

PSYCHIATRY POSTGRADUATE EXAMS

Weave Study Guides

Paper IV, Neurology, Medicine and Recent Advances

Twenty-two guides across Papers I to IV, plus the cross-paper supplement. Study notes, model answers, mnemonics, high-yield comparisons, PYQ frequency, and quick review for every topic.

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PART IV

Paper IV

Neurology, Medicine & Recent Advances

The interface with medicine and neurology, and the recent advances that examiners keep returning to.

Epilepsy Psychiatry

Paper IV · Neurology, Medicine & Recent Advances. Six study modes, from notes to quick review.

Study Notes

Sources: *Kaplan & Sadock's Comprehensive Textbook of Psychiatry (10th ed.)*, *Stahl's Essential Psychopharmacology (5th ed.)*, *Trimble & Schmitz, Seizures, Affective Disorders and Anticonvulsant Drugs*, *Engel & Pedley, Epilepsy: A Comprehensive Textbook*, *Oxford Textbook of Epileptology*

SECTION 1: SEIZURE CLASSIFICATION: ILAE 2017

EXAM PEARL

The ILAE revised its classification in 2017. Older terminology (simple partial, complex partial, secondary generalised) is obsolete in exams, use the 2017 terms. However, expect older terms in clinical vignettes. Know both.

1.1 The Three-Level Framework

The 2017 ILAE classification operates at three levels:

LEVEL	QUESTION ASKED	CLINICAL UTILITY
Seizure Type	What kind of seizure?	Immediate management
Epilepsy Type	What pattern of seizures?	Syndrome classification
Epilepsy Syndrome	Which defined syndrome?	Specific treatment & prognosis

1.2 Seizure Onset Classification

1.3 Focal Seizures: Detailed Classification

FEATURE	AWARE FOCAL	IMPAIRED AWARENESS FOCAL
Old term	Simple partial	Complex partial
Consciousness	Preserved	Impaired
Memory of event	Present	Absent or partial
Duration	Usually < 2 min	Usually 1–3 min
Postictal state	Minimal	Often present (confusion, fatigue)
EEG	Contralateral focal discharge	Often temporal, bilateral spread
Common origin	Any lobe	Often temporal lobe (70%)

Focal seizure descriptors (motor):

- Automatisms: Repetitive semi-purposeful movements (lip smacking, hand fumbling)
- Atonic: Loss of muscle tone in one body part
- Clonic: Rhythmic jerking
- Epileptic spasms: Brief sustained muscle contraction
- Hyperkinetic: Pedalling, thrashing movements
- Myoclonic: Brief irregular jerks
- Tonic: Sustained increased tone

Focal seizure descriptors (non-motor):

- Autonomic: Pallor, flushing, piloerection, cardiovascular changes
- Behaviour arrest: Cessation of activity
- Cognitive: Dysphasia, déjà vu, jamais vu, forced thinking
- Emotional: Fear, anxiety, joy, ictal emotions
- Sensory: Somatosensory, visual, auditory, olfactory, gustatory, vestibular
- Sensory, special: The "dreamy state" of Jackson (temporal lobe)

CLINICAL ANCHOR

Déjà vu and jamais vu as seizure phenomena originate from the hippocampus/entorhinal cortex. When a patient reports "episodic feelings of familiarity or unreality," temporal lobe epilepsy should be in the differential.

1.4 Generalised Seizures: Detailed**Tonic-Clonic (Grand Mal):**

- Tonic phase: 10–30 seconds, rigid extension, ictal cry (forced expiration through adducted cords), cyanosis
- Clonic phase: 30–120 seconds, rhythmic jerking, gradually slowing
- Postictal: Confusion, deep sleep, headache, myalgia, Todd's paralysis possible
- EEG: 10 Hz polyspikes during tonic; spike-wave during clonic; postictal flattening

Typical Absence (Petit Mal):

- Abrupt onset and offset, 3–20 seconds
- Staring, mild automatisms (eye blinking), no postictal phase
- 3 Hz spike-wave on EEG (pathognomonic)
- Precipitated by hyperventilation (useful in clinic)
- Age: 4–12 years, remits at puberty in 60–70%

Atypical Absence:

- Slower onset/offset, longer duration
- Associated with intellectual disability, multiple seizure types
- 1.5–2.5 Hz slow spike-wave
- Associated with Lennox-Gastaut syndrome

Myoclonic Seizures:

- Brief (<0.1 sec), bilateral, synchronous muscle jerks
- No loss of consciousness
- Worst in morning (characteristic of JME)
- Polyspike-wave on EEG

Atonic Seizures (Drop Attacks):

- Sudden loss of muscle tone
- High injury risk (helmet needed)
- EEG: Burst of polyspikes followed by slow waves
- Associated with Lennox-Gastaut

Tonic Seizures:

- Sustained muscle contraction, 2–30 seconds
- Usually during sleep
- Associated with Lennox-Gastaut

1.5 Epilepsy Types and Syndromes

EPILEPSY TYPE · CHARACTERISTICS

Focal Consistent with network in one hemisphere

Generalised Networks rapidly engage both hemispheres

Combined focal + generalised Both types present (e.g., Dravet syndrome)

Unknown Insufficient information

SECTION 2: EPILEPSY SYNDROMES RELEVANT TO PSYCHIATRY

2.1 Temporal Lobe Epilepsy (TLE)

EXAM PEARL

TLE is the most psychiatrically relevant epilepsy syndrome. It is the most common form of focal epilepsy and the most common cause of drug-resistant epilepsy. Know it cold.

Epidemiology:

- Most common focal epilepsy (60% of focal epilepsies)
- Onset: Any age, but peaks in childhood and adolescence
- Drug resistance: 30–40% of cases

Aetiology:

- Hippocampal sclerosis (mesial temporal lobe epilepsy, MTLE), most common structural cause
- Cortical dysplasia
- Tumours (ganglioglioma, DNET)
- Vascular malformations
- Encephalitis (especially HSV, limbic encephalitis)
- Perinatal injury, febrile convulsions (controversial causality)

Mesial TLE (MTLE), Key Features:

- Aura: Epigastric rising sensation (most common), fear, déjà vu / jamais vu, olfactory / gustatory hallucinations
- Automatisms: Oral (lip smacking, chewing), manual (fumbling, picking)
- Impaired awareness during seizure
- Postictal confusion (>30 min), aphasia if dominant hemisphere
- Unilateral tonic posturing (contralateral to focus)

Lateral (Neocortical) TLE:

- Auditory hallucinations (superior temporal gyrus)
- Receptive aphasia (Wernicke's area, dominant hemisphere)
- Experiential phenomena: Forced memories, déjà vu
- Rare automatisms

MRI in MTLE:

- Hippocampal sclerosis: Atrophy + T2/FLAIR hyperintensity + loss of internal architecture
- FDG-PET: Hypometabolism in ipsilateral temporal lobe (interictal)
- Wada test: For lateralisation of language and memory before surgery

Psychiatric Comorbidity in TLE:

CONDITION	PREVALENCE IN TLE	GENERAL POPULATION
Depression	30–50%	10–15%
Anxiety	25–40%	15–20%

CONDITION	PREVALENCE IN TLE	GENERAL POPULATION
Psychosis	5–10%	1–2%
Personality changes	20–40%	Variable
ADHD features	30–40%	5–10%

2.2 Juvenile Myoclonic Epilepsy (JME)

EXAM PEARL

JME is the most common generalised epilepsy syndrome (5–10% of all epilepsies). It is lifelong in most patients. The triad of seizure types is classic exam material.

Classic Triad:

1. Myoclonic jerks, worse on awakening, early morning
2. Generalised tonic-clonic seizures, often triggered by sleep deprivation
3. Absence seizures, in ~30% of patients

Features:

- Onset: 12–18 years (adolescence)
- Normal intelligence, normal neurological exam
- EEG: Generalised polyspike-wave, 4–6 Hz, frontally dominant
- Photosensitivity: 30–50%
- Strong genetic component (CACNB4, GABRA1, EFHC1 mutations)
- AED of choice: Valproate (most effective); levetiracetam, lamotrigine alternatives

Psychiatric Considerations in JME:

- Higher rates of ADHD, anxiety, depression vs. general population
- Personality profile: Impulsivity, poor self-regulation (controversial, may reflect shared neurobiology)
- Valproate: Risk of cognitive side effects, teratogenicity, significant for female patients of reproductive age
- Sleep deprivation, alcohol, stress are key triggers, lifestyle factors matter
- JME patients often have insight into triggers but struggle to modify behaviour (ADHD overlap)

2.3 Childhood Absence Epilepsy (CAE)

Features:

- Age of onset: 4–12 years
- Multiple daily absences (50–100/day)

- Normal development, normal neurological exam
- EEG: Classic 3 Hz generalised spike-wave
- Remission: 60–70% by puberty; persistent in 30–40%

Psychiatric Relevance:

- Academic difficulties secondary to frequent undetected seizures
- Attention and learning problems independent of AEDs
- Misdiagnosis: Often mistaken for daydreaming or ADHD
- AEDs: Ethosuximide (first-line for pure absence), valproate (also covers GTC), lamotrigine

CLINICAL ANCHOR

A child referred for "ADHD" with frequent staring spells, always consider absence epilepsy. Hyperventilation test in the clinic (3 minutes of deep breathing) can precipitate typical absences. This is a simple, zero-cost bedside diagnostic.

2.4 West Syndrome (Infantile Spasms)

EXAM PEARL

The classic triad, infantile spasms + hypsarrhythmia on EEG + developmental regression. Know it. ACTH or vigabatrin are first-line treatments.

Triad:

1. **Infantile spasms**, brief (1–2 sec), symmetric flexion or extension, clusters on awakening
2. **Hypsarrhythmia** on EEG, chaotic, high-amplitude, asynchronous slow waves with superimposed multifocal spikes
3. **Developmental regression**, loss of previously acquired milestones

Epidemiology:

- Onset: 3–12 months (peak 4–6 months)
- Incidence: 1 / 4000 births

Aetiology:

- Structural (40%): Tuberous sclerosis (most common structural cause, ALWAYS think TSC in infantile spasms), cortical dysplasia, hypoxic-ischaemic injury, Down syndrome
- Genetic/metabolic (10%)
- Unknown (cryptogenic) (50%)

Treatment:

- First-line: ACTH (most evidence), vigabatrin (especially if TSC, superior response)

- Second-line: High-dose prednisolone, ketogenic diet, pyridoxine
- Early treatment = better neurodevelopmental outcome

Psychiatric Outcome:

- Autism spectrum disorder: 30–50%
- Intellectual disability: 70–80% (varies with aetiology)
- ADHD-like features: Common
- If TSC-associated: Higher psychiatric burden

2.5 Lennox-Gastaut Syndrome (LGS)

EXAM PEARL

LGS triad, multiple seizure types + slow spike-wave EEG pattern (< 2.5 Hz) + intellectual disability. Drug-resistant. Know which AEDs help.

Triad:

1. **Multiple seizure types**, tonic (especially nocturnal), atonic (drop attacks), atypical absence; also GTC, myoclonic
2. **EEG**, slow spike-wave (< 2.5 Hz), generalized; also paroxysmal fast activity (> 10 Hz) during sleep
3. **Intellectual disability**, cognitive regression is common

Features:

- Onset: 1–7 years (peak 3–5 years)
- Preceded by West syndrome in 30%
- Drop attacks: Major safety concern; helmets required
- Tonic seizures during sleep: Characteristic, dangerous
- Drug-resistant in 90%

AEDs Used in LGS:

AED	EVIDENCE LEVEL	NOTES
Valproate	High	First-line
Lamotrigine	High	Add-on; may worsen myoclonus
Clobazam	High	Add-on
Rufinamide	Moderate	Especially for drop attacks
Topiramate	Moderate	Cognitive side effects
Cannabidiol (CBD)	High (newer)	For seizure reduction

AED	EVIDENCE LEVEL	NOTES
Felbamate	Moderate	Aplastic anaemia risk

Psychiatric Comorbidity:

- Intellectual disability: Core feature
- Autism features: 20–30%
- Behavioural problems: Aggression, self-injury, high frequency
- ADHD: Significant overlap
- Psychiatric management: Challenging due to polypharmacy and cognitive burden

SECTION 3: TEMPORAL LOBE EPILEPSY AND PSYCHIATRIC PHENOMENA

3.1 Geschwind Syndrome (Interictal Behavioral Syndrome)

EXAM PEARL

Geschwind syndrome is highly exam-tested. Know the five core features. Note: its existence as a distinct syndrome is debated, but it remains in exam syllabi.

Historical Context:

Norman Geschwind (1975) described a cluster of personality and behavioural traits in patients with TLE, particularly MTLE with hippocampal pathology. The original description was based on clinical observation rather than controlled studies.

The Five Classic Features (Geschwind Syndrome):

FEATURE	DESCRIPTION	FREQUENCY
Hypergraphia	Compulsive, excessive writing; detailed journals, letters, notes	10–30%
Hyperreligiosity	Intense religiosity, mystical experiences, spiritual preoccupations	10–30%
Hyposexuality	Decreased sexual interest and activity (opposite of what many expect)	Variable
Viscosity / Stickiness	Circumstantial thinking, difficulty ending conversations, adhesiveness	Common

FEATURE	DESCRIPTION	FREQUENCY
Deepened affect	Intense emotional responses, everything feels profound and meaningful	Common

Memory aid, 5 H's: Hypergraphia, Hyperreligiosity, Hyposexuality, "Hurts to leave" (viscosity), Heightened affect

Critical caveats:

- Not all patients with TLE show these features
- The syndrome is not specific to TLE
- Hypergraphia is the most specific feature
- Geschwind did not describe this as a psychiatric disorder, it is a personality style
- Trimble and Bear popularised the concept
- Recent research: Methodological criticisms; comparison studies show much weaker effects

EXAM STRATEGY

If asked about Geschwind syndrome, give the five features, note it's associated with TLE particularly MTLE, mention the controversy about specificity and whether it constitutes a true syndrome. This shows examination depth.

3.2 Interictal Dysphoric Disorder (IDD)

EXAM PEARL

Blumer's concept. Know the eight symptoms. IDD is specific to epilepsy, it does not map neatly onto DSM depression or cyclothymia.

Blumer's Description (2004):

Dietrich Blumer described a pattern of affective disturbance specific to epilepsy that differs from standard mood disorder classifications. It is characterised by:

Eight Core Symptoms:

Depressive-type (4):

1. Depressive mood
2. Anergia (lack of energy)
3. Pain (somatic complaints)
4. Insomnia

Labile/Irritable-type (4):

1. Fear/anxiety (episodic)
2. Euphoric moods (episodic)
3. Irritability
4. Paroxysmal affective disturbances

Key Features of IDD:

- Intermittent, not continuous
- Dysphoric in character (mixed low mood + irritability)
- Pleiotropy: Combines features of dysthymia, cyclothymia, and anxiety disorder
- Temporally related to seizure activity but not strictly peri-ictal
- Responds to SSRI + low-dose lamotrigine (anecdotally)

IDD vs. Major Depressive Disorder in Epilepsy:

FEATURE	IDD	MDD IN EPILEPSY
Course	Intermittent, fluctuating	Sustained episodes
Irritability	Prominent	May be present
Euphoric periods	Yes (short)	Absent
Anhedonia	Mild	Often severe
DSM fit	Poor	Good
AED response	May vary	Standard antidepressants work

3.3 Interictal Psychosis

See Section 5.2 for detailed coverage.

SECTION 4: ICTAL PSYCHIATRIC PHENOMENA

4.1 Overview of Peri-Ictal Psychiatric Phenomena

EXAM PEARL

The peri-ictal classification is critical, ictal, postictal, and interictal phenomena are distinct. Knowing which phase produces which symptom is fundamental to both diagnosis and management.

Temporal Framework:

PHASE	TIMING	PSYCHIATRIC PHENOMENA
Pre-ictal (prodromal)	Hours-days before	Mood change, irritability, anxiety

PHASE	TIMING	PSYCHIATRIC PHENOMENA
Ictal	During seizure	Fear, psychosis, automatisms, forced thoughts
Postictal	Minutes-hours after	Confusion, psychosis, depression, aggression
Interictal	Between seizures	Depression, anxiety, psychosis, personality changes

4.2 Ictal Fear

Characteristics:

- Most common ictal emotion (60–70% of emotional seizures)
- Sudden, intense, unprovoked fear
- Duration: Seconds to 1–2 minutes
- Origin: Amygdala activation (mesial temporal focus)
- Patient retains memory of the fear if aware
- Quality: Unlike normal fear, no clear object, sudden onset, reproducible

Differential Diagnosis:

- Panic disorder: Longer duration, builds up, no EEG correlate, no stereotypy
- Generalised anxiety: Chronic, not paroxysmal
- PTSD: Triggered by stimuli, narrative content
- Pheochromocytoma: Hypertension, flushing, sweating

Clinical Implication:

Patients with TLE presenting to psychiatry with "panic attacks", especially brief, stereotyped, with no identifiable trigger, and with other TLE features, should have EEG performed.

4.3 Ictal Psychosis

Definition: Psychotic symptoms occurring during an ictal discharge, with EEG confirmation.

