your eyes? Are you seeing anything that is disturbing to you? Are you seeing things you know are not there?" Observation.
0 not present
1 very mild sensitivity
2 mild sensitivity
3 moderate sensitivity
4 moderately severe hallucinations
5 severe hallucinations
6 extremely severe hallucinations
7 continuous hallucinations

ANXIETY -- Ask "Do you feel nervous?" Observation.
0 no anxiety, at ease
1 mild anxious
2
3
4 moderately anxious, or guarded, so anxiety is inferred
5
6
7 equivalent to acute panic states as seen in severe delirium or acute schizophrenic reactions

HEADACHE, FULLNESS IN HEAD -- Ask "Does your head feel different? Does it feel like there is a band around your head?" Do not rate for dizziness or lightheadedness. Otherwise, rate severity.
0 not present
1 very mild
2 mild
3 moderate
4 moderately severe
5 severe
6 very severe
7 extremely severe

A.15 The CIWA-Ar (Clinical Institute Withdrawal Assessment for Alcohol, revised). The ten-item scale for alcohol-withdrawal severity: nine items scored 0 to 7 and orientation scored 0 to 4, for a total out of a possible 67; the form's own anchor is that patients scoring below 10 do not usually need additional medication, and any severity bands above that are protocol-dependent. Reproduced as its actual form; the CIWA-Ar is not copyrighted and may be reproduced freely (Sullivan et al., 1989).



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APPENDIX 1
Clinical Opiate Withdrawal Scale

For each item, circle the number that best describes the patient's signs or symptom. Rate on just the apparent relationship to opiate withdrawal. For example, if heart rate is increased because the patient was jogging just prior to assessment, the increase pulse rate would not add to the score.

Patient's Name:_____ Date and Time ____/____/____:_____

Reason for this assessment:_____

Resting Pulse Rate: _____beats/minute *Measured after patient is sitting or lying for one minute* 0 pulse rate 80 or below 1 pulse rate 81-100 2 pulse rate 101-120 4 pulse rate greater than 120	**GI Upset**: *over last 1/2 hour* 0 no GI symptoms 1 stomach cramps 2 nausea or loose stool 3 vomiting or diarrhea 5 multiple episodes of diarrhea or vomiting
Sweating: *over past 1/2 hour not accounted for by room temperature or patient activity.* 0 no report of chills or flushing 1 subjective report of chills or flushing 2 flushed or observable moistness on face 3 beads of sweat on brow or face 4 sweat streaming off face	**Tremor** *observation of outstretched hands* 0 no tremor 1 tremor can be felt, but not observed 2 slight tremor observable 4 gross tremor or muscle twitching
Restlessness *Observation during assessment* 0 able to sit still 1 reports difficulty sitting still, but is able to do so 3 frequent shifting or extraneous movements of legs/arms 5 unable to sit still for more than a few seconds	**Yawning** *Observation during assessment* 0 no yawning 1 yawning once or twice during assessment 2 yawning three or more times during assessment 4 yawning several times/minute
Pupil size 0 pupils pinned or normal size for room light 1 pupils possibly larger than normal for room light 2 pupils moderately dilated 5 pupils so dilated that only the rim of the iris is visible	**Anxiety or Irritability** 0 none 1 patient reports increasing irritability or anxiousness 2 patient obviously irritable or anxious 4 patient so irritable or anxious that participation in the assessment is difficult
Bone or Joint aches *If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored* 0 not present 1 mild diffuse discomfort 2 patient reports severe diffuse aching of joints/muscles 4 patient is rubbing joints or muscles and is unable to sit still because of discomfort	**Gooseflesh skin** 0 skin is smooth 3 piloerrection of skin can be felt or hairs standing up on arms 5 prominent piloerrection
Runny nose or tearing *Not accounted for by cold symptoms or allergies* 0 not present 1 nasal stuffiness or unusually moist eyes 2 nose running or tearing 4 nose constantly running or tears streaming down cheeks	Total Score _____ The total score is the sum of all 11 items Initials of person completing assessment: _____

Score: 5-12 = mild; 13-24 = moderate; 25-36 = moderately severe; more than 36 = severe withdrawal

This version may be copied and used clinically.

