WEAVE SPRINT . PAPER II

Substance Use

Substance use disorders in one document: the dependence syndrome, the neurobiology of addiction and the screening scales; alcohol, opioid and every other substance by intoxication, withdrawal and complication; the emergencies from delirium tremens to opioid overdose; and the treatment, motivational interviewing and relapse prevention alongside the opioid substitution and anti-craving pharmacotherapy, led by the BAP guidelines with the Indian position throughout.

CONTENTS

- General concepts and assessment
- Alcohol use disorder
- Opioid use disorder
- Other substances of misuse
- Psychosocial treatment and relapse prevention
- Anti-craving and aversive pharmacotherapy
- Apply and consolidate

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Routine referrals only. This is not an emergency route.

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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.

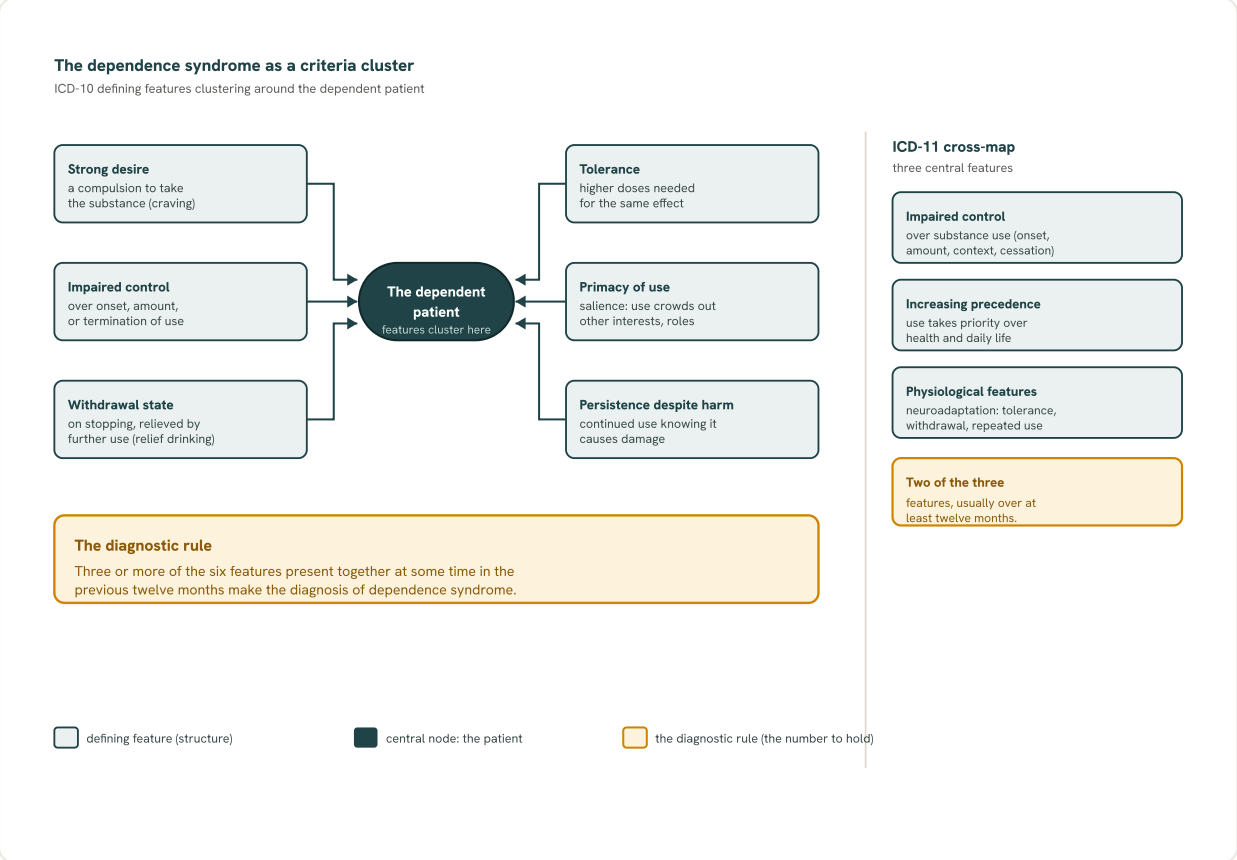


Fig 13.1 The dependence syndrome: the criteria cluster and the ICD-11 cross-map. In ICD-10 the dependent patient sits at the centre of six defining features: a strong desire or compulsion to use, impaired control, a physiological withdrawal state, tolerance, primacy or salience of use over other interests, 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.

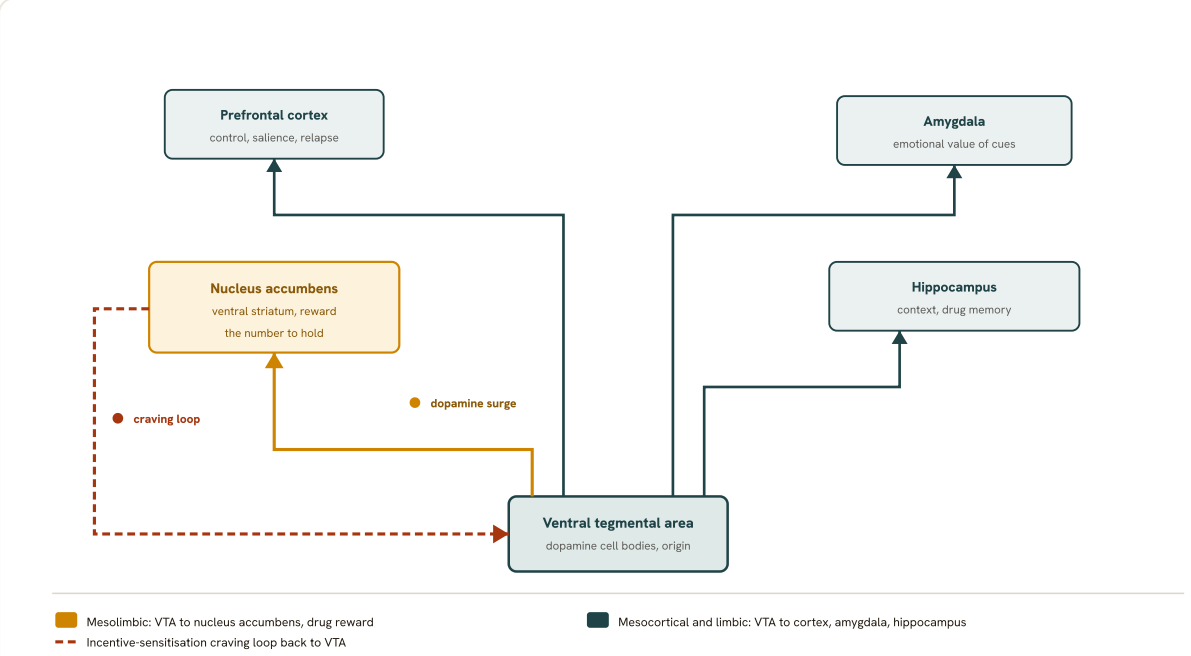


Fig 13.2 The mesolimbic reward circuit and the neurobiology of addiction. Dopamine cell bodies in the ventral tegmental area project along the mesolimbic tract to the nucleus accumbens, where drug reward drives a dopamine surge far larger than any natural reinforcer. Parallel projections reach the prefrontal 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