Features:

- Rare (< 1% of TLE patients)
- Usually brief (minutes)
- Hallucinations: Visual, auditory, olfactory more common than in schizophrenia
- Delusions: Simple, poorly formed
- Associated with continuous EEG abnormality

- Non-convulsive status epilepticus (NCSE) can present as psychosis, this is the critical clinical scenario

EXAM PEARL

Non-convulsive status epilepticus (NCSE) presenting as acute psychosis is a psychiatric emergency. Any acute-onset psychosis with altered consciousness, fluctuating course, subtle automatisms, get an EEG. Missing NCSE = serious harm.

Ictal hallucinations by lobe:

LOBE · HALLUCINATION TYPE

Temporal (anterior) Olfactory ("uncinate fits"), gustatory

Temporal (posterior/superior) Auditory (simple or complex)

Occipital Visual (simple, lights, shapes; not complex)

Parietal Somatosensory, body image disturbance

Frontal Less common; often motor phenomena

4.4 Forced Normalisation (Landolt's Phenomenon)

EXAM PEARL

Heinrich Landolt (1953) described this. Know the paradox: when seizures stop, psychosis can emerge. The EEG normalises, hence "forced normalisation."

Definition:

The phenomenon in which the cessation of seizures (either spontaneous or pharmacologically induced) is associated with the emergence of psychosis. The EEG, previously showing epileptiform activity, becomes paradoxically normal.

Historical Context:

- Landolt (1953): First EEG description, "forced normalisation" referring to the EEG finding
- Tellenbach (1965): "Alternative psychosis", emphasising the alternating, competitive relationship between psychosis and seizures
- The terms are sometimes used interchangeably but are distinct:
- Forced normalisation = EEG phenomenon (normalisation)
- Alternative psychosis = clinical phenomenon (psychosis when seizures remit)

Mechanism (Theoretical):

- Competing inhibitory mechanisms: Seizures may temporarily suppress psychosis-generating processes
- Dopamine hypothesis: Seizures may modulate mesolimbic dopamine; normalization removes this effect
- GABA-glutamate balance shifts
- Not fully understood

Clinical Scenario:

Patient with known TLE, previously seizure-prone, started on new AED (e.g., vigabatrin, levetiracetam). Seizures stop. Two weeks later: acute psychosis, florid hallucinations, EEG now normal.

Management:

- Reduce or discontinue the offending AED (discuss with neurologist)
- Short-term antipsychotic (lowest dose)
- Do NOT automatically increase AED dose, may worsen psychosis
- Monitor EEG during psychosis

AEDs Most Associated with Forced Normalisation:

- Vigabatrin (highest risk)
- Ethosuximide
- Lamotrigine (occasionally)
- Levetiracetam (behavioural side effects, but forced normalisation less clearly established)

SECTION 5: POSTICTAL AND INTERICTAL PSYCHOSIS

5.1 Postictal Psychosis (PIP)

EXAM PEARL

The lucid interval is the signature feature of postictal psychosis. Know it. Know the timing. Know the risk factors. This is a classic exam question.

Definition:

Psychosis emerging after a seizure or cluster of seizures, with a lucid interval (clear period) of 24–48 hours between seizure and psychosis onset.

Epidemiology:

- Prevalence: 7–10% of TLE patients
- More common in: Bilateral seizure foci, longer duration of epilepsy, poor seizure control

The Lucid Interval:

- Critical distinguishing feature
- Duration: Typically 24–48 hours (range: 12 hours to 7 days)
- During this period: Patient is relatively clear, may seem recovered
- Then: Acute psychosis emerges

Clinical Features of PIP:

Onset 24–48 h after seizure cluster (lucid interval)

Trigger Usually cluster of GTC or complex partial seizures

Duration Days to weeks (usually < 2 weeks without treatment)

Mood Often elevated, grandiose, religious, not always paranoid

Hallucinations Auditory, visual, both common

Insight Partial to absent

EEG Usually normalises (cf. Landolt's phenomenon)

Risk Harm to self/others possible, treat actively

Risk Factors for PIP:

1. Bilateral (or dual) seizure foci
2. History of febrile convulsions
3. Longer duration of epilepsy (> 10 years)
4. Male sex (some studies)
5. Temporal lobe focus
6. Prior postictal psychosis (strongest predictor)

Management of PIP:

1. **Immediate:** Observation, safety, supportive care
2. **Antipsychotics:** Low-dose haloperidol or olanzapine (avoid clozapine, lowers seizure threshold; avoid phenothiazines)
3. **Benzodiazepines:** For agitation
4. **AED optimisation:** Reduce seizure frequency to prevent recurrence
5. **Psychoeducation:** Family must understand lucid interval, they may think patient is fine, then decompensate

Natural History:

- Self-limiting in most cases (days to weeks)
- Risk of progression to chronic interictal psychosis with repeated episodes (~15%)
- Does not require long-term antipsychotic in most cases

5.2 Interictal Psychosis (IIP) / Schizophrenia-Like Psychosis of Epilepsy (SLPE)

EXAM PEARL

Slater and Beard (1963) is the foundational paper. Know the features that distinguish SLPE from schizophrenia, the "positive without negative" pattern and preserved affect are classic exam content.

Slater and Beard (1963):

Classic study describing psychosis in 69 epilepsy patients. Found psychosis resembling schizophrenia but with key differences.

Definition:

Chronic psychosis occurring in epilepsy patients, not time-locked to seizure activity (interictal), persisting for months to years.

Prevalence:

- 5–10% of TLE patients
- Risk vs. general population: 6–12x higher (depending on study)
- Most common in: MTLE, bilateral foci, long duration, poor control

Clinical Features, SLPE vs. Schizophrenia:

FEATURE	SLPE (INTERICTAL PSYCHOSIS)	SCHIZOPHRENIA
Positive symptoms	Prominent (hallucinations, delusions)	Prominent
Negative symptoms	Mild or absent, KEY DISTINCTION	Often prominent
Affect	Preserved, warm, KEY DISTINCTION	Often flat/blunted
Social deterioration	Milder	More severe
Formal thought disorder	Less severe	Common
Religious content	Often present	Less specific
Catatonia	Rare	Possible
Premorbid function	Often normal	Often impaired
Onset	After epilepsy onset (mean: 11 years after)	Early adulthood

FEATURE	SLPE (INTERICTAL PSYCHOSIS)	SCHIZOPHRENIA
FH of schizophrenia	Not elevated	Elevated
First rank symptoms	Present	Present

The "Positive Without Negative" Pattern:

This is the most testable feature of SLPE. Hallucinations and delusions are present, but the patient retains warmth, maintains relationships, and shows preserved emotional responsiveness. This "schizophreniform" picture without the typical deterioration distinguishes it.

Risk Factors for SLPE:

1. TLE (especially MTLE and bilateral TLE)
2. Long duration of epilepsy
3. Poor seizure control
4. Alien tissue lesions (ganglioglioma, hamartoma, DNET)
5. Bilateral or left-sided foci
6. Ictal fear as prominent symptom
7. History of postictal psychosis

Mechanism Hypotheses:

1. **Kindling:** Repeated sub-threshold stimulation → permanent neuronal changes
2. **Structural:** Hippocampal, amygdala, and parahippocampal atrophy → psychotic vulnerability
3. **Neurotransmitter:** Dopaminergic dysregulation secondary to limbic pathology
4. **Shared vulnerability:** Common genetic/neurodevelopmental substrate for epilepsy and psychosis

Management of SLPE:

- Antipsychotics: Atypical antipsychotics preferred
- Aripiprazole: Least proconvulsant
- Risperidone: Effective; moderate proconvulsant risk
- Olanzapine: Effective; moderate proconvulsant
- Clozapine: Avoid (highest proconvulsant risk); reserve for treatment-resistant
- Haloperidol: Useful acutely; chronic use less favoured
- Continue AEDs, do NOT reduce AEDs expecting this to help psychosis
- Monitor EEG when starting antipsychotics

Proconvulsant Risk of Antipsychotics (Low → High):

Aripiprazole < Haloperidol < Risperidone < Quetiapine < Olanzapine < Clozapine

SECTION 6: DEPRESSION IN EPILEPSY

6.1 Epidemiology and Prevalence

Prevalence:

- 20–55% of epilepsy patients (most consistent estimate: ~30%)
- Most common psychiatric comorbidity in epilepsy
- More common in:
 - TLE
 - Drug-resistant epilepsy
 - Active seizures (vs. well-controlled)
 - Left hemisphere focus (some evidence)
 - Limbic involvement

The Bidirectional Relationship:

EXAM PEARL

The relationship between epilepsy and depression is bidirectional, each increases the risk of the other. This is not coincidence; it reflects shared neurobiology. Examiners love this concept.

DIRECTION · EVIDENCE

Epilepsy → Depression High seizure frequency, AED effects, social stigma, functional limitations

Depression → Epilepsy Depression itself is a risk factor for developing epilepsy (RR ~1.5–2.0)

Shared neurobiology Both involve serotonergic, GABAergic, noradrenergic dysregulation

Shared pathology TLE + hippocampal atrophy + amygdala changes correlate with both

Mechanisms of Depression in Epilepsy:

CATEGORY · MECHANISM

Neurobiological Limbic-serotonin disruption; HPA axis dysregulation; interictal hypometabolism

Pharmacological AED side effects (phenobarbital, topiramate, levetiracetam, zonisamide)

Psychosocial Stigma, driving restrictions, employment limitations, dependency

Ictal/postictal Postictal depression (distinct entity)

6.2 Postictal Depression

- Occurs within 24–48 hours of seizure
- Duration: Hours to 1–2 days
- Features: Sadness, hopelessness, fatigue, suicidal ideation (can be dangerous)
- May be part of postictal psychiatric syndrome (postictal psychosis, agitation, mania also occur)
- Management: Short-term support; SSRI if persistent or severe

6.3 NDDI-E (Neurological Disorders Depression Inventory for Epilepsy)

EXAM PEARL

NDDI-E is the validated, preferred screening tool for depression in epilepsy. Know the cutoff score.

Why NDDI-E and not PHQ-9?

- PHQ-9 includes somatic items that overlap with AED side effects and seizure effects (fatigue, sleep disturbance, concentration)
- NDDI-E excludes somatic items; focuses on cognitive-emotional features
- Developed and validated specifically for epilepsy populations

NDDI-E Items (6 items, each scored 1–4):

1. Everything is a struggle
2. Nothing I do is right
3. Feel guilty
4. I'd be better off dead
5. Frustrated
6. Difficulty finding pleasure

Scoring:

- Total: 6–24
- Cutoff ≥ 15 : Probable major depressive disorder (sensitivity 81%, specificity 90%)
- Scores 11–14: Subclinical, monitor

GAD-7 for Anxiety:

- GAD-7 is recommended for anxiety screening in epilepsy
- Same rationale, validated and less somatic overlap than other scales

6.4 Antidepressants in Epilepsy

Proconvulsant Risk, Antidepressants:

ANTIDEPRESSANT	SEIZURE RISK	NOTES
SSRIs (sertraline, citalopram, escitalopram)	Low	First-line in epilepsy
SNRIs (venlafaxine, duloxetine)	Low-moderate	Acceptable
Mirtazapine	Low	Good option, sedating
TCAs (amitriptyline, imipramine)	High	Avoid, especially at high doses
Bupropion	High	Avoid, most proconvulsant antidepressant
Maprotiline	High	Avoid
Clomipramine	High	Avoid
Fluoxetine	Low-moderate	CYP interactions

EXAM PEARL

SSRIs are the antidepressants of choice in epilepsy. Bupropion is the most proconvulsant antidepressant, it is contraindicated in epilepsy.

6.5 Suicide Risk in Epilepsy

Prevalence:

- Suicide attempts: 5x higher than general population
- Completed suicide: 3–5x higher
- SUDEP (Sudden Unexpected Death in Epilepsy): 1 / 1000 patient-years (competing cause)

Risk Factors for Suicide in Epilepsy:

1. TLE (especially MTLE)
2. Depression (strongest modifiable risk factor)
3. Drug-resistant epilepsy
4. Young age, male sex
5. Recent diagnosis
6. Social isolation, unemployment
7. AED side effects (particularly topiramate and levetiracetam)

FDA Black Box Warning (2008):

All AEDs carry an FDA black box warning for increased suicidality. This applies to the class as a whole, not specific agents. Meta-analysis showed approximately 2x increased risk. The absolute risk is small.

EXAM PEARL

The FDA 2008 warning covers ALL AEDs for suicidality. This is frequently tested. The risk is real but small, do not withhold AEDs because of this.

SECTION 7: ANXIETY IN EPILEPSY

7.1 Prevalence and Types

Prevalence: 20–40% of epilepsy patients

Anxiety Disorders in Epilepsy:

TYPE · NOTES

Panic disorder Difficult to distinguish from ictal fear; needs careful characterisation

Generalised anxiety Common; chronic worry about seizures, driving, employment

Phobia Specific: fear of having seizures in public (ictal phobia)

PTSD Following traumatic seizure experiences, injuries

Social anxiety Stigma-related

Interictal anxiety As part of IDD

7.2 Anticipatory Anxiety

- Fear of the next seizure, "living on the edge"
- Leads to avoidance behaviour, activity restriction
- Reduced quality of life independent of seizure frequency
- Cognitive-behavioural interventions are effective
- AED optimisation helps by reducing uncertainty

7.3 Treatment

- **SSRIs/SNRIs:** First-line for GAD, panic, social anxiety in epilepsy
- **Buspirone:** Safe; no proconvulsant risk; useful for GAD
- **Benzodiazepines:** Use with caution (tolerance, sedation, cognitive impairment, respiratory depression)
- **CBT:** Evidence-based; strongly recommended alongside pharmacotherapy

- **Mindfulness-based interventions:** Growing evidence

SECTION 8: ANTIEPILEPTIC DRUGS AND PSYCHIATRIC EFFECTS

8.1 Overview

EXAM PEARL

AEDs have both positive (mood-stabilising, anxiolytic) and negative (depression, psychosis, cognitive impairment) psychiatric effects. The table below is essential exam content.

Master Table, AED Psychiatric Profiles:

AED	MECHANISM	POSITIVE PSYCH EFFECTS	NEGATIVE PSYCH EFFECTS	NOTES
Valproate	GABA enhancement, sodium channel blockade	Mood stabiliser (mania, bipolar), anxiety reduction	Weight gain, cognitive dulling, teratogenicity	First-line mood stabiliser; also used in BD-I
Carbamazepine	Sodium channel blockade	Mood stabilisation, aggression reduction	Hyponatraemia (SIADH), sedation, cognitive effects	Structurally similar to TCA; also used in BD
Lamotrigine	Sodium/calcium channel, glutamate reduction	Mood stabilisation (especially bipolar depression), reduced mood cycling	Rash (serious), insomnia, rarely psychosis	Superior for bipolar depression
Levetiracetam	SV2A binding	Minimal sedation, no cognitive impairment	Irritability, aggression, depression, psychosis (most psychiatric side effects of newer AEDs)	Psychiatric side effects in ~10%; dose-dependent
Topiramate	Multiple (GABA, glutamate, sodium channel, carbonic anhydrase)	Weight loss (can be a "positive")	Cognitive impairment (word-finding difficulty, processing speed), "Dope-iramate", depression, suicidality, psychosis (rarely)	Cognitive effects are dose-dependent

AED	MECHANISM	POSITIVE PSYCH EFFECTS	NEGATIVE PSYCH EFFECTS	NOTES
Phenobarbital	GABA-A enhancement	Sedation (occasionally desired)	Depression , cognitive impairment, hyperactivity in children, tolerance, dependence	Worst for depression among older AEDs
Phenytoin	Sodium channel blockade	Low psychiatric burden when used appropriately	Cognitive effects at high doses, gingival hyperplasia	Drug interactions significant
Oxcarbazepine	Sodium channel blockade	Similar to carbamazepine	Hyponatraemia, dizziness	Fewer drug interactions than carbamazepine
Clonazepam	GABA-A	Anxiolytic, antimyoclonic	Dependence, sedation, cognitive impairment, paradoxical disinhibition	Use cautiously long-term
Vigabatrin	GABA transaminase inhibitor	Effective for infantile spasms, TSC	Depression, psychosis, forced normalisation	Visual field defects, irreversible; monitor
Lacosamide	Slow inactivation sodium channel	Low psychiatric burden	Dizziness, diplopia; psychiatric effects minimal	Well tolerated psychiatrically
Zonisamide	Multiple	Modest weight loss	Cognitive effects, depression, kidney stones	Similar to topiramate profile
Gabapentin/Pregabalin	Alpha-2-delta subunit	Anxiolytic, pain; used as adjuncts	Sedation, weight gain, misuse potential (pregabalin especially)	Pregabalin: Schedule 5 in UK; abuse potential
Perampanel	AMPA antagonist	Good tolerability	Aggression, irritability, hostility (dose-dependent)	Warn patients about behavioural effects

8.2 Valproate: Psychiatric Indications

Epilepsy uses:

- Generalised epilepsy (JME, childhood absence, idiopathic)
- Focal epilepsy (second-line)
- Lennox-Gastaut syndrome

- Status epilepticus (IV formulation)

Psychiatric uses:

- Bipolar disorder I, acute mania (first-line), maintenance
- Augmentation in schizoaffective disorder
- Impulse control disorders
- Aggression/behavioural problems in dementia, ID
- Migraine prophylaxis (neurological)

EXAM PEARL

Valproate teratogenicity is exam gold. Neural tube defects (spina bifida aperta): 1–2% risk (vs. ~0.05% baseline). Overall major congenital malformations: ~10%. Neurodevelopmental effects: IQ reduction, autism risk. AVOID in women of childbearing potential unless other options exhausted. VALPROATE MUST NOT be used in girls/women without effective contraception unless clearly necessary (MHRA 2018, revised guidance 2024).