Source: Wesson, D. R., & Ling, W. (2003). The Clinical Opiate Withdrawal Scale (COWS). *J Psychoactive Drugs*, 35(2), 253–9.

A.16 The COWS (Clinical Opiate Withdrawal Scale). The eleven-item clinician-rated scale for opioid-withdrawal severity, for a total out of a possible 48, with 5 to 12 mild, 13 to 24 moderate, 25 to 36 moderately severe and more than 36 severe withdrawal. Reproduced from the NIDA form, freely reproducible with acknowledgement (Wesson and Ling, 2003).

NIDA Clinical Trials Network

Fagerstrom Test for Nicotine Dependence (FND)

Segment: _ _

Visit Number: _ _

Date of Assessment: (mm/dd/yyyy) _ _/_ _/_ _ _ _

Do you currently smoke cigarettes?

☐No ☐Yes

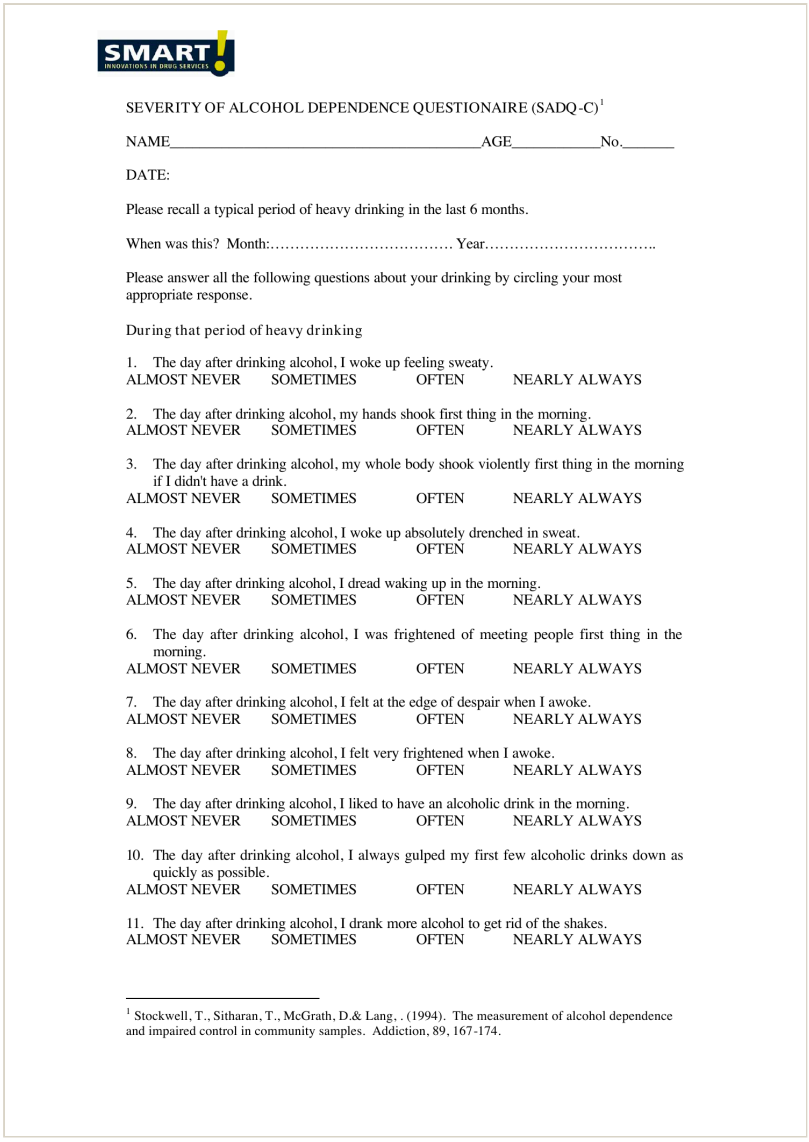
If "yes," read each question below. For each question, enter the answer choice which best describes your response.