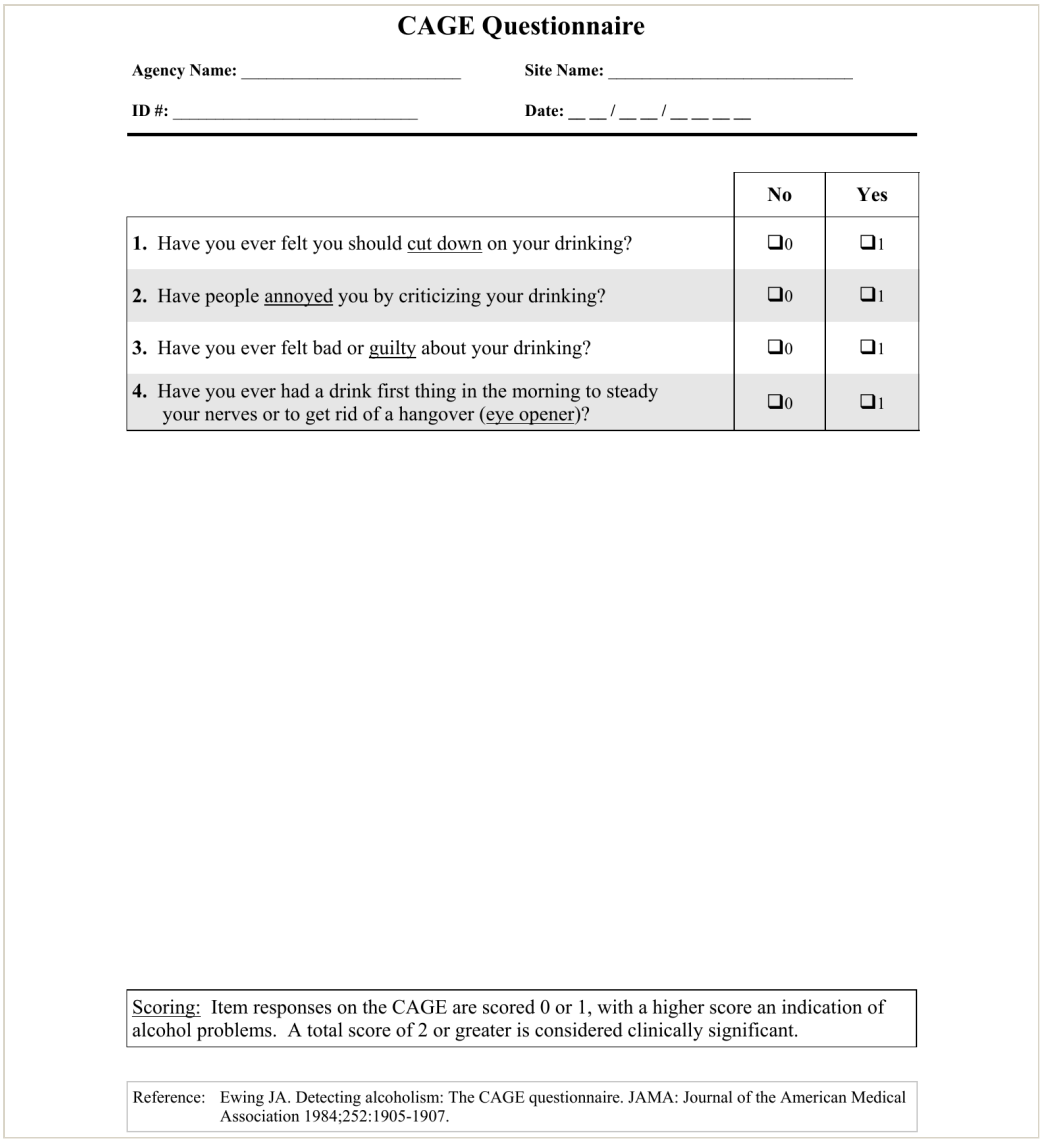
The Alcohol Use Disorders Identification Test: Self-Report Version

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.

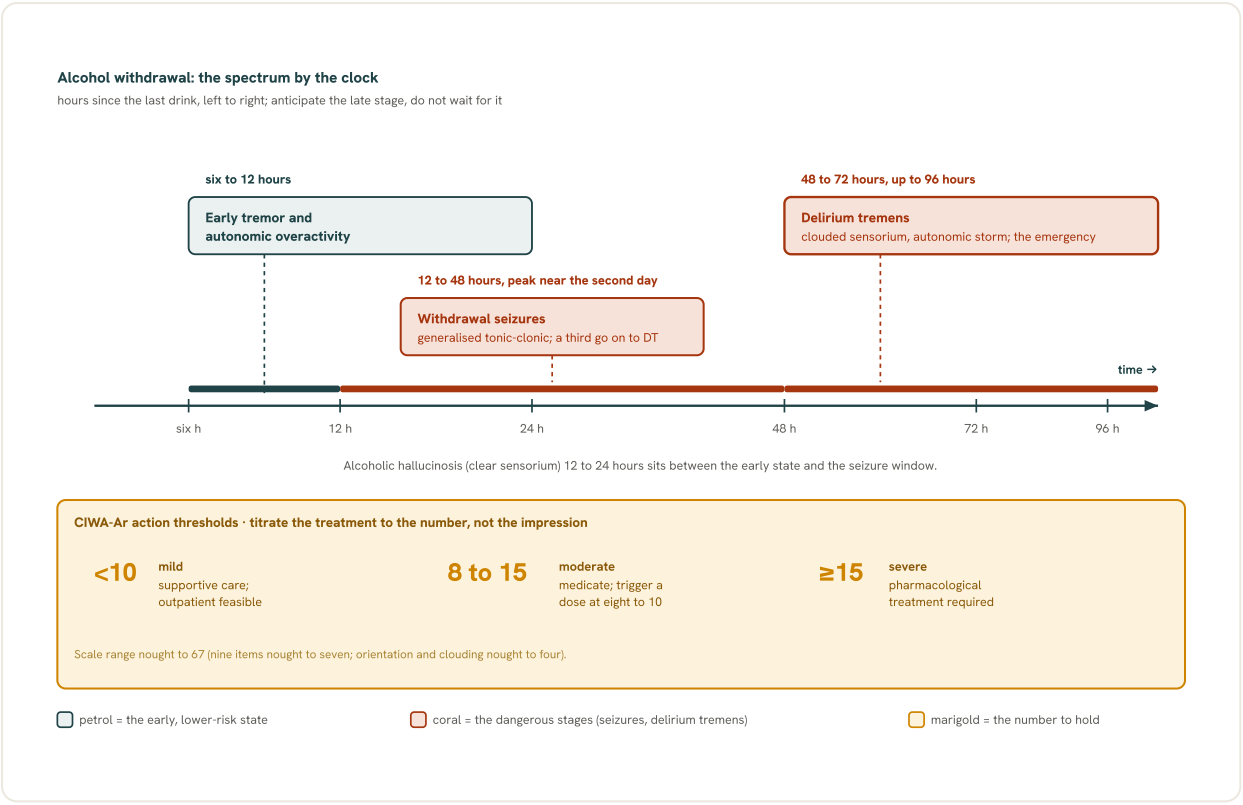


Fig 13.4 The alcohol-withdrawal spectrum read off the clock. Early tremor and autonomic overactivity begin at six to 12 hours, generalised withdrawal seizures cluster at 12 to 48 hours (peaking near day two, and about a third go on to delirium tremens), and delirium tremens, the high-mortality emergency, 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