8.3 Carbamazepine: Psychiatric Considerations

- Mood stabiliser: Particularly for rapid cycling, mixed states, BD with dysphoric mania
- Drug interactions: Strong CYP3A4 inducer
- Reduces plasma levels of: Haloperidol, olanzapine, risperidone, aripiprazole, quetiapine, valproate, lamotrigine
- Oral contraceptives: Efficacy reduced (important, counsel women)
- SIADH and hyponatraemia: Especially in elderly; can cause encephalopathy
- Aplastic anaemia/agranulocytosis: Rare but potentially fatal; monitor FBC
- Oxcarbazepine: Less enzyme induction, better tolerated

8.4 Lamotrigine: Psychiatric Considerations

- Mood stabilisation: Evidence-based for bipolar depression maintenance
- NOT first-line for acute mania
- Rash: 10% mild rash; 0.1–0.3% severe (Stevens-Johnson syndrome, TEN)
- Risk reduced by slow titration
- Risk increased with: Rapid titration, concomitant valproate (doubles lamotrigine levels → double rash risk)
- Interaction with oral contraceptives: OCP reduces lamotrigine levels by ~50%; monitor doses if OCP started/stopped
- Psychosis: Rare; associated with forced normalisation in some patients

8.5 Levetiracetam: Psychiatric Side Effects

EXAM PEARL

Levetiracetam (Keppra) is the AED most associated with psychiatric side effects among newer agents. Irritability and agitation in ~10% of patients. Depression and psychosis less common but recognised.

Psychiatric side effects:

- Irritability / agitation: 10–15% (dose-dependent)
- Depression: 5–10%
- Anxiety: 5–8%
- Psychosis: 0.5–2% (can be severe, acute onset)
- Associated with forced normalisation

Mechanism hypothesis: SV2A binding modulates neurotransmitter release; unclear why this produces behavioural effects in some patients.

Management:

- Dose reduction often helps
- Adjunctive pyridoxine (vitamin B6): Some evidence for reducing irritability in children; less clear in adults
- Switching to alternative AED if intolerable
- Antidepressants / antipsychotics as needed

8.6 Topiramate: Cognitive Effects

EXAM PEARL

"Dopamax" or "Dope-iramate", the cognitive side effects of topiramate are clinically significant and exam-testable. Word-finding difficulty (anomia) is most characteristic.

Cognitive effects:

- Word-finding difficulty: Most prominent, distressing to patients
- Processing speed: Reduced
- Working memory: Impaired
- Attention: Impaired
- Effects: Dose-dependent (much worse at > 200 mg/day)

Other notable effects:

- Weight loss (positive for some patients, negative in underweight individuals)

- Nephrolithiasis (carbonic anhydrase inhibition → alkaline urine → calcium phosphate stones)
- Oligohidrosis (reduced sweating), rare but dangerous in hot weather
- Depression and suicidality: Monitor

8.7 Phenobarbital: Depression Risk

- Oldest AED; first-line in low-income countries (cheap, available)
- Depression: Most clearly linked to phenobarbital among all AEDs
- Mechanism: GABA-A enhancement → sedation, CNS depression
- Hyperactivity in children: Paradoxical effect
- Sedation: Prominent, limits use
- Cognitive impairment: Significant with chronic use
- Tolerance: Develops to sedative effects
- Dependence: Physical dependence; withdrawal seizures if stopped abruptly

SECTION 9: AED INTERACTIONS WITH PSYCHOTROPICS

9.1 Enzyme Induction by AEDs

Strong CYP3A4 Inducers (AEDs):

- Carbamazepine
- Phenytoin
- Phenobarbital
- Primidone (metabolised to phenobarbital)

Effect on Psychotropics:

These AEDs dramatically reduce plasma levels of most antipsychotics and antidepressants. Clinical consequence: Apparent treatment resistance.

PSYCHOTROPIC AFFECTED · EFFECT OF ENZYME INDUCTION

Haloperidol Levels reduced 50–70%

Olanzapine Levels reduced 40–60%

Risperidone Levels reduced 40–50%

Aripiprazole Levels reduced 50–60%

Quetiapine Levels reduced 50–70%

Clozapine Levels reduced 40–60%

Valproate Levels reduced (by carbamazepine especially)

Lamotrigine Levels reduced by phenytoin, carbamazepine, phenobarbital

Clinical implication: When starting enzyme-inducing AEDs, anticipate need to increase psychotropic doses. When stopping them, reduce psychotropic doses (risk of toxicity).

9.2 Enzyme Inhibition by AEDs

Valproate inhibits CYP2C9, CYP2C19, and is a UGT inhibitor:

- Doubles lamotrigine levels (important, rash risk)
- Increases phenobarbital levels
- May increase levels of certain SSRIs (via CYP2C19)

9.3 Psychotropic Effects on AED Levels

PSYCHOTROPIC · AED EFFECT

Fluoxetine, fluvoxamine CYP2C9/2C19 inhibition → increased phenytoin, carbamazepine, valproate levels

Sertraline Minimal interactions

Citalopram/escitalopram Minimal interactions (safest SSRIs for epilepsy)

Haloperidol May lower seizure threshold; minimal pharmacokinetic interaction

Clozapine Lowers seizure threshold; avoid with carbamazepine (both agranulocytosis risk)

EXAM PEARL

Clozapine + carbamazepine = CONTRAINDICATED. Both cause agranulocytosis independently; combination dramatically increases risk.

9.4 Seizure Threshold and Psychotropics

Psychotropics that Lower Seizure Threshold:

DRUG	SEIZURE RISK LEVEL	NOTES
Clozapine	Very High	3–5% at high doses; EEG monitoring recommended
Chlorpromazine	High	Older antipsychotics generally more proconvulsant
Bupropion	High	Most proconvulsant antidepressant
Tricyclics	High	Especially at toxic levels

DRUG	SEIZURE RISK LEVEL	NOTES
Maprotiline	High	Tetracyclic
Lithium	Moderate-high	Especially at toxic levels (tremor → seizure cascade)
Haloperidol	Moderate	
Olanzapine, risperidone	Low-moderate	
SSRIs	Low	Safest class
Aripiprazole	Low	Safest antipsychotic

SECTION 10: PSEUDOSEIZURES / PNES

10.1 Terminology

EXAM PEARL

"PNES", Psychogenic Non-Epileptic Seizures, is the preferred current term. "Pseudoseizures" is outdated but still used clinically. "Functional seizures" is increasingly used (part of functional neurological disorder, FND spectrum). Know all three terms.

Current preferred terminology: Psychogenic Non-Epileptic Seizures (PNES) or Functional Seizures

Why terminology matters: "Pseudo" implies faking. These are not voluntary. They are genuine, disabling, and medically serious. This distinction matters in court, in medical letters, and in therapeutic relationships.

10.2 Epidemiology

- Prevalence: 2–33/100,000 (community); higher in epilepsy monitoring units
- 20–30% of patients referred to epilepsy monitoring units have PNES
- 10–30% of PNES patients also have comorbid epilepsy (dual diagnosis), critical point
- Sex: Female:male ratio ~3:1 to 7:1
- Age of onset: Bimodal, adolescence and 30s
- Misdiagnosis duration: Average 7 years before correct diagnosis

10.3 Differentiating Epileptic Seizures from PNES

EXAM PEARL

The gold standard for diagnosis is Video-EEG telemetry with a captured event. No other test is definitive. Know the clinical features, but know the gold standard.

Gold Standard: Video-EEG monitoring with ictal EEG recording (or absence of EEG change during typical event)

Clinical Differentiators:

FEATURE	EPILEPTIC SEIZURE (TLE/GTC)	PNES
Onset	Sudden, stereotyped	Gradual, variable
Duration	Usually < 3 min	Often prolonged (>3–5 min)
Motor features	Stereotyped, rhythmic (GTC), automatisms (TLE)	Asynchronous, thrashing, pelvic thrusting, opisthotonus
Side-to-side head movement	Rare	Common (positive likelihood ratio ~8)
Eye position	Open, deviated (GTC); blank (TLE)	Closed; resistance to opening eyes
Ictal crying/weeping	Very rare	Common
Responsiveness	Absent (if impaired awareness)	Variable, sometimes present even in apparent unconsciousness
Postictal confusion	Prominent, prolonged	Minimal or absent
Self-injury	Common (tongue bite, lateral; falls)	Tongue bite rare (tip not lateral); rare falls
Incontinence	Common in GTC	Less common
Recall	Absent for GTC	May have partial recall
Triggers	Sleep deprivation, alcohol, illness	Psychosocial stressors, trauma contexts, sometimes suggestion
Witnesses	Irrelevant	Often occurs with audience
Ictal prolactin	Elevated 10–20 min post-GTC/CPS	Not elevated
Postictal EEG	Slowing	Normal

Semiology features suggesting PNES:

- Pelvic thrusting (though not specific)
- Forward pelvic thrusting (more specific for PNES)
- Opisthotonus (arc de cercle)
- Bicycling leg movements
- Atypical motor features (e.g., gradual onset, build-up)
- Eye closure and resistance
- Crying during or immediately after event

- Out-of-phase limb movements
- Prolonged duration

Semiology features suggesting epilepsy:

- Stereotypy across events
- Brief duration (< 3 minutes)
- Postictal confusion
- Todd's paralysis (postictal focal weakness)
- Lateral tongue bite
- Clear postictal coma

10.4 Investigation

INVESTIGATION	FINDING IN PNES	FINDING IN EPILEPSY
Video-EEG (gold standard)	Normal EEG during event	Epileptiform discharge or generalised change
Interictal EEG	Usually normal (may have non-specific changes)	May show epileptiform discharges
Serum prolactin (20 min post-event)	Not elevated	Elevated after GTC/CPS (not absence)
CK	May rise with intense PNES	Rises significantly after GTC
MRI brain	Usually normal	May show structural lesion
Neuropsychological testing	May reveal dissociative features	Cognitive profile depends on syndrome

Note on prolactin: Not reliable enough alone. Sensitivity 60%; specificity 96% for GTC/CPS (not absence, frontal, or postictal period > 60 min). Use only as adjunct.

10.5 Psychiatric Comorbidity in PNES

DIAGNOSIS · PREVALENCE IN PNES

Depression 50–80%

Anxiety disorders 50–70%

PTSD 30–60%

Dissociative disorders 30–50%

Personality disorders (Cluster B especially) 30–50%

Somatic symptom disorder Overlap

History of trauma/abuse 50–80%

Comorbid epilepsy 10–30%

10.6 Management of PNES

EXAM PEARL

Disclosing the diagnosis is therapeutic, but HOW it is disclosed matters enormously. The wrong approach drives patients away. Know the communication framework.

Step 1, Establish diagnosis definitively (Video-EEG)

Step 2, Communicating the diagnosis:

- Lead with what it IS, not what it isn't: "Your spells are a type of functional neurological disorder..."
- Do NOT say: "It's all in your head" or "There's nothing wrong with you"
- Emphasise: Real symptoms, not faking, treatable
- Acknowledge the diagnostic journey
- Explain the diagnosis as a brain-body communication problem (mind-brain framework)
- Joint consultation (neurologist + psychiatrist ideally)

Step 3, Psychiatric treatment:

- **Psychotherapy:** CBT with seizure-specific components (strongest evidence); trauma-focused therapy if PTSD; EMDR; psychodynamic
- **Treat comorbidities:** Depression, PTSD, anxiety, standard treatments
- **Address iatrogenic harm:** Many patients have been overmedicated with AEDs, suffered AED side effects; gradual AED withdrawal after diagnosis (if no comorbid epilepsy)
- **Physiotherapy/rehabilitation:** For functional neurological disorder comorbidities

Step 4, Withdrawal of AEDs (if no comorbid epilepsy):

- Gradual, not abrupt
- Done jointly with neurology
- Expect potential short-term worsening of PNES (extinction burst)
- Long-term: AED withdrawal reduces PNES burden in many patients

Prognosis:

- 30–40% remit completely with treatment
- 50% improve substantially
- Poorer prognosis: Longer duration of misdiagnosis, comorbid personality disorder, secondary gain, multiple comorbidities

SECTION 11: EEG IN PSYCHIATRY

11.1 Normal EEG Rhythms

RHYTHM	FREQUENCY	LOCATION	STATE
Alpha (α)	8–13 Hz	Occipital, posterior	Relaxed, eyes closed; blocks with eye opening
Beta (β)	13–30 Hz	Frontocentral	Alert, active mental activity; drugs (benzos)
Theta (θ)	4–7 Hz	Temporal, frontal	Drowsiness; normal in children; frontotemporal TLE
Delta (δ)	0.5–3 Hz	Diffuse	Deep sleep; pathological if awake (focal or diffuse)
Gamma (γ)	>30 Hz	Widespread	Cognitive processing; being studied
Mu (μ)	8–13 Hz	Central (Rolandic)	Motor cortex at rest; blocks with movement

Normal variants (not epileptiform):

- Wicket spikes: Benign temporal variant
- SREDA (subclinical rhythmic EEG discharges of adults)
- 14 and 6 Hz positive bursts
- Benign epileptiform transients of sleep (BETS/BETS)
- Hypnagogic hypersynchrony (children)

11.2 Epileptiform Discharges

PATTERN	DESCRIPTION	ASSOCIATED CONDITION
Interictal epileptiform discharges (IEDs)	Spikes (< 70 ms), sharp waves (70–200 ms), isolated	Focal or generalised epilepsy
3 Hz spike-wave	Regular, generalised	Childhood absence epilepsy
Hypsarrhythmia	Chaotic, high-amplitude, asynchronous	West syndrome
Slow spike-wave (< 2.5 Hz)	Diffuse, slow	Lennox-Gastaut
Polyspike-wave	Multiple spikes + slow wave	JME and other myoclonic epilepsies

PATTERN	DESCRIPTION	ASSOCIATED CONDITION
Focal spike-wave	Temporal, frontal, etc.	Focal epilepsy
PLEDS (Periodic Lateralised Epileptiform Discharges)	Unilateral, periodic	Acute brain damage (HSV encephalitis, stroke)
GPEDS (Generalised Periodic Epileptiform Discharges)	Bilateral, periodic	CJD, anoxic encephalopathy, NCSE
Ictal EEG	Clear evolution of frequency and amplitude	Seizure activity

11.3 EEG in Psychiatric Conditions

CONDITION · EEG FINDING

Schizophrenia Increased theta, reduced alpha power, non-specific; IEDs not expected

Depression Frontal alpha asymmetry (right > left frontal alpha in depression, reflects left frontal hypoactivity); non-specific

Bipolar disorder Non-specific; some studies show theta / delta changes in mania

Delirium Diffuse slowing (theta / delta); hallmark EEG finding

Dementia (Alzheimer's) Progressive slowing; alpha reduction; delta in late stages

CJD PSWCs (Periodic Sharp Wave Complexes) 1–2 Hz, pathognomonic

Lithium toxicity Diffuse slowing, focal / generalised epileptiform; triphasic waves

Benzodiazepine Increased beta activity (drug effect)

ECT Post-ictal flattening; postictal slowing → gradual return to baseline

NCSE (Non-convulsive SE) Continuous or near-continuous epileptiform activity, diagnosis of exclusion

EXAM PEARL

Delirium = diffuse slowing on EEG. This is the most clinically important EEG finding in a psychiatry inpatient setting. When a patient's sensorium is fluctuating acutely on your ward, EEG can help distinguish delirium (diffuse slowing) from NCSE (epileptiform activity) from functional / psychiatric (normal EEG).

11.4 Indications for EEG in Psychiatry

CLINICAL SCENARIO · INDICATION LEVEL

First-episode psychosis Routine (to rule out organic cause)

Fluctuating consciousness with psychiatric symptoms Urgent (rule out NCSE)

Episodic psychiatric symptoms with motor features Important

Treatment-resistant epilepsy before surgery Mandatory

Suspected PNES Essential (video-EEG)

Lithium toxicity Useful

After clozapine dose increase Consider (seizure monitoring)

Pre-ECT workup In selected patients (not routine)

SECTION 12: STATUS EPILEPTICUS

12.1 Definition and Classification

EXAM PEARL

The 2015 ILAE definition changed the threshold. Know the operational definition: 5 minutes for convulsive SE, 10 minutes for absence SE. This replaced the old "30 minutes" definition.