1. **How soon after you wake up do you smoke your first cigarette?**
   ☐Within 5 minutes ☐31 to 60 minutes
   ☐6 to 30 minutes ☐After 60 minutes
2. **Do you find it difficult to refrain from smoking in places where it is forbidden** (e.g., in church, at the library, in the cinema)**?**
   ☐No ☐Yes
3. **Which cigarette would you hate most to give up?**
   ☐The first one in the morning ☐Any other
4. **How many cigarettes per day do you smoke?**
   ☐10 or less ☐21 to 30
   ☐11 to 20 ☐31 or more
5. **Do you smoke more frequently during the first hours after waking than during the rest of the day?**
   ☐No ☐Yes
6. **Do you smoke when you are so ill that you are in bed most of the day?**
   ☐No ☐Yes

Comments:

Heatherton TF, Kozlowski LT Frecker RC (1991). The Fagerström Test for Nicotine Dependence: A revision of the Fagerström Tolerance Questionnaire. British Journal of Addiction 86:1119-27.

A.17 The Fagerstrom Test for Nicotine Dependence (FTND). The six-item measure of nicotine dependence, for a total out of a possible 10, with 0 to 2 very low, 3 to 4 low, 5 moderate, 6 to 7 high and 8 to 10 very high dependence. Reproduced from the NIDA government-hosted form, freely reproducible with acknowledgement (Heatherton, Kozlowski, Frecker and Fagerstrom, 1991).



SMART
INNOVATIONS IN DRUG SERVICES

SEVERITY OF ALCOHOL DEPENDENCE QUESTIONAIRE (SADQ-C)[1]

NAME_____AGE_____No._____

DATE:

Please recall a typical period of heavy drinking in the last 6 months.

When was this? Month:…… Year……..

Please answer all the following questions about your drinking by circling your most appropriate response.

During that period of heavy drinking

1. The day after drinking alcohol, I woke up feeling sweaty.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS

2. The day after drinking alcohol, my hands shook first thing in the morning.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS

3. The day after drinking alcohol, my whole body shook violently first thing in the morning if I didn't have a drink.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS

4. The day after drinking alcohol, I woke up absolutely drenched in sweat.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS

5. The day after drinking alcohol, I dread waking up in the morning.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS

6. The day after drinking alcohol, I was frightened of meeting people first thing in the morning.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS

7. The day after drinking alcohol, I felt at the edge of despair when I awoke.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS

8. The day after drinking alcohol, I felt very frightened when I awoke.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS

9. The day after drinking alcohol, I liked to have an alcoholic drink in the morning.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS

10. The day after drinking alcohol, I always gulped my first few alcoholic drinks down as quickly as possible.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS

11. The day after drinking alcohol, I drank more alcohol to get rid of the shakes.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS

[1] Stockwell, T., Sitharan, T., McGrath, D.& Lang, . (1994). The measurement of alcohol dependence and impaired control in community samples. Addiction, 89, 167-174.

A.18 The SADQ (Severity of Alcohol Dependence Questionnaire). The 20-item self-report measure of alcohol-dependence severity, each item scored 0 to 3, for a total out of a possible 60, with below 16 mild, 16 to 30 moderate and 31 or more severe dependence (16 or more is the usual threshold at which an assisted detoxification regime is considered). Reproduced with acknowledgement for non-commercial use (Stockwell, Hodgson, Edwards and colleagues).