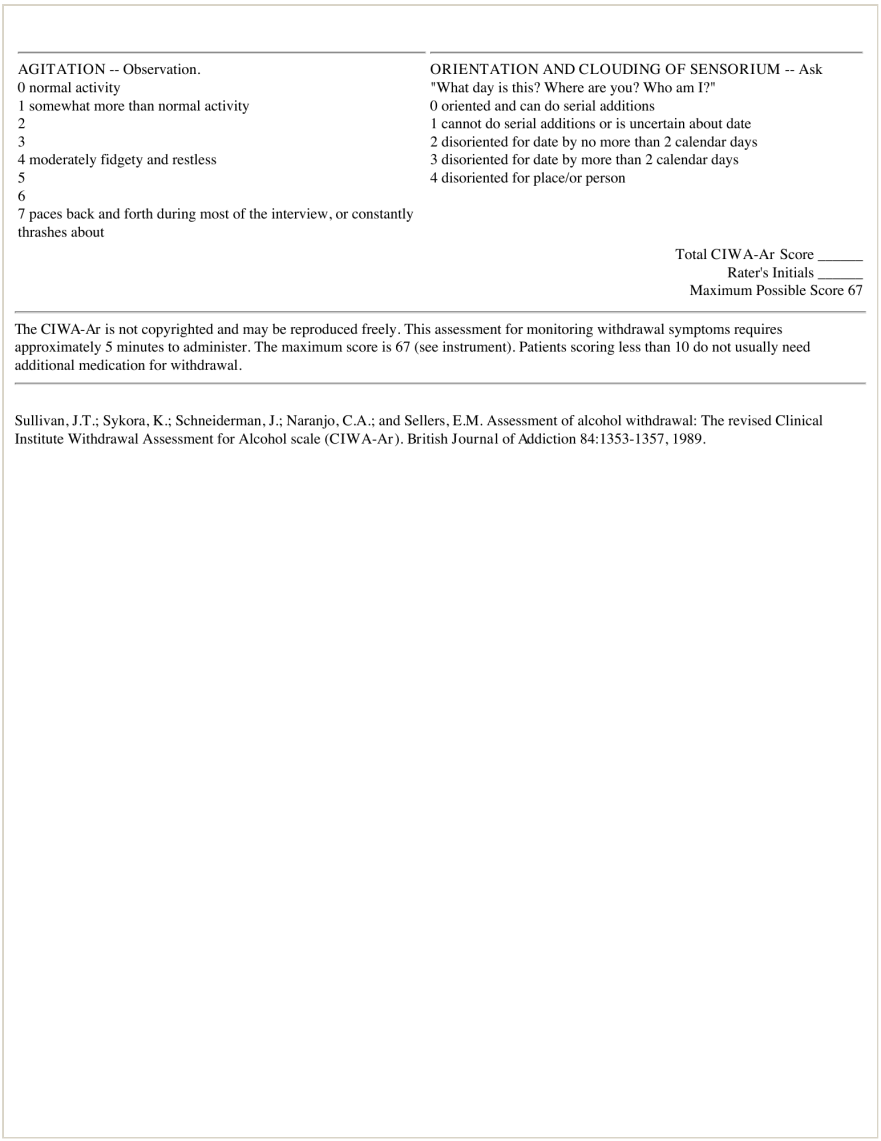
AUDITORY DISTURBANCES -- Ask "Are you more aware of sounds around you? Are they harsh? Do they frighten you? Are you hearing anything that is disturbing to you? Are you hearing things you know are not there?" Observation.
0 not present
1 very mild harshness or ability to frighten
2 mild harshness or 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

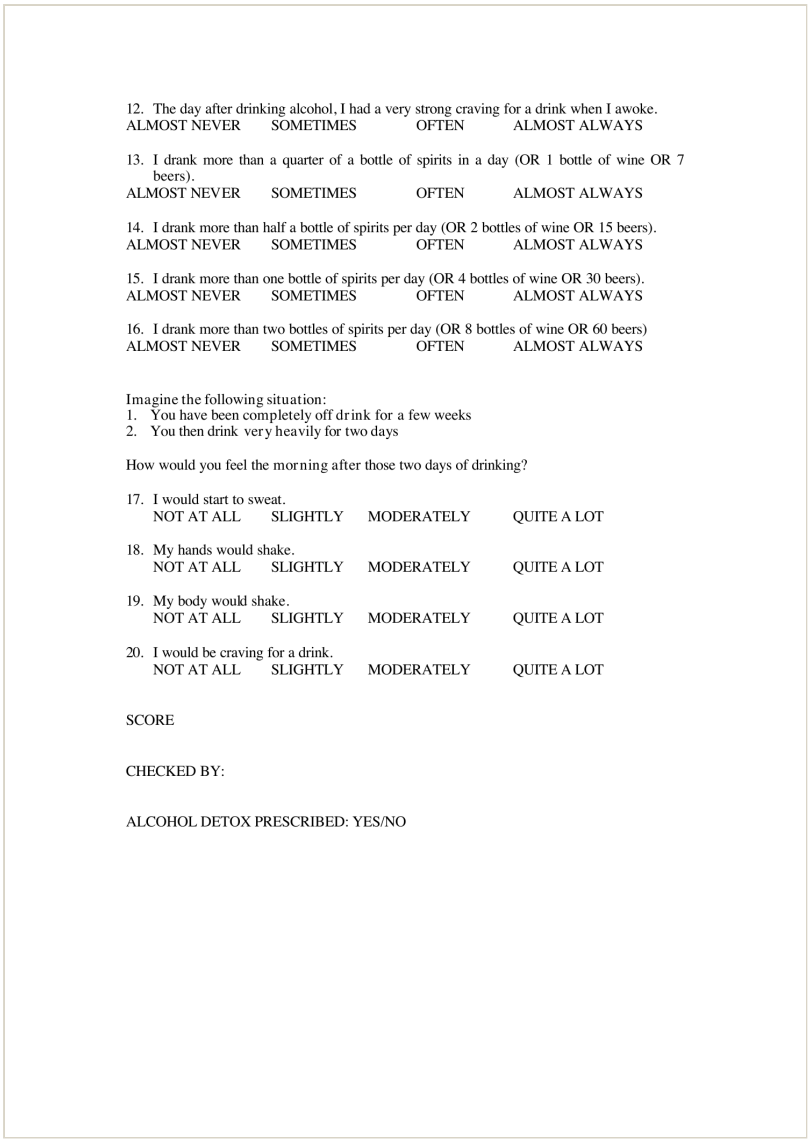
8. The day after drinking alcohol, I felt very frightened when I awoke.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS

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.