ILAE 2015 Operational Definitions:

SE TYPE	OPERATIONAL DEFINITION (T1)	FUNCTIONAL DEFINITION (T2)
Convulsive SE	≥ 5 minutes of seizure activity	≥ 30 minutes (long-term consequences)
Absence SE	≥ 10 minutes	≥ 30 minutes
Focal SE with impaired awareness	≥ 10 minutes	≥ 60 minutes

Classification of SE:

TYPE	FEATURES	PSYCHIATRIC RELEVANCE
Convulsive (Generalised Tonic-Clonic SE)	Overt motor manifestations; most common	Medical emergency; post-SE depression/psychosis common
Non-convulsive SE (NCSE)	Altered awareness without overt convulsions; EEG-confirmed	Can present as acute psychosis, psychiatric emergency
Absence SE	Continuous absence; subtle behaviour change	Misdiagnosed as psychiatric; patient appears "spacey"

TYPE	FEATURES	PSYCHIATRIC RELEVANCE
Focal SE with impaired awareness	Previously complex partial SE	TLE-related; prolonged confusional states
Refractory SE	Not responding to first and second-line AEDs	ICU management
Super-refractory SE	Ongoing ≥ 24 h despite general anaesthesia	Extremely high morbidity / mortality

12.2 Management Protocol for Convulsive SE

Time-based Protocol:

0–5 min (Stabilisation Phase):

- ABC, oxygen, IV access, glucose (check and treat if low)
- Blood: FBC, EUC, glucose, LFTs, AED levels, toxicology
- Position: Recovery position if no spinal injury concern
- Do NOT restrain

5–20 min (First-line, Benzodiazepines):

- **Lorazepam IV** 0.1 mg/kg (max 4 mg per dose); preferred if IV access
- **Diazepam IV** 0.2 mg/kg (max 10 mg)
- **Midazolam IM/buccal/intranasal** 10 mg, if no IV access (equivalent efficacy)
- Can repeat once after 5–10 minutes if seizure continues

20–40 min (Second-line, Non-benzodiazepine):

- **Levetiracetam IV** 60 mg/kg (max 4500 mg), now often first choice for second-line
- **Valproate IV** 40 mg/kg (max 3000 mg), avoid in hepatic disease, pregnancy, mitochondrial disease
- **Phenytoin IV** 20 mg/kg (max 1500 mg), fosphenytoin preferred if available; cardiac monitoring needed
- **Lacosamide IV**, emerging second-line option

40–60 min (Third-line, Refractory SE):

- ICU transfer
- Anaesthetic agents: Midazolam infusion, propofol, thiopental, ketamine
- EEG monitoring (continuous)
- Burst suppression target

12.3 NCSE: Psychiatric Presentation

Why NCSE Is a Psychiatric Emergency:

NCSE can present with:

- Acute onset psychosis
- Fluctuating consciousness
- Bizarre behaviour
- Mutism
- Automatic behaviour with post-event amnesia

Red Flags for NCSE in a Psychiatric Setting:

- Known epilepsy history
- Fluctuating, not continuous symptoms
- Subtle motor features (lip smacking, eye blinking, subtle facial twitching)
- Amnesia for the episode
- Impaired response to commands despite apparent wakefulness
- EEG-confirmed (required for diagnosis)

Management: IV benzodiazepine diagnostic trial; AED optimisation; treat underlying cause

SECTION 13: EPILEPSY SURGERY AND PSYCHIATRIC OUTCOMES

13.1 Surgical Options

SURGERY TYPE	DESCRIPTION	BEST CANDIDATE
Anterior temporal lobectomy (ATL)	Resection of anterior temporal lobe + hippocampus	MTLE with hippocampal sclerosis, best outcomes
Selective amygdalohippocampectomy (SAH)	More limited resection	Preserves more neocortex; comparable seizure outcomes
Lesionectomy	Removal of MRI-visible lesion	Tumour, cavernoma, cortical dysplasia
Hemispherectomy/hemispherotomy	Disconnection of hemisphere	Rasmussen's encephalitis, large unilateral lesions in children
Corpus callosotomy	Section of corpus callosum	Drop attacks in LGS; palliative
Vagal nerve stimulation (VNS)	Implantable device	Non-resectable; adjunctive
Deep brain stimulation (DBS)	Thalamic stimulation	Non-resectable; emerging
Responsive neurostimulation (RNS)	Closed-loop stimulation at seizure focus	Emerging

13.2 Psychiatric Outcomes Post-Surgery

EXAM PEARL

Surgery does NOT reliably improve psychiatric comorbidity. In fact, de novo psychiatric disorders can emerge post-surgery. This is frequently tested.

Post-ATL Psychiatric Outcomes:

PSYCHIATRIC DOMAIN · OUTCOME

Seizure freedom (Engel I) ~70% in MTLE with hippocampal sclerosis

Depression pre-surgery Major predictor of poor psychiatric outcome

De novo depression post-surgery 5–20% develop new depression; highest in first year

De novo psychosis post-surgery 1–5%; especially with history of postictal psychosis

Anxiety Often improves with seizure freedom

Quality of life Generally improves with seizure freedom

Forced normalisation Can occur post-surgery, psychosis when seizures stop

Predictors of Good Post-Surgery Psychiatric Outcome:

- Absence of pre-surgical psychiatric disorder
- High baseline IQ
- Seizure freedom achieved
- Strong social support
- Younger age at surgery

Predictors of Poor Psychiatric Outcome:

- Pre-existing depression or psychosis
- History of postictal psychosis
- Bilateral foci
- Right temporal resection (some studies suggest higher depression risk)
- Failure to achieve seizure freedom

Pre-surgical psychiatric assessment:

- Mandatory in most epilepsy surgery centres
- Wada test (intracarotid amobarbital test): Assesses language lateralisation and memory function of each temporal lobe separately
- Neuropsychological assessment: Predicts post-operative cognitive change

- Structured psychiatric interview: Identifies risk factors for post-surgical psychiatric complications

SECTION 14: WOMEN WITH EPILEPSY

14.1 Teratogenicity of AEDs

EXAM PEARL

Teratogenicity is a major exam topic. Know the hierarchy, valproate is the most teratogenic. Neural tube defects are the hallmark of valproate / carbamazepine. Lamotrigine has the lowest risk of major congenital malformations among common AEDs.

Relative Teratogenicity:

AED	MAJOR CONGENITAL MALFORMATION RATE	KEY MALFORMATIONS	NOTES
Valproate	~10–11%	Neural tube defects (NTD: 1–2%), cardiovascular, orofacial clefts, hypospadias, limb defects	HIGHEST RISK; also neurodevelopmental, IQ loss, autism risk
Carbamazepine	~2–3%	NTD (0.5%), cardiovascular, orofacial clefts	Dose-dependent
Phenobarbital	~5–7%	Cardiovascular, orofacial, digital defects	
Phenytoin	~3–7%	Fetal hydantoin syndrome (NTDs, hypoplastic nails / fingers, dysmorphic facies)	
Lamotrigine	~2%	Orofacial clefts (slight increase in some registries)	Lowest overall risk; safer option
Levetiracetam	~2–3%	No specific pattern; limited data	Relatively new; emerging evidence
Topiramate	~3–9%	Orofacial clefts	Avoid in first trimester
Oxcarbazepine	~3–4%	Cardiovascular, NTDs	

Valproate-specific developmental effects:

- IQ: Children exposed to valproate in utero have ~7–9 point lower IQ on average vs. unexposed

- Autism risk: ~6x higher
- ADHD: Increased risk
- Language and verbal abilities: Specifically impaired
- These effects are independent of major structural malformations

Folic acid supplementation:

- ALL women with epilepsy on AEDs planning pregnancy: High-dose folic acid 5 mg/day (not 0.4 mg)
- Start at least 3 months before conception
- Continue through first trimester at minimum
- Reduces (but does not eliminate) NTD risk

14.2 Contraception and AEDs

EXAM PEARL

Enzyme-inducing AEDs reduce efficacy of combined oral contraceptives. This is clinically important, unintended pregnancy on an AED is a serious issue.

AED · EFFECT ON CONTRACEPTION

Carbamazepine, phenytoin, phenobarbital, primidone, oxcarbazepine, topiramate Reduce OCP efficacy (enzyme induction); need alternative or higher-dose OCP

Lamotrigine OCP reduces lamotrigine levels by ~50%, reduced seizure control; double-check doses

Valproate, levetiracetam, lacosamide, gabapentin, vigabatrin No significant interaction

Recommended for women on enzyme-inducing AEDs Intrauterine device (IUD), not affected by enzyme induction

14.3 Pregnancy and Epilepsy

Pre-conception counselling:

1. Confirm diagnosis, is epilepsy definite?
2. Review AED choice, switch from valproate if possible
3. High-dose folate started pre-conception
4. Consider AED monotherapy at lowest effective dose
5. Discuss risks openly, untreated seizures also harm foetus

Changes during pregnancy:

- AED levels often fall due to: Increased volume of distribution, renal clearance, decreased protein binding
- Lamotrigine: Levels fall significantly in pregnancy; increase dose with monitoring
- Levetiracetam: Levels also fall; monitor
- Seizure frequency may increase due to: Sleep deprivation, AED level changes, hormonal changes, medication non-compliance

Delivery:

- Vaginal delivery: Preferred; risk of seizures during labour is low
- IV benzodiazepines: Available for rescue
- Vitamin K: Neonates should receive at delivery (AED enzyme induction reduces neonatal vitamin K)

Breastfeeding:

- Generally encouraged
- Most AEDs: Low concentrations in breast milk
- Exceptions: Phenobarbital, lamotrigine (significant amounts), monitor baby for sedation
- Valproate, carbamazepine, levetiracetam: Relatively low breast milk levels; generally safe

14.4 Catamenial Epilepsy

Definition: Epilepsy with seizures clustering around menstrual cycle, defined as $\geq 2\times$ increase in seizure frequency in specific cycle phase vs. baseline.

Three patterns (Herzog):

1. **Perimenstrual (C1):** Seizure cluster around menstruation (days -3 to +3)
2. **Periovulatory (C2):** Seizure cluster around ovulation (days 10–13)
3. **Anovulatory (C3):** Entire second half of cycle (days 10–28)

Mechanism: Estrogen (proconvulsant) increases; progesterone (anticonvulsant via GABA-A action) falls abruptly at menstruation

Treatment:

- Acetazolamide (carbonic anhydrase inhibitor): Perimenstrual use
 - Clonazepam intermittently
 - Progesterone supplementation (luteal phase support)
 - OCP (continuous): Eliminates cycle variation
 - Optimise baseline AED
-

SECTION 15: DRIVING AND EPILEPSY: INDIAN REGULATIONS

EXAM PEARL

Indian driving regulations for epilepsy are distinct from UK/international guidelines. Know the seizure-free period requirements.

15.1 Indian Motor Vehicles Act: Epilepsy

Current Indian Regulations (Motor Vehicles Act 1988, Central Motor Vehicles Rules 1989):

- **Epilepsy is a disqualifying condition** for obtaining a driving licence under standard eligibility
- A person with epilepsy may be considered for driving licence if: Seizure-free for **≥ 2 years** (on or off medication)
- This is different from the UK (1 year seizure-free) and many Western countries

Practical Clinical Advice:

1. Always document seizure-free dates in records
2. Counsel all patients about driving restrictions at diagnosis and at every follow-up
3. Document that counselling was given (medicolegal protection)
4. Report to licensing authority if a patient continues to drive against advice (duty to protect third parties)
5. Consider: Employment implications, alternative transport planning

15.2 Fitness to Drive: Clinical Assessment

Factors Affecting Driving Clearance:

- Type of seizure (absence vs. GTC vs. nocturnal-only)
- Seizure-free duration
- AED compliance and stability
- Occupational vs. private driving (higher standard for commercial/HGV)
- Prodromal warning (if adequate warning, some jurisdictions allow driving)

Nocturnal Seizures Only:

In many guidelines (UK, India provisions): If seizures are exclusively nocturnal for **≥ 3 years**, driving may be permitted. Discuss with licensing authority.

SECTION 16: SPECIAL TOPICS

16.1 Psychiatric Disorders in Epilepsy: Summary Framework

Using the Temporal Framework (critical for MCQs):

16.2 Cognitive Impairment in Epilepsy

Sources of Cognitive Impairment:

SOURCE · EXAMPLES

Underlying aetiology Hippocampal sclerosis, TSC, structural lesions

Seizure effects Each GTC causes some neuron loss; frequent seizures → cumulative loss

AED effects Topiramate (worst), phenobarbital, phenytoin, benzodiazepines

Psychosocial Poor education due to frequent absences, hospitalisation

Depression Cognitive symptoms of depression overlap with epilepsy effects

Seizure type Absence seizures, "microseconds" of cognitive absence during events

16.3 Limbic Encephalitis: Epilepsy-Psychiatry Crossover

EXAM PEARL

Limbic encephalitis (LE) is the key differential diagnosis when new-onset TLE presents with psychiatric symptoms, especially in younger patients without prior epilepsy history.

Types of Limbic Encephalitis:

TYPE	ANTIBODY	PSYCHIATRIC FEATURES	SEIZURE TYPE
Anti-NMDAR encephalitis	Anti-GluN1 (NR1)	Psychosis, behavioural disturbance, catatonia	Focal and generalised; can progress to SE
Anti-LGI1 encephalitis	Anti-LGI1	Memory impairment, psychiatric symptoms, hyponatraemia	Faciobrachial dystonic seizures (FBDS), pathognomonic
Anti-CASPR2	Anti-CASPR2	Amnesia, behavioural changes, neuropathic pain	Less prominent seizures
Anti-GABA-B	Anti-GABA-B	Less psychiatric; more classical LE	Temporal lobe seizures, frequent
Paraneoplastic (anti-Hu, Yo, Ma2)	Various	Memory impairment, personality change	Multifocal

Anti-NMDAR Encephalitis, Know this:

1. Most common autoimmune encephalitis
2. Young women; associated with ovarian teratoma (40%)
3. Sequence: Psychiatric phase → seizures → movement disorders → autonomic instability → coma
4. MRI: Often normal initially; may show FLAIR changes
5. CSF: Pleocytosis; CSF antibody more sensitive than serum
6. Treatment: Immunotherapy (steroids, IVIG, plasmapheresis) + tumour removal; antipsychotics for safety
7. Antipsychotics may worsen movement disorder phase, use cautiously

SECTION 17: QUICK REFERENCE TABLES

Table 1: Key Syndromes Summary

SYNDROME	AGE	KEY EEG	PSYCHIATRIC RELEVANCE	AED OF CHOICE
CAE	4–12	3 Hz SWD	ADHD-like, misdiagnosis	Ethosuximide, VPA
JME	12–18	4–6 Hz poly-spike-wave	ADHD, impulsivity	VPA, LEV, LTG
West	3–12 mo	Hypsarrhythmia	ASD, ID	ACTH, Vigabatrin
LGS	1–7 y	Slow SWD <2.5 Hz	ID, aggression, ASD	VPA, LTG, Clobazam
TLE	Any	Temporal spikes, rhythmic	Full psychiatric spectrum	CBZ, VPA, LEV, LTG

Table 2: AED Psychiatric Effects: Quick Reference

AED · REMEMBER FOR

Valproate Mood stabiliser; teratogen

Carbamazepine Mood stabiliser; enzyme inducer

Lamotrigine Bipolar depression; rash; OCP interaction

Levetiracetam Irritability / psychosis (psychiatric effects)

Topiramate Cognitive impairment ("Dopamax")

Phenobarbital Depression; cognitive effects

Vigabatrin Forced normalisation; visual field defects

Table 3: Psychosis Timing in Epilepsy

TYPE	TIMING	KEY FEATURE	DURATION
Ictal	During seizure	EEG-confirmed discharge	Seconds-minutes
Forced normalisation	After seizure control	Paradoxical EEG normalisation	Days-weeks
Postictal	24–48h post-seizure	Lucid interval	Days-weeks
Interictal (SLPE)	Independent of seizures	Preserved affect/warmth	Months-years

REFERENCES: KAPLAN & SADOCK'S COMPREHENSIVE TEXTBOOK OF PSYCHIATRY, 10TH ED.	TRIMBLE MR, SCHMITZ B, NEUROPSYCHIAT RY OF EPILEPSY, 2ND ED.	ENGEL J, PEDLEY TA, EPILEPSY: A COMPREHENSIVE TEXTBOOK	OXFORD TEXTBOOK OF EPILEPSY AND EPILEPTIC SEIZURES	STAHL'S ESSENTIAL PSYCHOPHARMA COLOGY, 5TH ED.

Model Answers

Sources: Kaplan & Sadock 10th ed., Trimble's Neuropsychiatry of Epilepsy, Oxford Textbook of Epilepsy, Stahl's 5th ed.

EXAM STRATEGY

Each answer below is structured for a 10-mark long answer. Target 2 A4 pages in the exam. Use the heading structure, examiners follow a marking key. Write definitions first, tables/lists over prose, end with clinical implications or management.

Answer 1: Classify seizures according to ILAE 2017. Describe the psychiatric relevance of temporal lobe epilepsy.