Global function and disability

GAF (TYPESET, NOT REPRODUCED)	VERIFIED STRUCTURE AND BANDS
Instrument	Global Assessment of Functioning, the DSM-IV Axis V single-number rating of overall psychological, social and occupational functioning
Scale	a single 1 to 100 scale read in ten anchored decile bands, each pairing a symptom clause with a functioning clause; higher scores mean better functioning
Anchor bands	**91 to 100 superior functioning, no symptoms; 81 to 90 absent or minimal symptoms; 71 to 80 transient, expectable reactions and slight impairment; 61 to 70 mild symptoms or some difficulty; 51 to 60 moderate symptoms or difficulty; 41 to 50 serious symptoms or serious impairment; 31 to 40 some impairment in reality testing or major impairment in several areas; 21 to 30 conduct strongly influenced by psychosis or serious impairment in judgment; 11 to 20 some danger to self or others or gross impairment; 1 to 10 persistent danger or persistent inability to maintain hygiene; 0 inadequate information**
Total	out of a possible 100 (higher is better functioning)

A.19 The Global Assessment of Functioning (GAF). The DSM-IV Axis V single-number rating of overall psychological, social and occupational functioning on a 1 to 100 scale, read in ten anchored decile bands where higher means better functioning, out of a possible 100. It derives from the Global Assessment Scale (Endicott et al., 1976); the American Psychiatric Association no longer licenses or endorses it and it was dropped from DSM-5, so its band structure is typeset here in our own words rather than lifted from the manual.

WHODAS 2.0 (TYPESET, NOT REPRODUCED)	VERIFIED STRUCTURE AND SCORING
Instrument	WHO Disability Assessment Schedule 2.0, a generic measure of functioning and disability across any health condition (WHO, 2010)
Versions	a 36-item full version and a 12-item short version; self-administered, interviewer-administered and proxy forms
Domains	six domains: cognition (understanding and communicating), mobility (getting around), self-care, getting along with people, life activities (household and work or school) and participation in society
Scoring	**each item rated none, mild, moderate, severe, or extreme or cannot do; a summary score is computed from 0 to 100, out of a possible 100, where 0 is no disability and 100 is full disability**

A.20 The WHO Disability Assessment Schedule 2.0 (WHODAS 2.0). The WHO generic measure of functioning and disability, in a 36-item full version and a 12-item short version, covering six domains (cognition, mobility, self-care, getting along, life activities and participation); items are rated from none to extreme and summarised on a 0 to 100 metric, out of a possible 100, where 0 is no disability and 100 is full disability. The WHODAS 2.0 is WHO copyright and free for clinicians to use with their own patients, but any other or electronic use requires written WHO permission, so it is typeset from the published structure rather than reproduced (WHO, 2010).

CGI (TYPESET)	VERIFIED ANCHORS
Instrument	Clinical Global Impression, a brief global clinician rating of illness severity and change (Guy, 1976)
CGI-Severity	rated 1 to 7: 1 normal, not ill; 2 borderline ill; 3 mildly ill; 4 moderately ill; 5 markedly ill; 6 severely ill; 7 among the most extremely ill
CGI-Improvement	rated 1 to 7: 1 very much improved; 2 much improved; 3 minimally improved; 4 no change; 5 minimally worse; 6 much worse; 7 very much worse
Scoring	**the two scales are rated separately, each out of a possible 7; the instrument does not yield a single summed total**

A.21 The Clinical Global Impression (CGI). The brief global clinician rating used across trials and clinics: CGI-Severity rates current illness from 1 (normal, not ill) to 7 (among the most extremely ill) and CGI-Improvement rates change from 1 (very much improved) through 4 (no change) to 7 (very much worse), each out of a possible 7 and rated separately rather than summed. The CGI is in the public domain (Guy W, ECDEU Assessment Manual for Psychopharmacology, 1976).