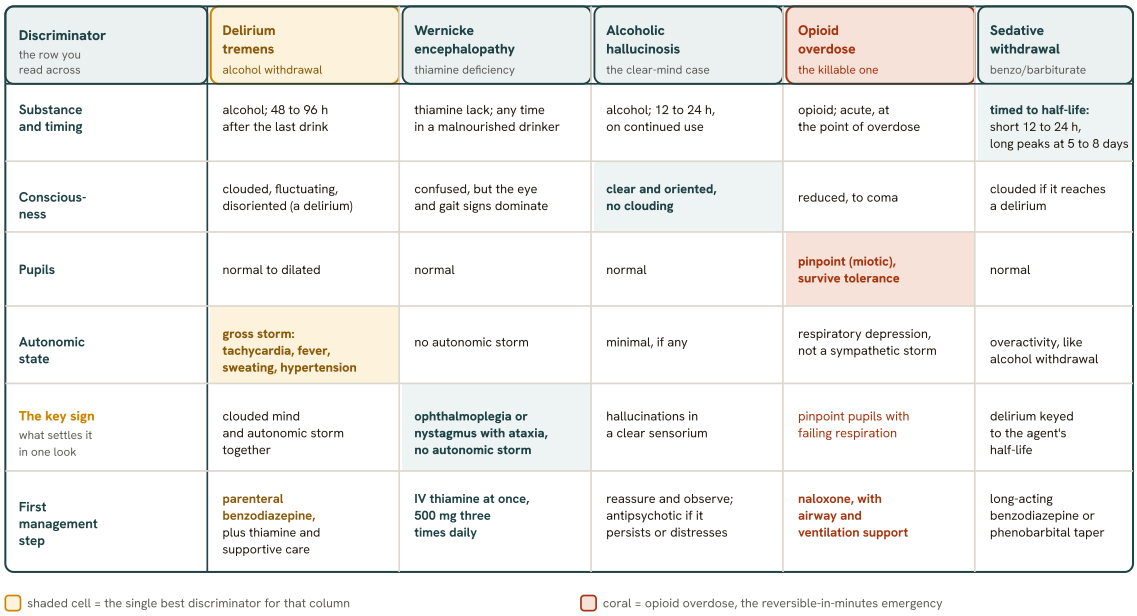
HOLD THIS

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.**

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

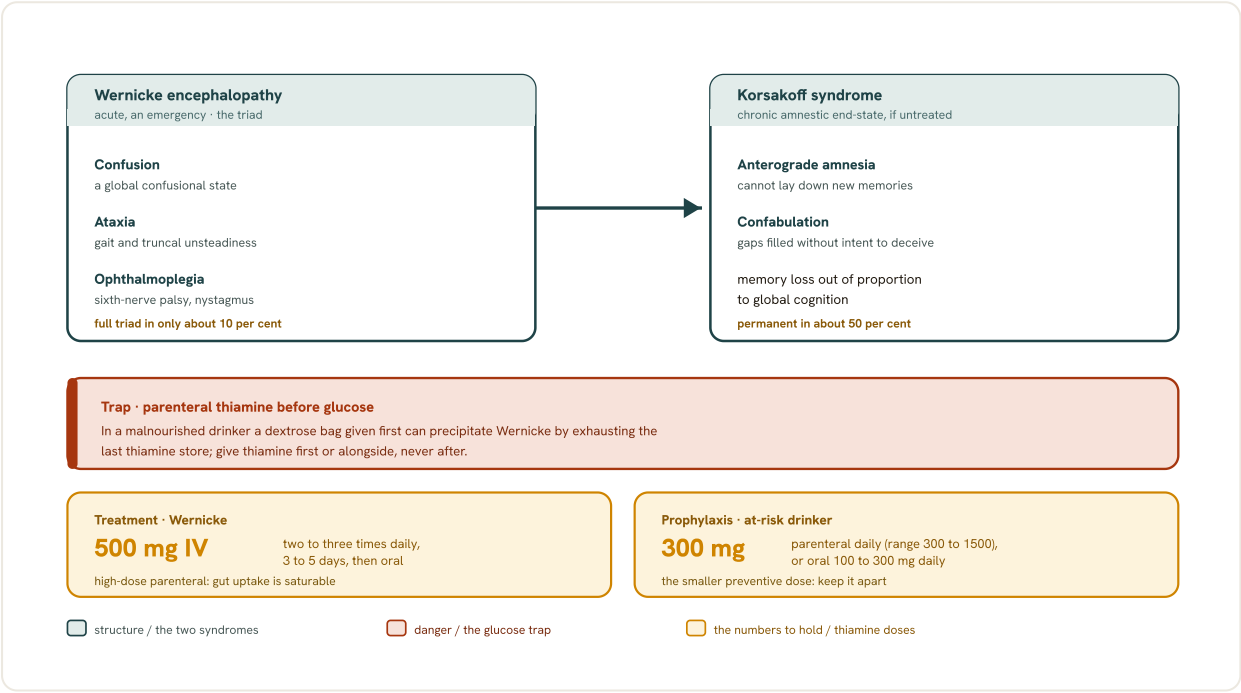


Fig 13.8 Wernicke encephalopathy to Korsakoff syndrome: the thiamine rule. The acute triad of confusion, ataxia and ophthalmoplegia is Wernicke, present in full in only about one patient in ten; untreated it fixes into Korsakoff, the chronic anterograde amnesia with confabulation. The non-negotiable 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)

FEATURE	ALCOHOLIC HALLUCINOSIS	DELIRIUM TREMENS	SCHIZOPHRENIA
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
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% OF DEPENDENT DRINKERS DEVELOP ALCOHOLIC HALLUCINOSIS	**1 month** TYPICAL TIME TO RESOLUTION ON ABSTINENCE	**3%** 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.

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 **biomarker**s 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
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.