Introduction

The International League Against Epilepsy (ILAE) 2017 classification revised the terminology of seizure types, abandoning older terms such as "simple partial" and "complex partial." It operates at three hierarchical levels: seizure type, epilepsy type, and epilepsy syndrome. (1 mark)

ILAE 2017 Seizure Classification (3 marks)

Level 1, Seizure Onset:

ONSET TYPE	SUBTYPES	FORMER TERM
Focal	Aware; Impaired Awareness; Focal to bilateral tonic-clonic	Simple partial; Complex partial; Secondary generalised
Generalised	Motor (tonic-clonic, tonic, clonic, myoclonic, atonic, spasms); Non-motor (absence: typical, atypical, myoclonic, eyelid)	Grand mal; Petit mal
Unknown	Motor (tonic-clonic, spasms); Non-motor (behaviour arrest)	

Level 2, Epilepsy Type: Focal, Generalised, Combined focal + generalised, Unknown.

Level 3, Epilepsy Syndrome: e.g., TLE, JME, Childhood absence epilepsy, West syndrome, Lennox-Gastaut.

Temporal Lobe Epilepsy (TLE): Overview (1 mark)

TLE is the most common focal epilepsy (60% of focal epilepsies). Mesial TLE (MTLE) arising from the hippocampus, amygdala, and parahippocampal gyrus is the most psychiatrically significant variant. Aura typically includes epigastric rising, fear, déjà vu / jamais vu, olfactory / gustatory hallucinations. Automatisms (oral, manual) and postictal confusion are characteristic.

Psychiatric Relevance of TLE (4 marks)

1. Depression (30–50% prevalence):

Most common psychiatric comorbidity in TLE. The relationship is bidirectional, TLE doubles depression risk, and depression is independently associated with increased seizure frequency. Mechanism involves serotonergic and limbic disruption. NDDI-E (Neurological Disorders Depression Inventory for Epilepsy) is the validated screening tool (cutoff ≥ 15).

2. Psychosis, Interictal (Schizophrenia-Like Psychosis of Epilepsy, SLPE):

Prevalence 5–10%. Described by Slater and Beard (1963). Key features: positive symptoms (hallucinations, delusions) WITHOUT prominent negative symptoms; preserved affect ("warmth"); no family history of schizophrenia. Develops 10–15 years after epilepsy onset on average.

3. Postictal Psychosis:

Occurs 24–48 hours after a seizure cluster (the "lucid interval" is pathognomonic). Duration: days to weeks. Features often include elevated mood, religious ideation, both visual and auditory hallucinations. Managed with low-dose antipsychotics; self-limiting in most cases.

4. Geschwind Syndrome (Interictal Personality Changes):

Cluster of personality traits: hypergraphia, hyperreligiosity, hyposexuality, viscosity (circumstantiality, "stickiness"), deepened affect. Existence as a distinct syndrome is debated but remains testable content.

5. Ictal Phenomena:

Ictal fear (most common ictal emotion, amygdala origin), ictal psychosis (rare, EEG-confirmed), forced normalisation (psychosis paradoxically emerging when seizures are controlled, Landolt, 1953).

6. Anxiety: 25–40% prevalence; includes ictal fear, anticipatory anxiety, and interictal generalised anxiety. Panic attacks must be distinguished from ictal fear (brevity, stereotypy, EEG correlation).

Clinical Implications (1 mark)

Any new-onset psychosis or atypical psychiatric presentation, especially if episodic, brief, stereotyped, associated with memory symptoms or olfactory aura, warrants EEG and

neurological evaluation. Non-convulsive status epilepticus presenting as acute psychosis is a psychiatric emergency.

Answer 2: Discuss postictal psychosis: features, pathophysiology, and management.

Definition (1 mark)

Postictal psychosis (PIP) is a transient psychotic episode emerging after a cluster of seizures, characterised by a lucid interval of 24–48 hours between the seizure(s) and the onset of psychosis. It occurs in 7–10% of patients with TLE and represents one of the most clinically significant peri-ictal psychiatric syndromes.

Epidemiology (0.5 marks)

- Prevalence: 7–10% of TLE patients
- Risk factors: Bilateral seizure foci, long duration of epilepsy (>10 years), history of febrile convulsions, prior PIP episodes (strongest predictor), male sex, dominant temporal focus

Clinical Features (3 marks)

Trigger Cluster of generalised tonic-clonic or complex partial seizures

Lucid interval 24–48 hours (range 12 hours–7 days), pathognomonic

Onset Abrupt psychosis after apparent recovery from seizures

Mood Often elevated, grandiose, euphoric, not always paranoid; religious colouration common

Hallucinations Both auditory AND visual, unlike typical schizophrenia where auditory predominates

Delusions Often grandiose, religious, persecutory

Insight Absent to partial

EEG during psychosis Often normal, mirrors Landolt's forced normalisation

Duration Usually < 2 weeks; may extend to 3 months

Self-limiting Yes, in most cases

Risk of harm Present, active management required

Pathophysiology (2 marks)

The mechanism of PIP is incompletely understood. Proposed mechanisms include:

1. **Forced normalisation:** Seizure activity may temporarily modulate limbic dopaminergic tone. When seizures cease, this modulating effect is removed, allowing dopaminergic dysregulation to emerge as psychosis. EEG normalisation during PIP supports this model.
1. **Transient dopaminergic hyperactivity:** Post-seizure rebound dopamine release in mesolimbic pathways.
1. **GABA/glutamate shift:** Postictal GABAergic inhibition followed by glutamatergic rebound → neuronal hyperexcitability in limbic circuits without convulsive threshold.
1. **Structural substrate:** Bilateral hippocampal and amygdala pathology in patients with bilateral foci increases risk; suggests an anatomical vulnerability.
1. **Immune/inflammatory:** Postictal neuroinflammation has been proposed; blood-brain barrier disruption following clusters of seizures may allow inflammatory mediators to trigger psychosis.

Management (3 marks)

Immediate:

- Safety assessment, risk to self and others
- Observation in a calm, low-stimulation environment
- Ensure family / carers aware (lucid interval phenomenon must be explained)

Pharmacological:

- **Low-dose antipsychotic:** Haloperidol 2–5 mg / day OR olanzapine 5–10 mg / day
- **Benzodiazepine:** For agitation (lorazepam 1–2 mg)
- **Avoid:** Clozapine (highest proconvulsant risk), high-dose typical antipsychotics
- **Duration:** Short-term (1–4 weeks typically sufficient)

AED Optimisation:

- Long-term reduction of seizure frequency reduces recurrence risk
- Review AED regimen; add or increase if poorly controlled

Psychoeducation:

- Explain the lucid interval, families and carers often misinterpret apparent recovery as full resolution
- Written crisis plan for future episodes

Follow-up:

- Monitor for progression to chronic interictal psychosis (~15% risk with recurrent PIP)
- Long-term antipsychotic generally NOT required after a single episode; consider prophylaxis after 2+ episodes

Prognosis (0.5 marks)

Most episodes are self-limiting within 2 weeks. With repeated episodes (3+), risk of persistent interictal psychosis rises to ~15%. Early recognition, adequate treatment, and seizure control are the primary modifiable factors.

Answer 3: Describe the schizophrenia-like psychosis of epilepsy. How does it differ from schizophrenia?

Introduction (1 mark)

Slater and Beard (1963) first systematically described a schizophrenia-like psychosis occurring in patients with epilepsy that differed from idiopathic schizophrenia in several important ways. Now termed "Interictal Psychosis" or "Schizophrenia-Like Psychosis of Epilepsy (SLPE)," it represents the most common form of chronic psychosis in epilepsy, occurring in 5–10% of temporal lobe epilepsy patients.

Epidemiology (0.5 marks)

- Prevalence in TLE: 5–10%
- Overall risk in epilepsy: 6–12x higher than general population
- Onset: Typically 10–15 years after epilepsy onset (mean age ~30–35 years)
- More common in MTLE, bilateral foci, alien tissue lesions (ganglioglioma, DNET, hamartoma)

Clinical Features of SLPE (3 marks)

Positive Symptoms (prominent):

- Auditory hallucinations, voices (similar to schizophrenia)
- Delusions, often persecutory, religious, grandiose
- Passivity phenomena (first rank symptoms may be present)

Negative Symptoms (characteristically ABSENT or mild):

- Flat affect: Rare in SLPE, affect is PRESERVED and often WARM
- Alogia: Not prominent
- Avolition/anhedonia: Mild at most
- Social withdrawal: Less severe than schizophrenia

Other Features:

- Mood congruent features may be present (elevation, dysphoria)
- Paranoid > disorganised presentations
- Preserved social functioning (relatively)
- No family history of schizophrenia
- Premorbid functioning often normal

Comparison: SLPE vs. Schizophrenia (4 marks)

FEATURE	SLPE	SCHIZOPHRENIA
Positive symptoms	Prominent	Prominent
Negative symptoms	Mild or absent, KEY	Often prominent, progressive
Affect	Preserved, warm, KEY	Often blunted / flat
Social deterioration	Mild	More severe
Formal thought disorder	Less severe	Common, prominent
Family history of psychosis	Not elevated	Elevated
Premorbid function	Often normal	Often impaired
Onset timing	After 10–15 yr of epilepsy	Early adulthood, no seizure trigger
Duration	Chronic if untreated	Chronic
First rank symptoms	May be present	Characteristic
Religious content	Often prominent	Less specific
Response to antipsychotics	Yes	Yes
Catatonia	Rare	Possible
Neuropathology	TLE substrate (hippocampal sclerosis)	Diffuse changes (reduced grey matter)
Neurodevelopmental basis	Epilepsy + kindling	Strong neurodevelopmental model

Pathophysiology (1 mark)

Four mechanisms are proposed:

1. **Kindling:** Repeated subthreshold limbic stimulation produces permanent neuronal sensitisation leading to psychotic vulnerability
2. **Structural:** Hippocampal, parahippocampal, and amygdala atrophy disrupts limbic-dopamine regulation
3. **Dopaminergic dysregulation:** Secondary to limbic epileptiform activity

4. **Shared neurodevelopmental substrate:** Common vulnerability for both epilepsy and psychosis (e.g., perinatal injury, genetic factors)

Management (0.5 marks)

- Atypical antipsychotics: Aripiprazole (lowest proconvulsant risk), risperidone, olanzapine
 - Continue AEDs, never reduce AED with the expectation that this will help psychosis
 - Do NOT use clozapine unless treatment-resistant (highest seizure risk)
 - Monitor EEG if clozapine is required
-

Answer 4: Discuss the role of AEDs in psychiatric disorders. Describe the psychiatric side effects of antiepileptic drugs.

Introduction (1 mark)

Antiepileptic drugs (AEDs) occupy a unique position in neuropsychopharmacology, several are used as primary treatments in psychiatric disorders (valproate, carbamazepine, lamotrigine) while others carry significant risks of inducing or worsening psychiatric symptoms. Understanding both dimensions is essential for safe practice at the neurology-psychiatry interface.

AEDs as Psychiatric Treatments (3 marks)

Valproate:

- Bipolar disorder I, acute mania: First-line (equivalent to lithium)
- Bipolar maintenance: Effective, especially for rapid cycling
- Schizoaffective disorder: Augmentation
- Impulse control disorders, aggression in intellectual disability
- Mechanism: GABAergic enhancement + sodium channel blockade + multiple downstream effects

Carbamazepine:

- Bipolar disorder: Second-line; particularly dysphoric mania, rapid cycling
- Acute mania: Less evidence than valproate/lithium but used
- Trigeminal neuralgia, PTSD augmentation
- Mechanism: Sodium channel blockade; structural resemblance to TCAs

Lamotrigine:

- Bipolar depression: Best evidence among all drugs for bipolar depression maintenance
- NOT first-line for acute mania; may precipitate mixed states
- Mechanism: Sodium + calcium channel blockade; reduces glutamatergic transmission

Clonazepam:

- Panic disorder, social anxiety (short-term)
- Acute mania (adjunct)
- Catatonia (IV lorazepam / diazepam)

Pregabalin/Gabapentin:

- Generalised anxiety disorder (pregabalin is licensed for GAD in Europe)
- Neuropathic pain comorbid with psychiatric disorders

Psychiatric Side Effects of AEDs (5 marks)

AED	PRIMARY PSYCHIATRIC SIDE EFFECTS	SEVERITY
Levetiracetam	Irritability, aggression, depression, psychosis (~10% affected)	High, most common psychiatric SE of newer AEDs
Topiramate	Cognitive impairment (word-finding, processing speed, "Dopamax"), depression, suicidality	High, cognitive effects very significant
Phenobarbital	Depression, cognitive impairment, hyperactivity (children), dependence	High, worst for depression
Vigabatrin	Depression, psychosis, forced normalisation	High
Zonisamide	Depression, cognitive effects, irritability	Moderate
Perampanel	Aggression, hostility, irritability (dose-dependent)	Moderate
Valproate	Mild sedation, cognitive dulling at high doses	Low-moderate
Carbamazepine	Mild sedation; hyponatraemia can cause confusion	Low-moderate
Lamotrigine	Insomnia, activation; rarely psychosis (with forced normalisation)	Low
Phenytoin	Cognitive impairment at toxic levels	Low at therapeutic levels
Lacosamide	Minimal psychiatric effects	Low

FDA 2008 Black Box Warning:

All AEDs carry a class warning for increased suicidality. Risk approximately doubles (from ~0.24% to 0.43% over study periods). The absolute risk is small but clinically relevant, monitor all patients starting AEDs for mood and suicidal ideation.

Levetiracetam, Psychiatric Effects (detailed):

Dose-dependent irritability and behavioural disinhibition in ~10% of patients. Thought to relate to SV2A binding modulating inhibitory neurotransmitter release. Adjunctive pyridoxine (Vitamin B6) has limited evidence for reducing irritability. Dose reduction or drug switch is the primary intervention.

Topiramate, Cognitive Effects (detailed):

Word-finding difficulty (anomia) is most characteristic. Processing speed and working memory also affected. Severity is dose-dependent, much less problematic at ≤ 100 mg/day. Labelled "Dopamax" by patients and clinicians colloquially. Cognitive testing before and after dose escalation is good practice.

Clinical Implications (1 mark)

When a patient with epilepsy presents with new psychiatric symptoms, always review:

1. Recent AED changes (new AED, dose increase)
2. AED interactions (enzyme induction reducing psychotropic levels)
3. Seizure control (improvement may trigger forced normalisation)
4. Temporal relationship (within weeks of AED change = likely AED-related)

Answer 5: Describe psychogenic non-epileptic seizures (PNES). How are they differentiated from epileptic seizures? Discuss management.

Definition and Terminology (1 mark)

Psychogenic Non-Epileptic Seizures (PNES), also termed functional seizures, are paroxysmal events resembling epileptic seizures in clinical appearance but occurring without the ictal neurophysiological changes (epileptiform EEG activity) characteristic of epilepsy. They represent a form of Functional Neurological Disorder (FND). The term "pseudoseizures" is outdated and stigmatising, it implies voluntary fabrication, which is incorrect.

Epidemiology (0.5 marks)

- Prevalence: 2–33/100,000 in community settings
- 20–30% of patients in epilepsy monitoring units have PNES
- 10–30% of PNES patients also have comorbid epilepsy
- Female:male ratio: 3:1 to 7:1
- Average delay to diagnosis: 7 years

- Average number of AEDs tried before diagnosis: 2–3

Differentiation: PNES vs. Epileptic Seizures (4 marks)

Gold standard: Video-EEG telemetry with a recorded typical event.

FEATURE	PNES	EPILEPTIC SEIZURE
Onset	Gradual, build-up	Abrupt, stereotyped
Duration	Prolonged (often >3–5 min)	Usually <3 min
Eye position during event	Closed (resistant to opening)	Open, may be deviated
Motor features	Asynchronous, thrashing, pelvic thrusting, opisthotonus	Rhythmic (GTC), stereotyped automatisms (TLE)
Side-to-side head movement	Common	Rare
Ictal crying/weeping	Common	Very rare
Responsiveness	May be partially present	Absent in GTC/CPS
Tongue bite	Rare; tip of tongue	Lateral tongue bite
Incontinence	Uncommon	Common (GTC)
Postictal confusion	Minimal/absent	Prolonged (>30 min in GTC)
Recall	Partial often present	Absent for GTC
Triggers	Psychosocial stressors	Sleep deprivation, alcohol, illness, hormonal
Audience effect	Events more common with observers	Not applicable
Serum prolactin (20 min post)	Not elevated	Elevated post-GTC/CPS
EEG during event	Normal	Ictal discharge or generalised change
Postictal EEG	Normal	Slowing
CK after event	Variable, usually normal	Elevated post-GTC

Semiology features strongly suggesting PNES:

- Asynchronous limb movements (arms and legs out of phase)
- Pelvic thrusting, especially forward thrusting
- Opisthotonus (arc de cercle)
- Eye closure with resistance
- Crying during or immediately after
- Gradual onset with emotional build-up

- Duration >5 minutes with preserved partial awareness

Psychiatric Comorbidity (1.5 marks)

COMORBIDITY · PREVALENCE IN PNES

Depression 50–80%

Anxiety disorders 50–70%

PTSD 30–60%

Dissociative disorders 30–50%

Borderline personality disorder 30–50%

Somatic symptom disorder High overlap

Childhood trauma/abuse 50–80%

Management (3 marks)

Step 1, Definitive Diagnosis:

Video-EEG monitoring with captured event. Do not diagnose PNES on clinical grounds alone, the consequences of misdiagnosis are severe (either undertreated epilepsy or continued AED treatment in non-epileptic patients).