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The psychotherapy, assessment and nosology content is grounded in the standard psychiatry sources (the source hierarchy below), with Kaplan and Sadock and the New Oxford Textbook as the depth bar for the modality models and the classification, Fish and Sims for the mental state examination and descriptive psychopathology, Gabbard for the psychodynamic material, Beck for cognitive therapy, Linehan for dialectical behaviour therapy and Yalom for group therapy, and Clinical Methods in Psychiatry for the Indian context, the rating scales and the forensic and capacity frame. The therapy indications are guideline-first, anchored on the Indian Psychiatric Society psychotherapy and disorder guidelines, with NICE, CANMAT and WHO mhGAP. The Indian legal provisions (the Mental Healthcare Act 2017, the Indian Penal Code Section 84 and its recodification) were checked against their primary texts. Every rating-scale cut-off, eponym count and nosology fact was checked against these sources, and anything that could not be confirmed was stated conservatively or omitted rather than guessed. Each journal identifier below was verified against PubMed this build and matched on title, first author and year; books, guidelines and statutes are cited by author or body, title and year.

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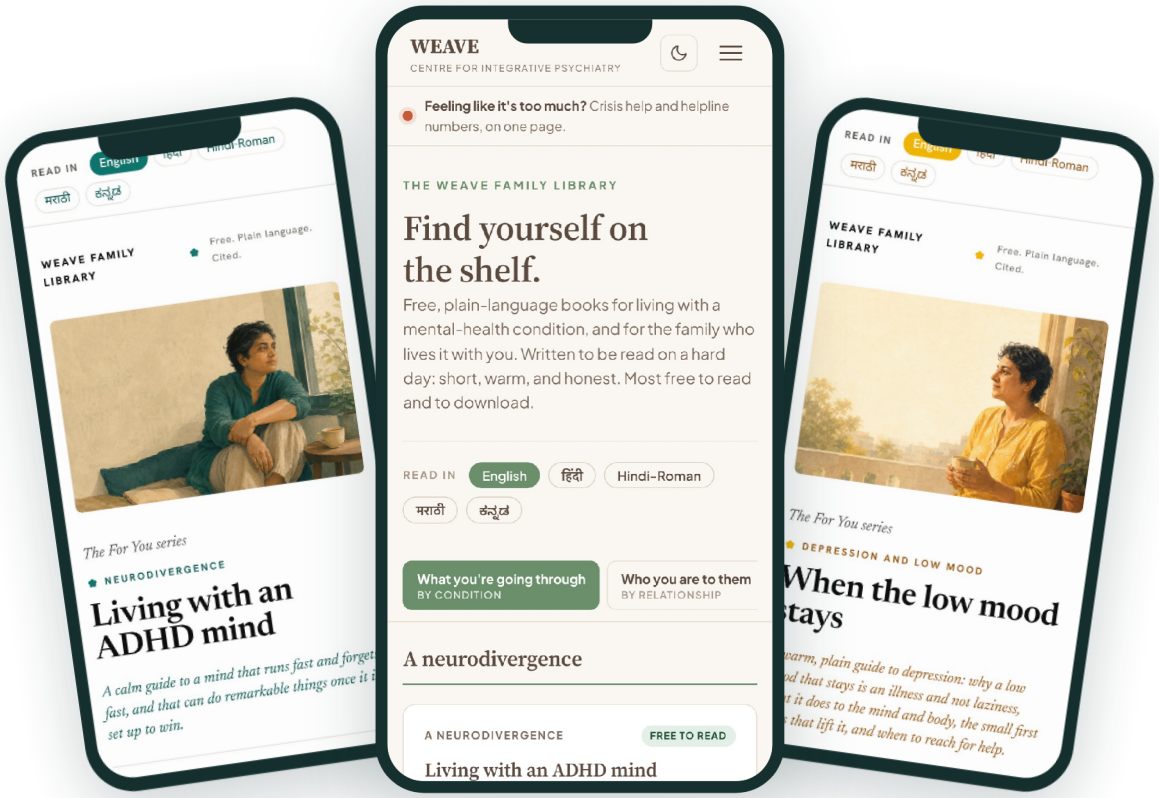
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