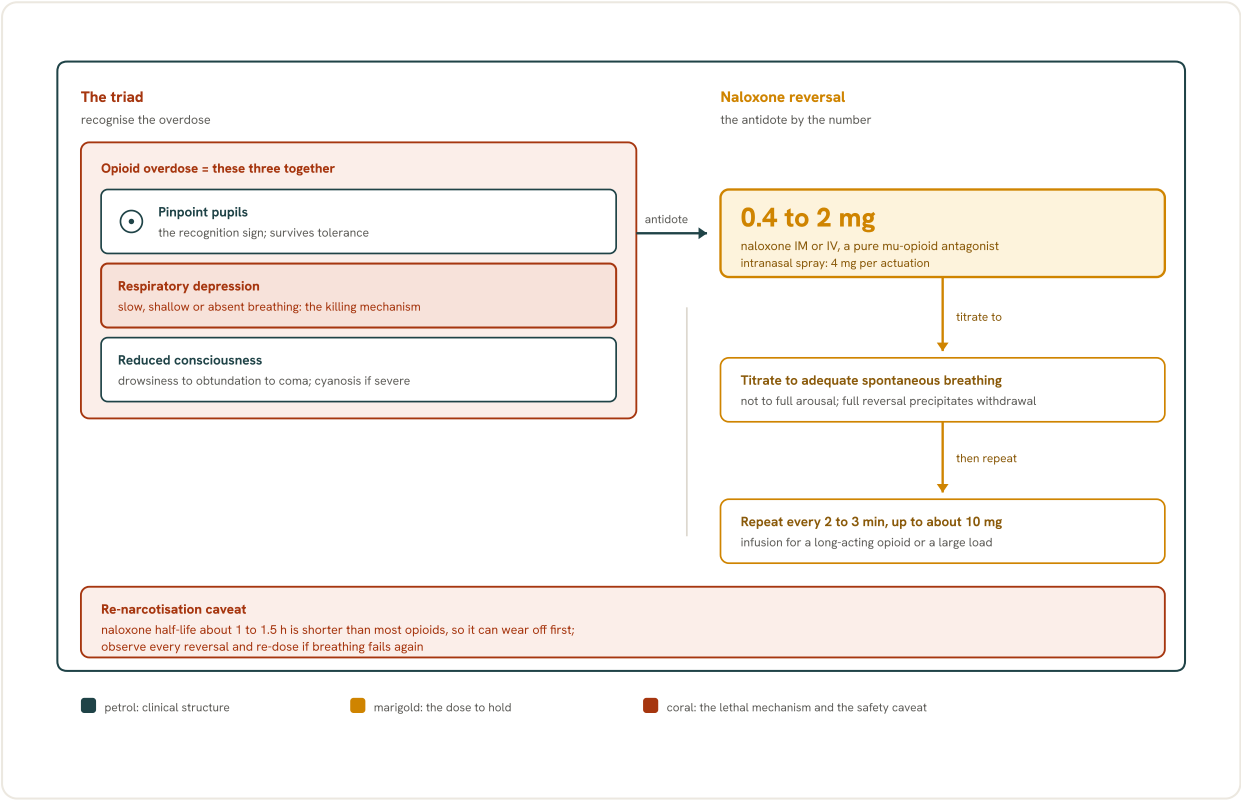


Fig 13.9 Opioid overdose: the triad and naloxone reversal. The overdose is the triad of pinpoint pupils, respiratory depression (the lethal component) and reduced consciousness taken together; the antidote is naloxone 0.4 to 2 mg IM or IV (intranasal 4 mg), titrated to adequate spontaneous breathing 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

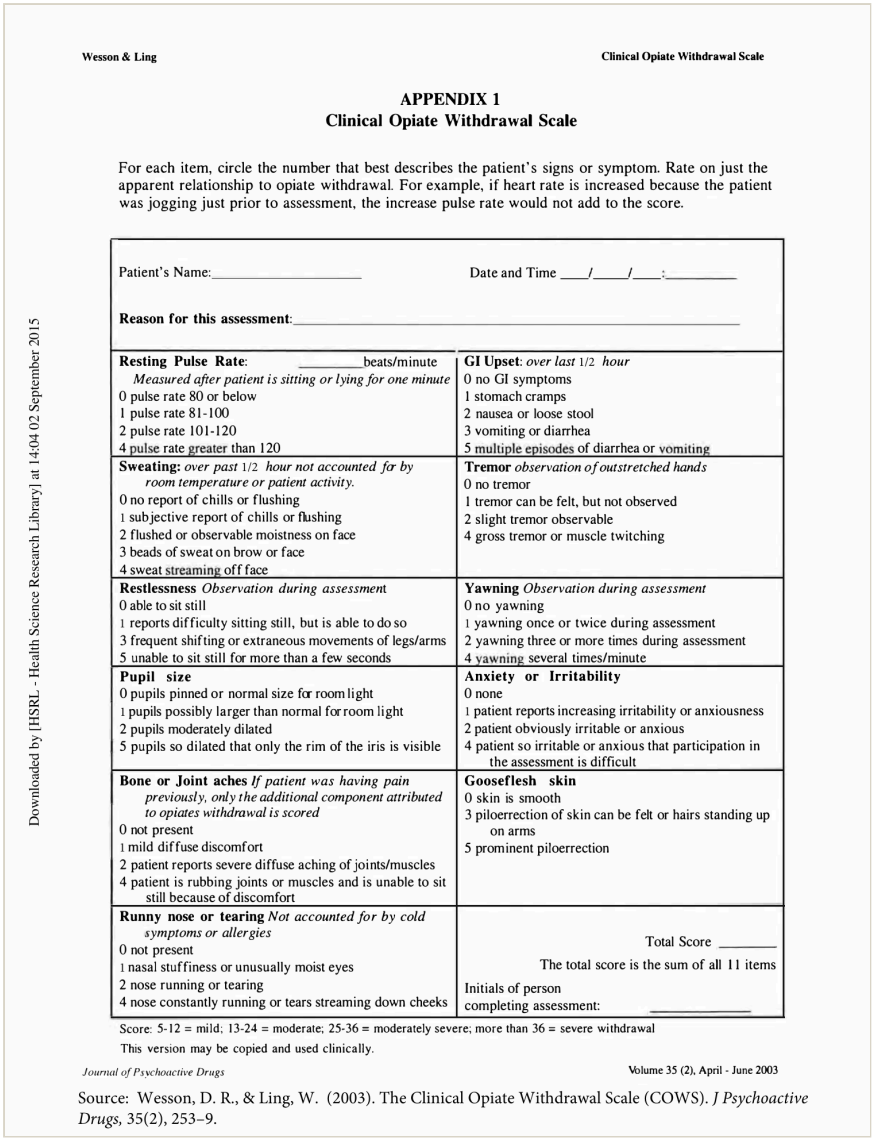
PPR then N

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.

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 13.10 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 13.11, the buprenorphine induction and precipitated-withdrawal timeline.