Step 2, Disclosure:

Delivery of the diagnosis is the first therapeutic act. Framework:

- Lead with what it IS: "Your brain is experiencing a type of functional nervous system difficulty..."
- Do NOT say: "It's not real," "you're fine," "it's psychological" (pejorative framing)
- Frame as: Real, disabling, treatable, not deliberate
- Acknowledge diagnostic journey and prior misdiagnosis
- Involve a neurologist and psychiatrist jointly

Step 3, Psychotherapy (Primary Treatment):

- **CBT:** Strongest evidence; seizure-specific CBT (cognitive restructuring + behavioural experiments targeting triggers)
- **Trauma-focused therapy:** If PTSD is present, trauma-focused CBT, EMDR
- **EMDR:** Growing evidence for PNES with trauma history
- **Psychodynamic therapy:** For patients with poor insight into emotional triggers
- **Group therapy:** Reduces isolation, shame

Step 4, AED Withdrawal (if no comorbid epilepsy):

- Gradual, collaborative with neurology
- Expect short-term worsening (extinction burst), prepare patient
- Long-term: AED withdrawal generally beneficial; reduces AED side effects

Step 5, Treat Comorbidities:

- Antidepressants for depression (SSRIs first-line)
- Trauma-focused work for PTSD
- DBT skills for BPD features

Prognosis (0.5 marks)

- Seizure freedom: 30–40% with treatment
 - Substantial improvement: 50%
 - Poorer prognosis: Long diagnostic delay, secondary gain, comorbid personality disorder, continued AED use (maintains sick role), lack of insight
-

Answer 6: Write a note on forced normalisation. Describe Landolt's phenomenon with clinical implications.

Historical Background (1 mark)

Heinrich Landolt (1953), a Swiss neurologist, described a paradoxical EEG phenomenon in epilepsy patients: when seizures were controlled, either spontaneously or pharmacologically, the EEG, previously showing epileptiform activity, would normalise (become apparently normal). Simultaneously, patients would develop acute psychiatric symptoms, most commonly psychosis. He termed this "forced normalisation" (erzwungene Normalisierung in German), referring to the EEG finding.

Tellenbach (1965) described the clinical counterpart, "alternative psychosis", emphasising the competitive, alternating relationship between epileptic seizures and psychosis.

Definition (1 mark)

Forced normalisation (Landolt): The paradoxical normalisation of EEG coinciding with the emergence of acute psychiatric symptoms (most commonly psychosis) when epileptic activity is suppressed.

Alternative psychosis (Tellenbach): The clinical alternating relationship between seizures and psychosis, when one is present, the other is absent.

These terms are related but distinct: Forced normalisation is an EEG description; alternative psychosis is a clinical description of the same phenomenon.

Clinical Features (3 marks)

Timing After seizure control is achieved (spontaneous or drug-induced)

EEG Paradoxically normalises or improves while psychiatric symptoms emerge

Psychiatric presentation Acute psychosis most common; may be mania, anxiety, agitation

Hallucinations Auditory and visual; often vivid

Delusions Paranoid, grandiose, religious

Mood Often elevated or mixed

Duration Days to weeks; resolves when seizures recur (or with treatment)

Reversibility Reverses when AED is reduced and seizures return, OR with antipsychotic treatment

AEDs Most Commonly Associated (1 mark)

AED · RISK LEVEL

Vigabatrin Highest

Ethosuximide High

Lamotrigine Moderate

Levetiracetam Moderate (behavioural side effects, though mechanism may differ)

Phenytoin, carbamazepine, valproate Lower risk

Pathophysiology (2 marks)

The mechanism is not fully established. Proposed models:

1. **Competing inhibition:** Seizure activity itself may paradoxically inhibit psychotic mechanisms (perhaps via postictal dopamine modulation). When seizures are suppressed, this inhibitory effect is removed, unmasking psychotic vulnerability.
1. **Dopamine hypothesis:** Seizures modulate mesolimbic dopamine tone. The anticonvulsant effect removes seizure-related dopaminergic modulation, allowing dopaminergic hyperactivity to emerge.
1. **GABA enhancement:** Vigabatrin increases GABA by inhibiting GABA transaminase. Excess GABAergic inhibition in limbic circuits may disrupt psychotic threshold regulation.

1. **Limbic network rebalancing:** Anticonvulsants shift the balance of excitation/inhibition across limbic networks; in vulnerable individuals, this rebalancing produces psychosis rather than normalcy.

Clinical Management (2 marks)

Step 1, Recognition: Clinician must know this phenomenon. Any acute psychosis emerging after seizure control (especially new AED or dose increase) should trigger assessment for forced normalisation.

Step 2, AED Reduction:

- Discuss with the treating neurologist
- Consider reducing the offending AED (especially vigabatrin, ethosuximide)
- The paradox: Allowing seizure recurrence may resolve psychosis
- Weigh seizure risk against psychiatric risk

Step 3, Antipsychotic:

- Low-dose antipsychotic for psychosis
- Avoid clozapine (increases seizure threshold paradoxically may help, but risk too high)
- Aripiprazole preferred (least proconvulsant)

Step 4, Monitor EEG:

- Serial EEG during psychotic episode
- Return of epileptiform activity often heralds resolution of psychosis

Key Clinical Principle: Do NOT automatically increase AED dose when psychosis emerges post-seizure control, this may worsen the psychiatric syndrome.

Answer 7: Discuss depression in epilepsy: prevalence, bidirectional relationship, screening, and treatment.

Introduction (0.5 marks)

Depression is the most common psychiatric comorbidity in epilepsy, affecting 20–55% of patients. It significantly impairs quality of life, often more than seizure frequency itself. The relationship between epilepsy and depression is uniquely bidirectional, reflecting shared neurobiological mechanisms.

Prevalence (0.5 marks)

- Overall in epilepsy: 20–55% (most consistent: ~30%)
- TLE specifically: 30–50%
- Drug-resistant epilepsy: Up to 55%

- Active seizures (vs. well-controlled): Higher prevalence
- Compared to general population (~10–15%): 2–4x higher

Bidirectional Relationship (3 marks)

KEY INSIGHT

This is a conceptually important exam topic, the relationship goes BOTH ways.

Epilepsy → Depression:

1. Neurobiological: Limbic hyperactivity disrupts serotonergic circuits; HPA axis dysregulation; interictal hypometabolism in frontal and limbic regions
2. AED effects: Phenobarbital, topiramate, levetiracetam, zonisamide directly increase depression risk
3. Psychosocial: Driving restrictions, employment limitations, stigma, dependency, loss of autonomy
4. Peri-ictal: Postictal depression (common after GTC) and interictal dysphoric disorder

Depression → Epilepsy:

1. Meta-analyses show: Individuals with depression have RR of 1.5–2.0 for subsequently developing epilepsy
2. Shared mechanisms: Serotonergic pathways, HPA axis dysregulation, hippocampal atrophy (depression causes hippocampal volume loss, same region vulnerable in MTLE)
3. Neuroinflammation: Depression and epilepsy both associated with elevated inflammatory markers

Shared Neurobiology:

- Both involve: Serotonin, GABA, glutamate dysregulation
- Both associated with: Hippocampal atrophy, amygdala hyperactivity
- Both benefit from: Anticonvulsant mood stabilisers (lamotrigine, valproate)

Screening Tools (1.5 marks)

NDDI-E (Neurological Disorders Depression Inventory for Epilepsy):

- Validated specifically for epilepsy, avoids somatic items that overlap with AED side effects
- 6 items, each scored 1–4
- Cutoff ≥ 15 : Probable MDD (sensitivity 81%, specificity 90%)
- Items: "Everything is a struggle," "Nothing I do is right," "Feel guilty," "I'd be better off dead," "Frustrated," "Difficulty finding pleasure"
- Preferred over PHQ-9 in epilepsy settings

GAD-7: Recommended for anxiety screening in epilepsy for the same reason.

Why not PHQ-9? Somatic items (sleep, fatigue, concentration, appetite) are confounded by AED side effects and postictal effects, inflates false positive rate.

Suicide Risk (1 mark)

- Suicide attempt rate: 5x higher than general population
- Completed suicide: 3–5x higher
- FDA 2008: All AEDs carry class black box warning for suicidality
- Risk factors: TLE, active depression, young male, drug-resistant epilepsy, recent diagnosis, social isolation

Treatment (3 marks)

Antidepressants:

DRUG	RECOMMENDATION	NOTES
SSRIs (sertraline, escitalopram, citalopram)	First-line	Low seizure risk; escitalopram and sertraline safest for interactions
SNRIs (venlafaxine, duloxetine)	Second-line	Acceptable; low-moderate proconvulsant risk
Mirtazapine	Useful adjunct	Sedating; low seizure risk; helpful for insomnia
TCA's	Avoid	High proconvulsant risk
Bupropion	Contraindicated	Highest proconvulsant risk of all antidepressants
Clomipramine	Avoid	High risk

Psychotherapy:

- CBT: Strong evidence; helps both depression and epilepsy adjustment
- IPT: Useful for interpersonal dimension of chronic illness adjustment
- Mindfulness-based CBT (MBCT): Growing evidence; particularly for relapse prevention

AED Optimisation:

- If AED is contributing (phenobarbital, topiramate, levetiracetam): Consider switching
- If seizure control is poor: Improving control often improves mood

Collaborative Care:

- Joint neuropsychiatry clinics are ideal
- Regular NDDI-E monitoring at follow-up

Interictal Dysphoric Disorder (0.5 marks)

Blumer's syndrome, intermittent dysphoria with eight symptoms (depressive: low mood, anergia, pain, insomnia; irritable: episodic fear, euphoria, irritability, paroxysmal affect). Does not map to DSM; may respond to SSRI + lamotrigine combination.

Answer 8: Discuss Women with Epilepsy (WWE): teratogenicity of AEDs, contraception, and pregnancy management.

Introduction (0.5 marks)

Women with epilepsy (WWE) face unique challenges at the intersection of reproductive health and neurological disease. Uncontrolled seizures during pregnancy carry foetal risks, while AEDs carry teratogenic risks. The clinical goal is to minimise seizure exposure and foetal drug exposure simultaneously, requiring careful pre-conception planning and ongoing monitoring.

Teratogenicity of AEDs (3.5 marks)

Background risk of major congenital malformation (MCM) in general population: ~1–2%.

AED	MCM RATE	SPECIFIC RISKS	NEURODEVELOPMENTAL
Valproate	~10–11%	Neural tube defects (1–2%), cardiac, orofacial clefts, limb anomalies, hypospadias	IQ –7–9 points; autism risk 6×; ADHD increased
Phenobarbital	~5–7%	Cardiac, orofacial, digital defects	Cognitive effects (less data)
Phenytoin	~3–7%	Fetal hydantoin syndrome: NTDs, hypoplastic nails, dysmorphic facies	Cognitive effects
Carbamazepine	~2–3%	NTDs (0.5%), cardiovascular, orofacial	Less than valproate
Topiramate	~3–9%	Orofacial clefts (strongly associated)	Limited data
Lamotrigine	~2%	Orofacial clefts (slight increase in some registries)	Lowest overall neurodevelopmental risk
Levetiracetam	~2–3%	No specific pattern; reassuring data accumulating	Limited long-term data
Oxcarbazepine	~3–4%	Cardiovascular, NTDs	Less data

Key valproate facts for exam:

- Highest structural AND neurodevelopmental teratogenicity
- Neurodevelopmental effects: Independent of structural malformations; dose-dependent
- MHRA 2018/2024: Valproate **MUST NOT** be used in women of childbearing potential without effective contraception and annual PREVENT review
- If valproate is absolutely necessary: Use minimum effective dose; folic acid 5 mg/day; detailed fetal anomaly scans

Folic acid:

- All WWE on AEDs planning pregnancy: **5 mg/day** (high dose, not 0.4 mg)
- Start ≥ 3 months before conception
- Reduces (does not eliminate) NTD risk
- Rationale: AEDs (especially enzyme inducers and VPA) deplete folate

Contraception and AED Interactions (2 marks)

CATEGORY	AEDS	CONTRACEPTIVE EFFECT
Enzyme-inducing AEDs	Carbamazepine, phenytoin, phenobarbital, primidone, oxcarbazepine, topiramate (>200 mg/day), rufinamide	Reduce OCP efficacy , breakthrough pregnancy possible; need higher-dose OCP or IUD
Lamotrigine		OCP reduces lamotrigine levels by $\sim 50\%$ $\rightarrow$ seizure breakthrough when OCP started; lamotrigine dose increase needed
Non-interacting AEDs	Valproate, levetiracetam, lacosamide, gabapentin, vigabatrin	No significant interaction
Safest contraceptive for WWE on enzyme inducers	IUD (copper or levonorgestrel)	Not affected by enzyme induction
Depot medroxyprogesterone (Depo-Provera)		Acceptable with enzyme inducers

Clinical Implication: WWE on carbamazepine, phenytoin, or oxcarbazepine taking the OCP need to be counselled about reduced OCP efficacy. IUD is the most reliable option.

Pregnancy Management (3.5 marks)

Pre-conception:

1. Review diagnosis, is epilepsy definitely present?

2. Rationalise AED: Switch from valproate if at all possible; prefer monotherapy at lowest effective dose
3. High-dose folate 5 mg / day
4. Counsel re: risks of uncontrolled seizures (foetal hypoxia, placental abruption, maternal injury) AND AED teratogenicity
5. Optimise seizure control before conception, accept some AED risk for good control

During Pregnancy:

- AED levels fall (increased Vd, renal clearance), especially lamotrigine and levetiracetam
- Monitor drug levels monthly (especially LTG); increase dose to maintain pre-pregnancy levels
- Serial anomaly scans: Detailed 20-week scan; fetal echocardiography if valproate / carbamazepine
- Neurology review each trimester
- Seizure risk in 3rd trimester: Sleep deprivation, non-compliance, level changes

Delivery:

- Vaginal delivery preferred; seizure risk during labour is low (~1–3%)
- IV lorazepam or diazepam available in delivery room
- Neonatal vitamin K at birth (enzyme-inducing AEDs reduce neonatal vitamin K → haemorrhage risk)

Breastfeeding:

- Encouraged in most cases
- Safe: Valproate, carbamazepine, oxcarbazepine (low breast milk levels)
- Monitor infant: Phenobarbital (sedation), lamotrigine (moderate levels), levetiracetam (moderate levels)
- Valproate: Low breast milk levels, generally safe

Catamenial Epilepsy (1 mark)

Seizures clustering with the menstrual cycle in $\geq 2\times$ increase in specific phase vs. baseline. Three patterns: perimenstrual (C1), periovulatory (C2), anovulatory (C3). Mechanism: estrogen proconvulsant, progesterone anticonvulsant (GABA-A modulation), premenstrual progesterone withdrawal triggers seizures. Treatment: intermittent acetazolamide, progesterone supplementation, continuous OCP.

Answer 9: Discuss Non-Convulsive Status Epilepticus (NCSE). Why is it relevant to psychiatry?

Definition (1 mark)

Non-Convulsive Status Epilepticus (NCSE) refers to a state of prolonged (≥ 10 minutes) epileptic seizure activity without major motor manifestations, manifesting primarily as altered consciousness, cognitive dysfunction, or behavioural changes. Diagnosis requires EEG confirmation. NCSE encompasses absence status epilepticus, complex partial status epilepticus (focal status with impaired awareness), and subtle generalised convulsive SE.

Psychiatric Relevance (3 marks)

NCSE is the most important differential diagnosis in a patient presenting acutely with:

- Sudden-onset psychosis
- Acute confusional state (delirium-like)
- Fluctuating consciousness
- Mutism
- Bizarre behaviour with partial recall
- Apparent dissociative states

Clinical presentations that mimic psychiatric disorders:

NCSE TYPE · PSYCHIATRIC MIMIC

Absence status "Spacey," inattentive, mild confusion, misdiagnosed as dissociation or intoxication

Complex partial SE (focal impaired awareness SE) Acute psychosis, automatisms mistaken for catatonia or mania

Subtle GCSE Post-ictal or persistent delirium with psychiatric features

Frontal lobe SE Bizarre motor behaviour, agitation, misdiagnosed as acute mania or conversion

Red Flags for NCSE in Psychiatric Settings:

1. Known epilepsy history
2. Recent change in AED
3. Fluctuating rather than sustained symptoms
4. Subtle motor features: lip smacking, eye blinking, facial twitching
5. Amnesia for the episode
6. Impaired command-following despite apparent wakefulness

Diagnosis (2 marks)

EEG is mandatory for diagnosis. NCSE cannot be reliably diagnosed clinically.