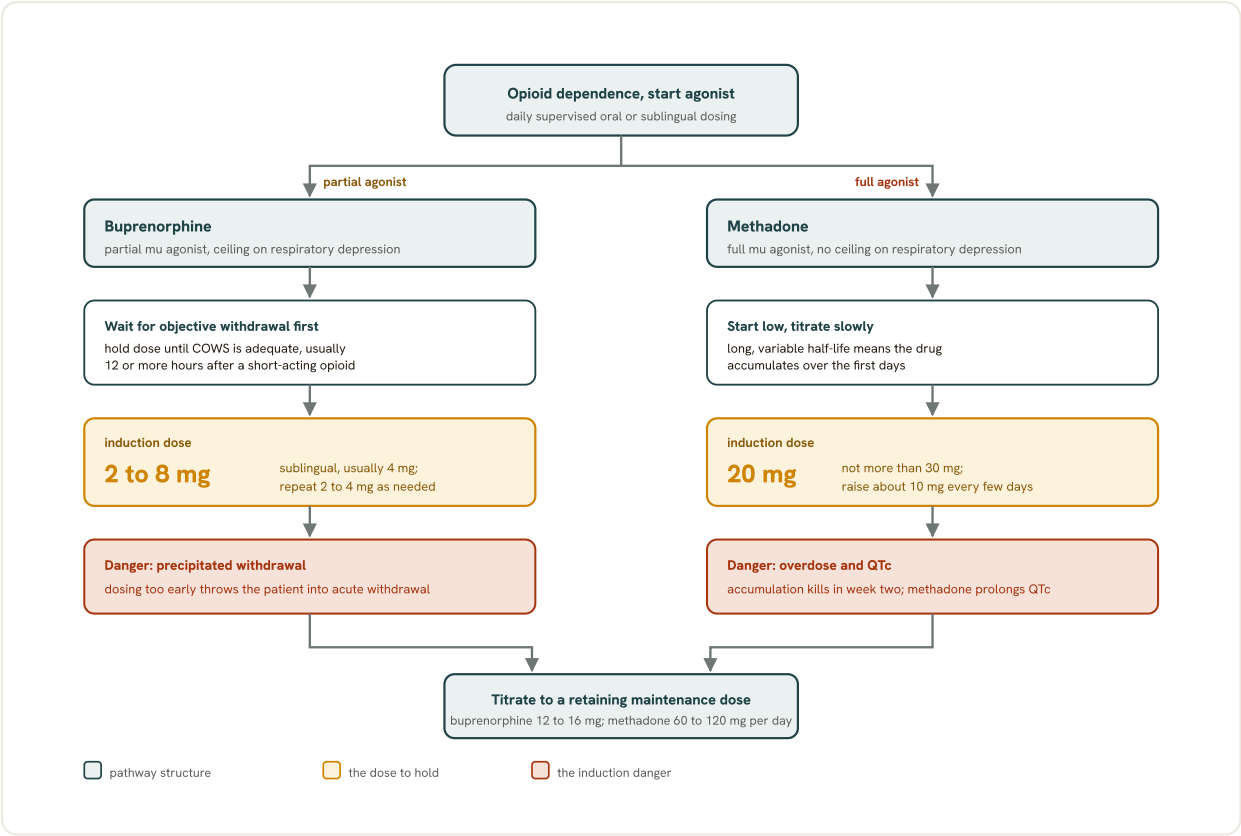


Fig 13.11 Opioid substitution: buprenorphine versus methadone induction. Buprenorphine is a partial mu agonist with a ceiling on respiratory depression: hold the first dose until objective withdrawal (an adequate COWS, usually 12 or more hours after a short-acting opioid), then induct at 2 to 8 mg sublingually, 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.

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).

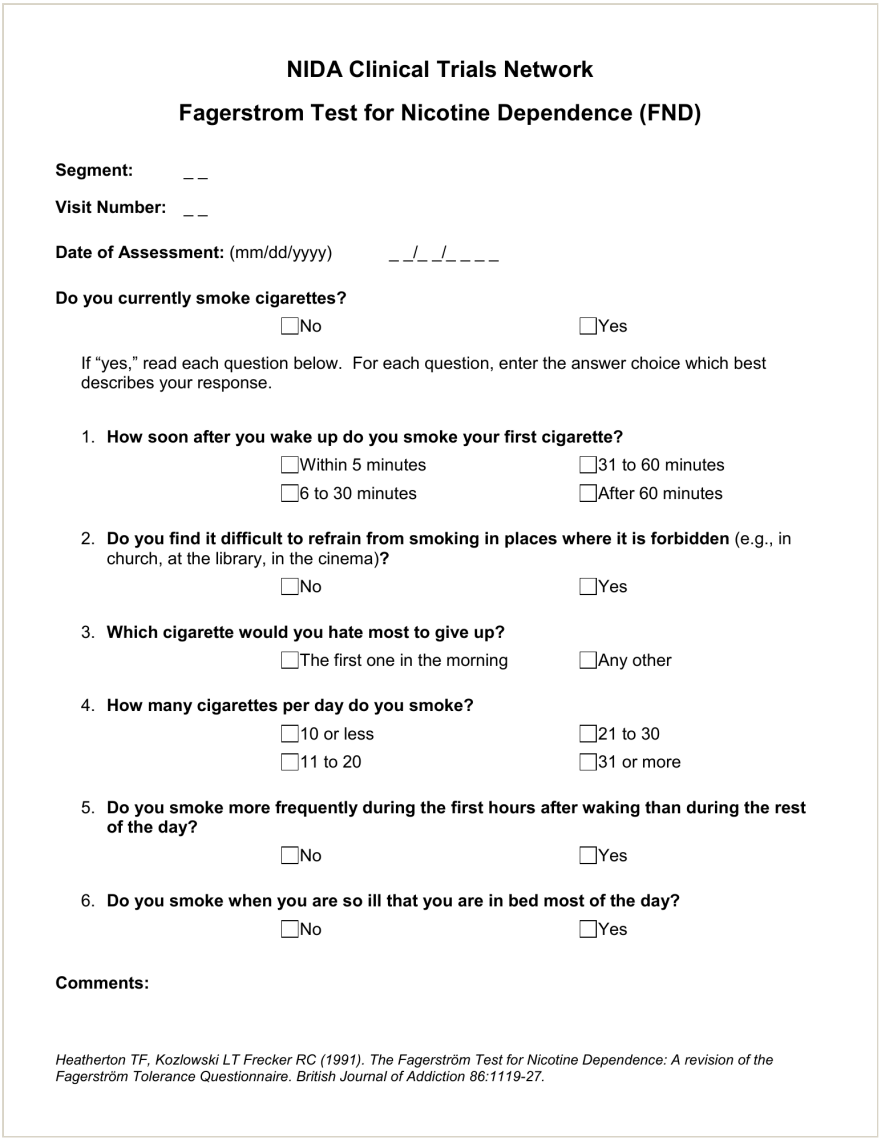
HOLD THIS

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 13.23, the FTND item map and its severity bands; and Fig 13.23, 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 13.12 The Fagerstrom Test for Nicotine Dependence (FTND)

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 13.13, 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.

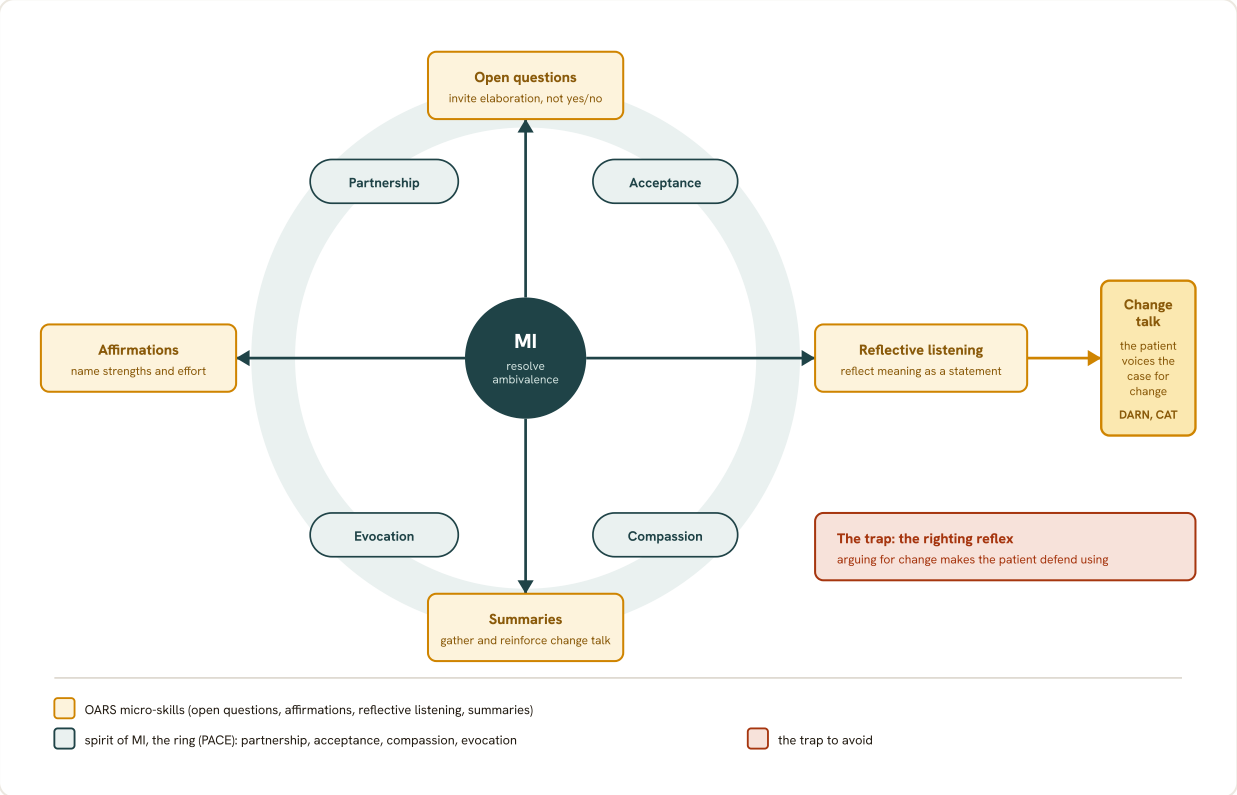


Fig 13.13 Motivational interviewing: the spirit and the OARS skills. The method sits at the centre, resolving ambivalence in favour of change. Around it are the four OARS micro-skills, open questions, affirmations, reflective listening and summaries, the moment-to-moment tools. Behind them is the ring 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.

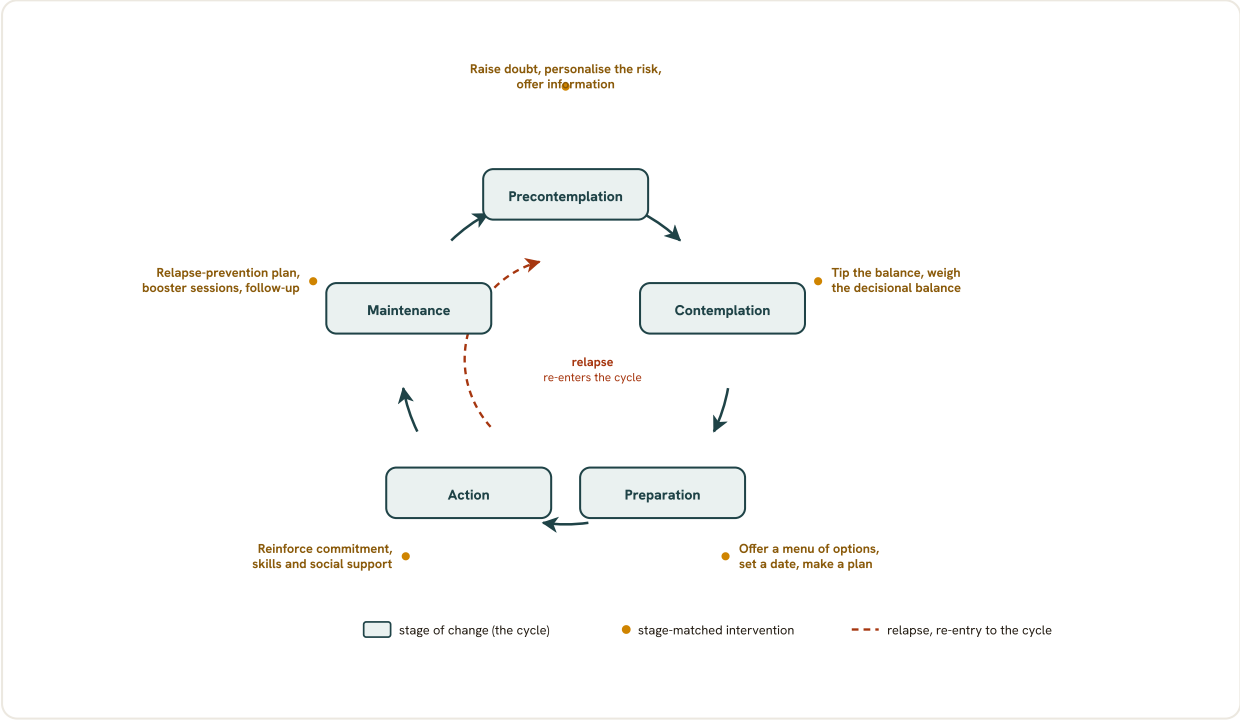


Fig 13.14 The stages of change and the stage-matched interventions. Change is a cycle, not a switch: a person moves from precontemplation through contemplation, preparation, action and maintenance, and relapse is a normal re-entry rather than a failure. Each stage calls for a different move, so the clinician 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 13.15, the Marlatt relapse-prevention model as a chain from high-risk situation through coping (or its failure) to lapse and the abstinence violation effect.