EEG Patterns in NCSE:

PATTERN · INDICATION

Generalised continuous/repetitive spike-wave at ≥ 2.5 Hz Generalised NCSE (absence SE)

Focal continuous epileptiform discharges Focal NCSE

Periodic lateralised epileptiform discharges (PLEDs) May indicate evolving focal NCSE

Generalised periodic discharges (GPDs) Subtle GCSE, post-anoxic

Triphasic waves Hepatic encephalopathy (DDx but can overlap)

Salzburg Criteria (2015): Most widely used criteria for NCSE diagnosis on EEG, requires epileptiform activity >2.5 Hz OR epileptiform activity at any frequency with clinical/EEG improvement on IV benzodiazepine.

Diagnostic therapeutic trial:

IV lorazepam 0.1 mg/kg or IV diazepam 0.2 mg/kg, if clinical and EEG improvement occurs, this confirms NCSE.

Management (3 marks)

Immediate:

- Call neurology/intensive care
- Airway protection; oxygen
- IV access; glucose check

First-line (Benzodiazepines):

- IV lorazepam 0.1 mg/kg OR diazepam 0.2 mg/kg
- Buccal/intranasal midazolam if no IV access

Second-line (if persistent at 20–40 min):

- IV levetiracetam 60 mg/kg (preferred)
- IV valproate 40 mg/kg
- IV lacosamide (emerging)

NCSE-Specific Considerations vs. Convulsive SE:

- Less urgency than convulsive SE (no immediate airway compromise or rhabdomyolysis risk)
- But prolonged NCSE causes neuronal injury, treat within 30–60 minutes

- De-escalation of treatment can be more gradual

After resolution:

- Review and optimise AED regimen
- Identify precipitant: AED non-compliance, infection, sleep deprivation, metabolic disturbance
- Monitor for postictal psychiatric syndromes (psychosis, depression, anxiety)

Key Teaching Point (1 mark)

Every psychiatric inpatient unit should have access to EEG services. The rule of thumb: **any acute-onset psychiatric syndrome with altered consciousness, fluctuating course, subtle motor features, or known epilepsy history, get an EEG before attributing to a primary psychiatric cause.** Missing NCSE in a psychiatric setting constitutes a serious clinical error.

Answer 10: Discuss the management of epilepsy with comorbid bipolar disorder. What are the challenges?

Introduction (1 mark)

The co-occurrence of epilepsy and bipolar disorder presents a complex therapeutic challenge. Both conditions share neurobiological substrates (limbic-monoaminergic dysregulation, ion channel dysfunction), and several AEDs double as mood stabilisers. However, the interaction of AEDs with psychiatric medications, the risk of drug-induced mood changes, and the competing demands of seizure control versus mood stabilisation create genuine clinical complexity.

Prevalence of Comorbidity (0.5 marks)

- Bipolar disorder in epilepsy: ~5–10% (vs. ~2% in general population)
- Higher in TLE, limbic epilepsy
- Bidirectional risk: History of bipolar disorder increases epilepsy risk (shared neurodevelopmental vulnerability)

Shared AEDs: Dual-Use Agents (3 marks)

AED / MOOD STABILISER	EPILEPSY EVIDENCE	BIPOLAR EVIDENCE	NOTES
Valproate	Generalised epilepsy, focal (second-line), SE	BD-I mania (first-line), maintenance, rapid cycling	Best overlap; teratogenic
Carbamazepine	Focal epilepsy	BD (especially dysphoric mania, rapid cycling)	Strong enzyme inducer, affects many drugs

AED / MOOD STABILISER	EPILEPSY EVIDENCE	BIPOLAR EVIDENCE	NOTES
Lamotrigine	Focal + generalised (adjunct)	BD depression (best evidence)	NOT for acute mania; rash risk
Oxcarbazepine	Focal epilepsy	BD (limited evidence)	Fewer interactions than CBZ
Lithium	Not an AED	BD (first-line)	Lowers seizure threshold at toxic levels

Strategic approach: When a patient has both epilepsy and bipolar disorder, prioritise AEDs with dual efficacy:

- **BD-I + epilepsy:** Valproate is optimal (covers seizures + mania)
- **BD + epilepsy depression:** Lamotrigine + valproate combination (covers both depression and seizures; but doubles LTG levels, titrate slowly, halve dose)
- **Rapid cycling BD + epilepsy:** Valproate ± lamotrigine

Specific Challenges (4 marks)

Challenge 1, AED-Induced Mood Episodes:

- Levetiracetam: Can cause irritability, depression, mania-like agitation, problematic in BD
- Topiramate: Depression and cognitive effects worsen BD depressive phases
- Vigabatrin: Can precipitate psychosis and mania
- Carbamazepine: Generally mood-stabilising, but rarely can activate
- **Management:** Monitor mood carefully when initiating AEDs; prefer valproate or lamotrigine in BD patients

Challenge 2, Drug Interactions:

- Carbamazepine reduces quetiapine levels by 60–70% → apparent antipsychotic failure
- Carbamazepine reduces lamotrigine levels → loss of mood stabilisation
- Valproate doubles lamotrigine levels → risk of Stevens-Johnson syndrome if titrated too quickly
- Enzyme-inducing AEDs reduce all psychotropic levels significantly

Challenge 3, Lithium + Epilepsy:

- Lithium is NOT an AED; lowers seizure threshold at toxic levels
- Lithium toxicity (levels >1.5 mM) can cause seizures, tremor, encephalopathy
- For BD patients with epilepsy: Prefer valproate over lithium if seizure threshold is a concern

Challenge 4, Clozapine in Refractory Cases:

- If treatment-resistant BD psychosis requires clozapine: Significant seizure risk (3–5% at high doses)
- EEG monitoring recommended before and during clozapine use
- Consider prophylactic AED (valproate) when clozapine dose escalates
- Do NOT combine clozapine + carbamazepine (dual agranulocytosis risk, absolute contraindication)

Challenge 5, Suicidality:

- Both epilepsy and BD independently elevate suicide risk
- Combined: Risk is substantially higher
- All AEDs carry FDA black box warning for suicidality
- Monitor closely; NDDI-E plus mood diary

Clinical Approach: Summary (1.5 marks)

1. **Establish each diagnosis independently**, avoid assuming mood symptoms are entirely seizure-related
2. **Monotherapy preferred**, minimise drug burden; prioritise dual-use agents (valproate, lamotrigine, carbamazepine)
3. **Interaction check mandatory** before adding any new agent
4. **Mood monitoring** at each visit, NDDI-E, mood diary
5. **Integrated care:** Neuropsychiatrist or epilepsy psychiatry liaison is optimal; if unavailable, maintain clear communication between neurologist and psychiatrist
6. **Teratogenicity counselling** in women, valproate concerns apply equally to BD and epilepsy

Answers 11–15: Additional Model Answers

Answer 11: Describe the EEG findings in epilepsy. What is the role of EEG in psychiatric practice?

EEG Fundamentals (1 mark)

Electroencephalography (EEG) records electrical activity of the cerebral cortex via scalp electrodes, measuring voltage fluctuations from ionic current flows in neurons. The International 10–20 system standardises electrode placement. A standard EEG records ~20–30 minutes; prolonged (24–72 hour) and video-EEG extend diagnostic yield.

Normal EEG Rhythms (1.5 marks)

RHYTHM	HZ	LOCATION	NORMAL CONTEXT
Alpha	8–13	Occipital	Relaxed, eyes closed; attenuates with eye opening
Beta	13–30	Frontocentral	Alert, active thinking; augmented by benzodiazepines
Theta	4–7	Temporal, frontal	Drowsiness; normal in children; pathological if focal and awake
Delta	0.5–3	Diffuse	Deep sleep; pathological if present awake (focal = structural; diffuse = encephalopathy)
Mu	8–13	Central (Rolandic)	Motor cortex at rest

Epileptiform Findings (2.5 marks)

PATTERN	MORPHOLOGY	CLINICAL SIGNIFICANCE
Spikes (<70ms)	Sharp, asymmetric	Focal IEDs, epileptogenic zone marker
Sharp waves (70–200ms)	Similar to spikes but slower	Focal or diffuse epilepsy
3 Hz spike-wave	Regular, generalised	Childhood absence epilepsy (pathognomonic)
Slow spike-wave (<2.5 Hz)	Irregular, slow, diffuse	Lennox-Gastaut
Polyspike-wave	Multiple spikes + SW	JME, myoclonic epilepsies
Hypsarrhythmia	Chaotic, high amplitude, asynchronous	West syndrome (infantile spasms)
PLEDs	Unilateral, periodic	Acute focal injury (HSV encephalitis, stroke)
GPEDs	Bilateral, periodic	CJD (PSWCs), anoxic encephalopathy
Ictal pattern	Evolving frequency, amplitude, morphology	Active seizure

Role of EEG in Psychiatry (4 marks)

1. Ruling out organic cause of psychiatric presentation:

- First-episode psychosis: EEG should be performed to exclude NCSE, encephalitis, structural/metabolic causes
- Acute confusional state: EEG distinguishes delirium (diffuse slowing), NCSE (epileptiform activity), functional (normal)

2. NCSE in acute psychiatric settings:

- Any fluctuating psychiatric syndrome with altered consciousness → urgent EEG
- Finding: Continuous or near-continuous epileptiform activity → confirms NCSE → emergency treatment

3. PNES evaluation:

- Gold standard: Video-EEG telemetry with captured event
- Normal EEG during typical event confirms PNES diagnosis

4. Monitoring drug effects:

- Clozapine: EEG before and after dose escalation; epileptiform activity = risk for clinical seizure
- Lithium toxicity: Diffuse slowing, triphasic waves
- Benzodiazepines: Increased beta activity (useful to confirm ingestion)

5. Delirium:

- Diffuse slowing is the hallmark EEG change in delirium, correlates with severity
- Monitoring treatment response in ICU delirium

6. ECT:

- Pre-ECT: Rule out structural lesions in selected patients
- Post-ECT: Postictal slowing; monitoring for adequate ictal duration

7. Dementia:

- Alzheimer's: Progressive slowing; alpha power reduction
- CJD: PSWCs 1–2 Hz (pathognomonic, present in ~70%)
- Frontotemporal: Less specific changes

Limitations (1 mark)

- Normal interictal EEG does NOT exclude epilepsy (30–50% of epilepsy patients have normal routine EEG)
 - Epileptiform discharges in ~1–2% of normal adults (not diagnostic alone)
 - Must interpret with clinical context always
 - Prolonged/ambulatory EEG significantly improves sensitivity
-

Answer 12: Discuss the management of status epilepticus. What are the psychiatric implications?

Definition (0.5 marks)

Status epilepticus (SE) is a seizure lasting ≥ 5 minutes OR two or more seizures without full recovery of consciousness between them (ILAE 2015 operational definition for convulsive SE). The functional definition (T2, when neuronal injury begins) for convulsive SE is 30 minutes.

Classification (1 mark)

TYPE	DEFINITION	PSYCHIATRIC RELEVANCE
Convulsive (GCSE)	Overt tonic-clonic activity	Post-SE psychiatric sequelae
Non-convulsive (NCSE)	Altered consciousness, EEG-confirmed	Presents as acute psychosis
Absence SE	Prolonged absence, subtle confusion	Misdiagnosed as psychiatric
Focal SE (impaired awareness)	Prolonged CPS	Prolonged psychotic-like states
Refractory SE	Not responding to first + second-line	ICU

Management Protocol (4 marks)

Phase 1, 0–5 min (Stabilisation):

- ABCDE assessment
- High-flow oxygen, IV access
- Glucose: Check and correct if < 3 mmol/L
- Blood: FBC, EUC, glucose, AED levels, toxicology, LFTs, Ca, Mg
- Thiamine 100 mg IV if alcoholism suspected (before glucose)

Phase 2, 5–20 min (First-line: Benzodiazepines):

DRUG	ROUTE	DOSE
Lorazepam	IV	0.1 mg/kg (max 4 mg), can repeat $\times 1$
Diazepam	IV/PR	0.2 mg/kg IV (max 10 mg); 10 mg PR
Midazolam	IM/buccal/IN	10 mg IM (preferred if no IV)

Phase 3, 20–40 min (Second-line: AED):

DRUG	DOSE	NOTES
Levetiracetam	60 mg/kg IV (max 4500 mg)	Preferred: few drug interactions, no cardiac monitoring
Valproate	40 mg/kg IV (max 3000 mg)	Avoid: hepatic disease, pregnancy, mitochondrial disorders
Phenytoin/Fosphenytoin	20 mg/kg IV	Cardiac monitoring required; slow infusion
Lacosamide	200–400 mg IV	Emerging option

Phase 4, 40+ min (Refractory SE: ICU):

- Anaesthetic agents: Midazolam infusion, propofol, thiopentone
- Continuous EEG monitoring (target: burst suppression)
- Ventilatory support
- Identify and treat underlying cause

Psychiatric Implications (3.5 marks)

1. NCSE as Psychiatric Emergency:

As discussed, acute psychosis, confusion, mutism as SE presentations. Every psychiatrist must know this differential. Emergency EEG in acutely confused patients with known epilepsy is mandatory.

2. Post-SE Psychiatric Sequelae:

After convulsive SE, the following can emerge:

- Postictal psychosis (24–48h later, lucid interval)
- Postictal depression
- Postictal aggression (in the immediate postictal period, not purposeful)
- Cognitive decline (especially after prolonged SE or recurrent SE)

3. AED Selection in Patients with Psychiatric Comorbidity:

- Prefer levetiracetam or lacosamide as second-line in patients with mood disorders (valproate is acceptable; phenytoin less so)
- Avoid phenobarbital maintenance post-SE in depression-prone patients

4. Neurological Injury → Psychiatric Sequelae:

Prolonged SE causes hippocampal neuronal loss → subsequent development of TLE → full psychiatric spectrum of TLE. This trajectory (SE → TLE → depression/psychosis) is well-described and justifies aggressive SE management.

5. Psychiatric Medications and SE:

Clozapine, chlorpromazine, TCAs, lithium toxicity, all can precipitate SE. When SE occurs in a psychiatric patient, review all medications for proconvulsant potential.

1 mark: Correctly note that the psychiatric team's role in SE is primarily: (a) recognition when presenting as psychiatric symptoms, (b) managing post-SE psychiatric sequelae, (c) ensuring ongoing AED optimisation in patients with psychiatric comorbidity.

Answer 13: Describe Lennox-Gastaut syndrome. What are its psychiatric implications?

Definition and Triad (1 mark)

Lennox-Gastaut syndrome (LGS) is a severe, age-related epileptic encephalopathy defined by three features: (1) multiple seizure types, (2) characteristic EEG pattern, and (3) cognitive/developmental impairment. It is one of the most challenging epilepsy syndromes to manage, with near-universal drug resistance.

Epidemiology and Aetiology (1 mark)

- Onset: 1–7 years; peak 3–5 years
- Preceded by West syndrome in 30%
- Structural causes: Cortical dysplasia, hypoxic-ischaemic injury, tuberous sclerosis, metabolic disorders
- Cryptogenic: 30–35%

Clinical Features: The Triad (3 marks)

1. Multiple Seizure Types:

SEIZURE TYPE · CHARACTERISTICS

Tonic (hallmark) Brief, nocturnal, bilateral sustained muscle contraction, pathognomonic for LGS

Atonic (drop attacks) Sudden loss of tone → falls; major injury risk; helmet required

Atypical absence Slow onset/offset; 1.5–2.5 Hz spike-wave

Myoclonic Variable

Generalised tonic-clonic Common

Focal May occur

2. EEG Features:

- Interictal: **Slow spike-and-wave complexes < 2.5 Hz** (typically 1.5–2 Hz), defines LGS EEG

- Sleep EEG: **Paroxysmal fast activity** (>10 Hz, 10–25 Hz "recruiting rhythm") during NREM sleep, highly specific
- Background: Diffuse slowing

3. Cognitive/Developmental Impairment:

- Intellectual disability: Present in >80%
- Progressive deterioration in many
- Regression common after LGS onset

Psychiatric Implications (4 marks)

1. Intellectual Disability and Adaptive Functioning:

- Ranges from mild to profound ID
- Requires educational placement, occupational therapy, structured daily routines
- Psychiatric assessment must be adapted for level of cognitive functioning, standard questionnaires may not apply

2. Behavioural Problems:

- Prevalence: 50–80% of LGS patients exhibit significant behavioural problems
- Types: Aggression, self-injurious behaviour, hyperactivity, stereotypies, non-compliance
- Management: Behavioural analysis, environmental modification, judicious use of medication
- Medications for aggression in ID: Risperidone, aripiprazole (evidence in ID/autism)

3. Autism Spectrum Disorder:

- ASD features: 20–30% of LGS
- Overlapping with tuberous sclerosis (when TSC is the aetiology, ASD rate is higher, 40–50%)
- ASD evaluation: Developmental history, CARS or ADOS adapted for level of function

4. ADHD Features:

- Hyperactivity, impulsivity, attention difficulties common
- May reflect frontal lobe dysfunction secondary to seizure activity
- AED polypharmacy (especially benzodiazepines, topiramate) worsens cognitive and attentional symptoms

5. AED-Related Psychiatric Effects in LGS:

- Clobazam: Sedation, paradoxical disinhibition (especially in ID patients)
- Topiramate: Cognitive effects worsening baseline ID
- Valproate: Sedation; preferred due to mood stabilisation properties

- Rufinamide: Generally well tolerated psychiatrically
- Cannabidiol (CBD): Emerging evidence; psychiatric side effects, somnolence, decreased appetite

6. Parental/Family Psychiatric Impact:

- Caregivers of LGS patients: High rates of depression (up to 60%), anxiety, burnout
- Respite care access, caregiver support groups, psychiatric monitoring of parents, part of comprehensive management

7. Quality of Life:

- Severely impaired in both patients and families
- Drop attacks are the feature most associated with poor QoL (physical danger, social restriction)
- Helmet use is necessary but stigmatising

Answer 14: Discuss the psychiatric aspects of West syndrome and infantile spasms.