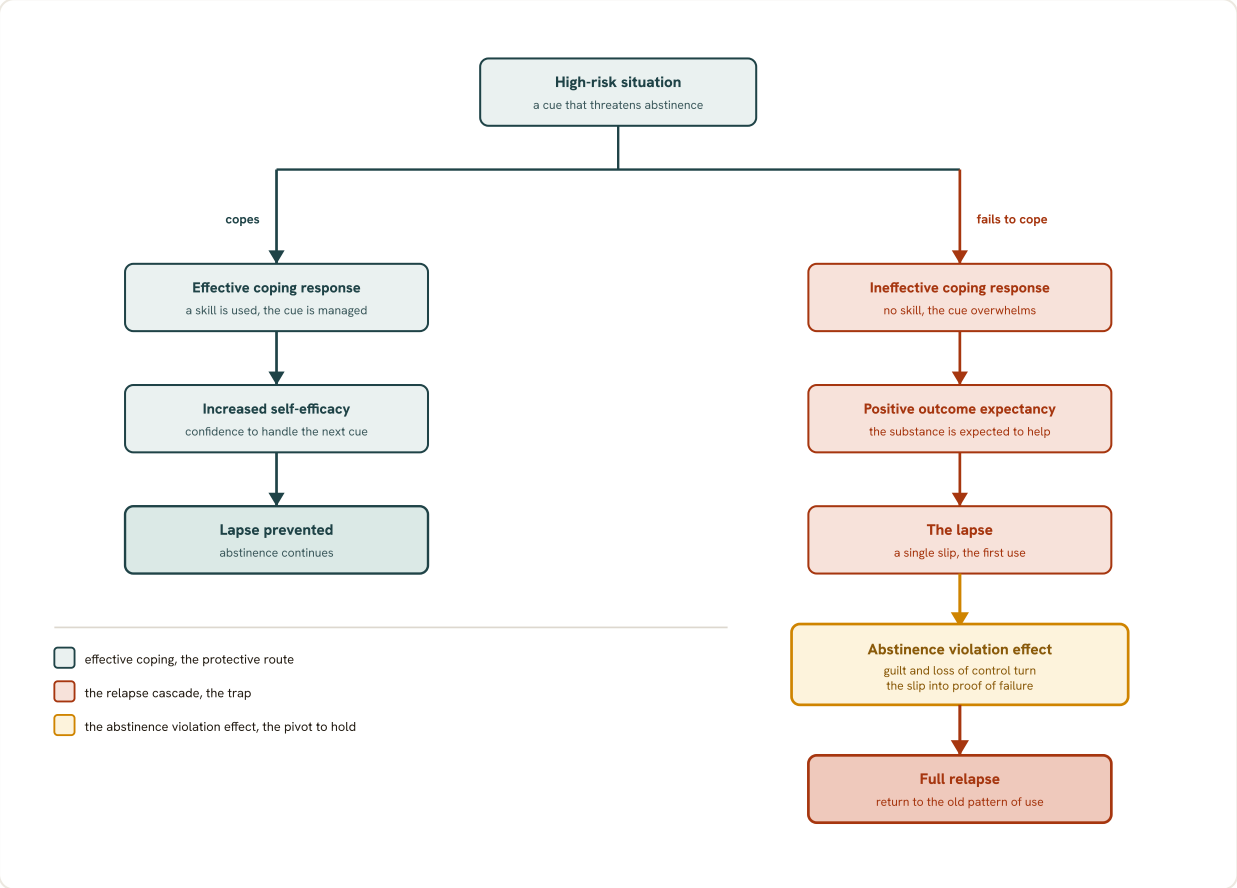


Fig 13.15 The Marlatt relapse-prevention model and the abstinence violation effect. A high-risk situation forces a choice. An effective coping response raises self-efficacy and the lapse is prevented, so abstinence holds. An ineffective response, driven by a positive outcome expectancy that the substance 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 13.16, 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

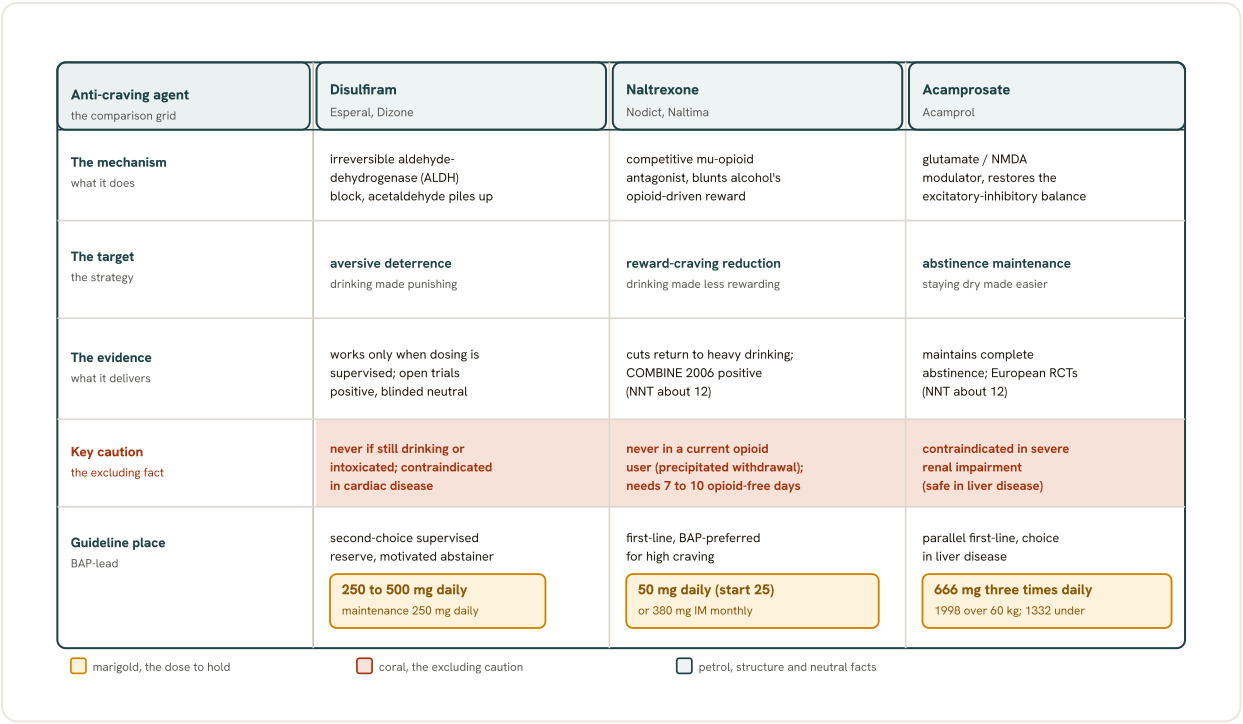


Fig 13.16 Anti-craving pharmacotherapy: disulfiram, naltrexone and acamprosate compared. Read down each column: disulfiram deters (ALDH block, aversive, supervised-only, never in a drinking or cardiac patient), naltrexone de-rewards (mu-opioid antagonist, first-line, never in an opioid user), and acamprosate 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 13.17).

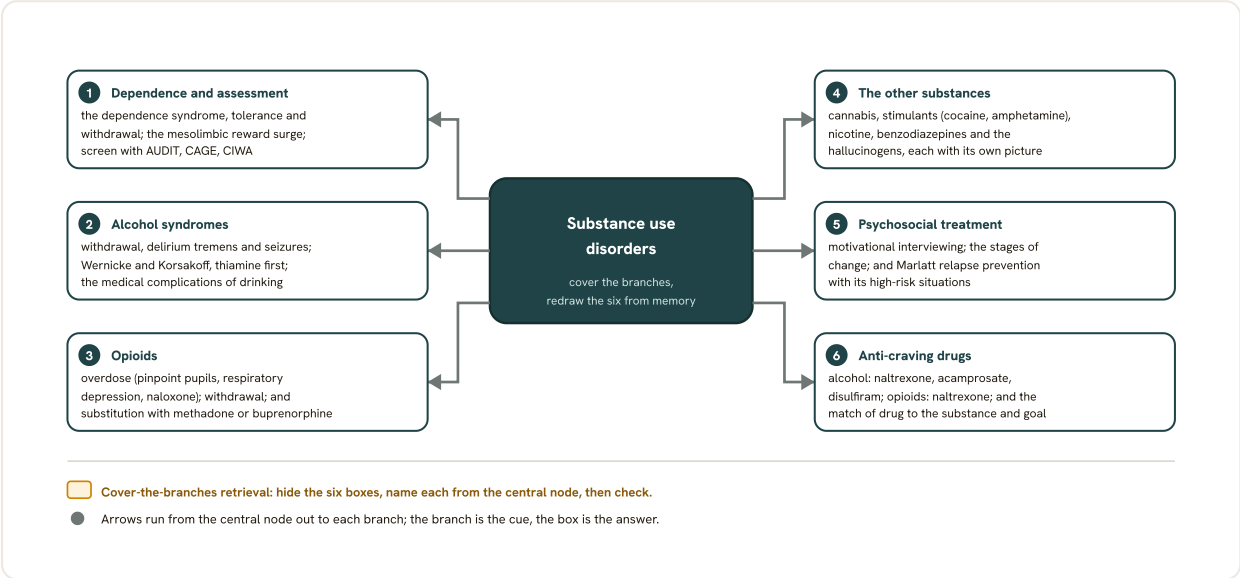


Fig 13.17 Chapter synthesis map: substance use disorders at a glance. Six branches radiate from the disorder at the centre: dependence and assessment with the reward neurobiology; the alcohol syndromes, emergencies and complications; opioid overdose, withdrawal and substitution; the other substances; 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 13.17).

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 13.17).

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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