Definition (1 mark)

West syndrome is an age-related epileptic encephalopathy of infancy, characterised by a classic triad: (1) epileptic (infantile) spasms, (2) hypsarrhythmia on EEG, and (3) developmental regression or arrest. It is the most common epileptic encephalopathy in infancy and one of the most psychiatrically significant, given its strong association with autism spectrum disorder and intellectual disability.

Epidemiology (0.5 marks)

- Incidence: ~1 / 4000 live births
- Age of onset: 3–12 months; peak 4–6 months
- Male slightly predominant

Aetiology (1 mark)

CATEGORY · EXAMPLES

Structural Cortical dysplasia, hypoxic-ischaemic injury, tuberous sclerosis complex (TSC), Down syndrome, lissencephaly

Genetic/Metabolic PKU, biotinidase deficiency, pyridoxine dependency

Unknown (cryptogenic) ~50%, better prognosis

Tuberous sclerosis (TSC) is the most common identifiable structural cause, always examine for TSC features (ash leaf macules, shagreen patches, adenoma sebaceum, cardiac rhabdomyoma).

Clinical Features (1.5 marks)

Infantile Spasms:

- Brief (1–2 seconds), symmetric contractions
- Flexion, extension, or mixed
- Occur in clusters, most prominent on waking
- Child may appear to startle or "scrunch up"
- Often preceded by a cry or giggle

Hypsarrhythmia (EEG):

- Chaotic, high-amplitude
- Asynchronous slow waves with multifocal spikes superimposed
- No organised background activity
- Pathognomonic for West syndrome

Developmental Regression:

- Loss of previously acquired milestones (smile, eye contact, reaching)
- Often noted by parents as "baby seems different"
- Regression is the most clinically alarming feature

Treatment (1 mark)

TREATMENT	EVIDENCE	NOTES
ACTH	Highest	Most evidence overall; rapid response
Vigabatrin	High	FIRST-LINE IF TSC, superior response in TSC
High-dose prednisolone	High	Non-inferiority to ACTH in some trials
Pyridoxine	Trial for 3–5 days	For pyridoxine-dependent epilepsy
Ketogenic diet	Moderate	If AEDs fail

Early treatment = better neurodevelopmental outcome. Every 1-week delay increases ASD risk.

Psychiatric Implications (4.5 marks)

1. Autism Spectrum Disorder (ASD):

- Prevalence of ASD in West syndrome: 30–50% overall; up to 60% in TSC-associated cases
- ASD features may emerge after seizure onset, often as developmental regression
- Mechanism: Epileptiform activity in limbic and association cortices disrupts critical periods of social-communicative brain development
- Diagnosis: Developmental surveillance at all follow-up appointments; formal ASD evaluation at 18–24 months
- Management: ABA, speech therapy, occupational therapy, structured educational programme

2. Intellectual Disability:

- 70–80% of West syndrome survivors have ID (ranges from mild to profound)
- Extent of ID correlates with: Underlying aetiology (TSC = better than anoxic injury), EEG duration of hypsarrhythmia, age at seizure onset, treatment latency
- Cryptogenic West syndrome: Better cognitive outcome (~50% normal or near-normal)

3. ADHD Features:

- Inattention, hyperactivity, impulsivity common in survivors
- May reflect frontal lobe involvement or medication effects (ACTH, steroids in early life)

4. Behavioural Disturbance:

- Irritability, sleep disturbance, self-injurious behaviour, all more common in TSC-associated cases
- ASD + seizures = complex behavioural management challenge

5. Impact on Caregivers:

- West syndrome diagnosis triggers significant parental crisis
- Parents require: Clear, compassionate communication; prognostic counselling; early referral to developmental services
- Parental depression: ~50–60% in first year after diagnosis
- Family counselling, social work input, essential components of management

6. Tuberous Sclerosis Complex (TSC), Special Case:

TSC-associated West syndrome warrants mention as a separate entity:

- Earlier vigabatrin treatment (pre-symptomatic in some guidelines) reduces ASD risk
 - Everolimus (mTOR inhibitor): Reduces tuber burden and some cognitive effects
 - Psychiatric manifestations in TSC beyond ASD: Anxiety, OCD, ADHD, aggression
-

Answer 15: Discuss the ILAE-defined epilepsy syndromes relevant to psychiatry. Compare their psychiatric profiles.

Introduction (1 mark)

Epilepsy syndromes are defined constellations of seizure types, EEG patterns, age of onset, aetiology, and natural history. For psychiatric practice, five syndromes are particularly relevant: Childhood Absence Epilepsy (CAE), Juvenile Myoclonic Epilepsy (JME), West syndrome, Lennox-Gastaut Syndrome (LGS), and Temporal Lobe Epilepsy (TLE). Each carries a distinct psychiatric profile.

Syndrome Profiles (5 marks)

FEATURE	CAE	JME	WEST SYNDROME	LGS	TLE
Age of onset	4–12 y	12–18 y	3–12 months	1–7 y	Any
Seizure types	Typical absence	Myoclonic, GTC, absence	Infantile spasms	Tonic, atonic, atypical absence	Focal (aura, automatisms), bilateral
Pathognomonic EEG	3 Hz SWD	4–6 Hz poly-spike-wave	Hypsarrhythmia	Slow SWD <2.5 Hz	Temporal spikes; ictal rhythmic theta
Intellectual disability	No	No	70–80%	Core feature	Not typical (except with lesion)
ASD	No	No	30–50%	20–30%	Not primary
Depression	Mild (reactive)	20–30%	(preverbal onset)	(ID complicates assessment)	30–50%, most prominent
Psychosis	Rare	Rare	Not described	Uncommon	5–10% (inter-ictal); PIP
ADHD features	Common (misdiagnosis)	30–40%	Common (survivors)	Common	30–40%
Personality changes	None	Impulsivity, poor self-regulation		Aggression, behavioural problems	Geschwind syndrome (20–40%)
Drug resistance	Rare	Common if untreated / life style	Common	Near-universal (90%)	30–40%

FEATURE	CAE	JME	WEST SYNDROME	LGS	TLE
AED of choice	Ethosuximide, VPA	VPA, LEV, LTG	ACTH, vigabatrin	VPA, LTG, clobazam, CBD	CBZ, OXC, LTG, LEV
Prognosis	Good (60% remit)	Lifelong (but manageable)	Variable (50% poor)	Poor	Variable
Psychiatric management priority	Identify, stop misdiagnosis as ADHD	Lifestyle, sleep, substance avoidance; mood screen	ASD surveillance, caregiver support	Behavioural management, caregiver burden	Full psychiatric comorbidity management

Key Differentiating Points (2 marks)

CAE vs. ADHD: CAE is the critical differential for inattentive ADHD in children. Brief, frequent staring spells with no postictal phase = CAE until proven otherwise.

Hyperventilation test in clinic: Induces typical absences. EEG confirms. Ethosuximide resolves both seizures and "attention problems."

JME lifestyle significance: JME is one of the few epilepsies where lifestyle modification is as important as medication. Sleep deprivation, alcohol, photic stimulation (common in adolescent social contexts) trigger seizures. Psychiatric input for sleep hygiene, impulse control, and substance use counselling is directly therapeutic.

LGS behavioural burden: LGS generates the highest caregiver psychiatric burden of all syndromes. Psychiatric support for families is not optional, depression and burnout in caregivers directly affects patient safety and treatment adherence.

TLE psychiatric depth: No other epilepsy syndrome generates as diverse or as clinically significant psychiatric comorbidity as TLE. Every psychiatrist working in a hospital setting will encounter TLE patients with depression, psychosis, or PNES, often simultaneously.

Clinical Synthesis (2 marks)

Psychiatric approach by syndrome priority:

1. **TLE**, Screen for depression (NDDI-E), psychosis, anxiety at every visit; joint neuropsychiatry input
2. **West/LGS**, Prioritise developmental assessment, ASD screening, caregiver psychiatric support
3. **JME**, Lifestyle counselling, mood monitoring, valproate teratogenicity counselling in women
4. **CAE**, Misdiagnosis awareness; once treated, most psychiatric issues resolve with seizure control

Mnemonics & Memory Tricks

15+ mnemonics covering all high-yield topics in Epilepsy & Psychiatry

EXAM STRATEGY

Each mnemonic includes the full decoded content immediately below it. Don't just memorise the acronym, rehearse the full expansion under exam conditions. These are retrieval cues, not replacements for understanding.

MNEMONIC 1: Geschwind Syndrome: "5 H's of TLE Personality"

H H H H H

LETTER	FEATURE	CLINICAL DETAIL
Hypergraphia	Compulsive, excessive writing	Most specific feature; detailed journals, letters, notes
Hyperreligiosity	Intense spiritual/religious preoccupation	Mystical experiences, conversion experiences
Hyposexuality	Decreased sexual interest	Note: hypO, not hyperSEXuality
Hurts to leave (Viscosity)	Circumstantial, "sticky" thinking	Difficulty ending conversations; tangential
Heightened affect	Everything feels profound, meaningful	Deepened emotional resonance

EXAM PEARL

Remember "5 H's" not "5 B's", the most common error is confusing hyposexuality with hypersexuality. It's hypo. Also note the syndrome is associated with TLE/MTLE, not generalised epilepsy.

MNEMONIC 2: Postictal Psychosis Key Features: "LUCID"

L U C I D

LETTER · FEATURE

Lucid interval 24–48 hours between seizure and psychosis onset

Usually self-limiting Most episodes resolve in < 2 weeks

Cluster of seizures triggers it Not a single seizure, usually bilateral/GTC cluster

Impaired insight Patient unaware of psychotic state

Dual features Both auditory AND visual hallucinations (unlike typical schizophrenia)

CLINICAL ANCHOR

The lucid interval is the single most testable feature of postictal psychosis. Examiners will give you a vignette of a patient who "seems fine" after seizures then develops psychosis 24–48h later, LUCID interval = Postictal Psychosis.

MNEMONIC 3: SLPE vs Schizophrenia: "PAWNS"

Schizophrenia-Like Psychosis of Epilepsy has PAWNS (not schizophrenia's full deck)

LETTER · FEATURE PRESENT IN SLPE (ABSENT/REDUCED VS. SCHIZOPHRENIA)

Positive symptoms Present (hallucinations, delusions, same as SCZ)

Affect Preserved Warm, intact affect, KEY distinction from schizophrenia

Warmth maintained Social connections preserved; less deterioration

Negatives absent Negative symptoms mild or absent, KEY distinction

Schizophrenia family history absent No elevated FH of psychosis (unlike SCZ)

EXAM PEARL

"SLPE has the POSITIVE features of schizophrenia without the NEGATIVE ones, and preserves AFFECT and WARMTH." Write this sentence in your answer.

MNEMONIC 4: ILAE 2017: Focal Seizure Descriptors, "SAME ACE"

Motor descriptors: SAME ACE

LETTER · DESCRIPTOR

Spasms (epileptic) Brief sustained contraction

Automatisms Repetitive semi-purposeful movements

Myoclonic Brief irregular jerks

Epileptic spasms (see Spasms above, same entry, confirms)

Atonic Loss of muscle tone

Clonic Rhythmic jerking

Epileptic spasms → **Hyperkinetic** Pedalling, thrashing

Non-motor: Autonomic, Behaviour arrest, Cognitive, Emotional, Sensory

MNEMONIC 5: West Syndrome Triad: "HIRS"

H I R S (Hypsarrhythmia In Regressing Spasms)

LETTER · FEATURE

Hypsarrhythmia Chaotic EEG, the pathognomonic EEG pattern

Infantile spasms Brief flexion/extension clusters, worse on waking

Regression Developmental regression/arrest

Salaam attacks Alternate name for infantile spasms (bowing movements)

EXAM PEARL

West = infantile; Lennox-Gastaut = childhood. The EEG distinguishes: Hypsarrhythmia (West) vs. Slow spike-wave <2.5 Hz (LGS). Treatment: ACTH (or vigabatrin if TSC).

MNEMONIC 6: Lennox-Gastaut: "DATS"

LGS = D A T S

LETTER · FEATURE

Drop attacks (atonic seizures) Most dangerous; helmet required

Atypical absence Slow onset/offset; 1.5–2.5 Hz spike-wave

Tonic seizures Nocturnal; hallmark seizure type

Slow spike-wave EEG <2.5 Hz; defining EEG feature

CLINICAL ANCHOR

"Tonic + Atonic + Atypical absence + Slow SWD + ID = Lennox-Gastaut." If you see drop attacks in a child with ID, think LGS until proven otherwise.

MNEMONIC 7: NDDI-E Items: "EVERYTHING FEELS LIKE A GUILTY STRUGGLE"

Six items of NDDI-E (Neurological Disorders Depression Inventory for Epilepsy):

ITEM · MEMORY HOOK

Everything is a struggle "EVERYTHING"

Nothing I do is right "NOTHING RIGHT"

Feel guilty "GUILTY"

I'd be better off dead "BETTER OFF DEAD"

Frustrated "FRUSTRATED"

Difficulty finding pleasure "PLEASURE"

GDNFEP, "Guilty Dead Nothing Frustrated Everything Pleasure"

Cutoff: ≥ 15 out of 24 = probable MDD (6 items $\times$ max 4 = 24)

EXAM PEARL

Why NDDI-E not PHQ-9? Because PHQ-9 has somatic items (fatigue, sleep, concentration) that overlap with AED side effects, produces false positives in epilepsy. NDDI-E avoids somatic items entirely.

MNEMONIC 8: AED Proconvulsant Risk for Antipsychotics: "AROQC" (Low to High)

A $\rightarrow$ R $\rightarrow$ O $\rightarrow$ Q $\rightarrow$ C (Aripiprazole $\rightarrow$ Risperidone $\rightarrow$ Olanzapine $\rightarrow$ Quetiapine $\rightarrow$ Clozapine)

DRUG · SEIZURE RISK LEVEL

Aripiprazole Lowest

Risperidone Low-moderate

Olanzapine Moderate

Quetiapine Moderate

Clozapine Highest (3–5%)

Memory: "A Royal Orchestra Quite Carefully", least to most risky

EXAM PEARL

Aripiprazole = safest antipsychotic in epilepsy. Clozapine = most dangerous. If clozapine is essential in a patient with epilepsy, add valproate prophylactically and monitor EEG.

MNEMONIC 9: Antidepressants to AVOID in Epilepsy: "BBC" (Bad For Brain Convulsions)

B B C

LETTER	DRUG	RISK
Bupropion	Most proconvulsant antidepressant	Contraindicated
Butriptyline / TCAs broadly	High seizure risk	Avoid
Clomipramine	Especially at high doses	Avoid

Safe alternatives: SSRIs (sertraline, escitalopram), SNRIs, mirtazapine

EXAM PEARL

Bupropion is THE answer to "which antidepressant is contraindicated in epilepsy?" It is dose-dependently proconvulsant.

MNEMONIC 10: Enzyme-Inducing AEDs: "CORP"

C O R P = AEDs that induce CYP3A4 (reduce psychotropic levels)

LETTER · AED

Carbamazepine Strong inducer

Oxcarbazepine Moderate

Rifampicin (Not AED but classic inducer, context)

Phenytoin / Phenobarbital / Primidone All strong inducers

Clinical consequence: Reduce levels of all antipsychotics and many antidepressants by 40–70%. When adding CORP drugs, expect apparent drug failure, increase psychotropic dose.

CLINICAL ANCHOR

"CORP drugs kill your psych drug levels." Clozapine + carbamazepine = contraindicated (not just pharmacokinetic, dual agranulocytosis risk).

MNEMONIC 11: Teratogenicity Hierarchy: "VERY BAD PILL, LAMOTRIGINE OK"

Teratogenicity: High → Low

RISK LEVEL	AED	MEMORY
HIGHEST	Valproate (~10%)	"Very Bad"
High	Phenobarbital (~5–7%)	Probably Bad
Moderate	Phenytoin, Topiramate (~3–9%)	
Lower	Carbamazepine (~2–3%)	"Cautious"
Lowest	Lamotrigine (~2%), Levetiracetam (~2–3%)	"Lamotrigine OK"

Folic acid: 5 mg/day for all WWE on AEDs, start 3 months pre-conception

EXAM PEARL

Valproate's teratogenicity is BOTH structural (NTDs, cardiac) AND neurodevelopmental (IQ –7–9 points, autism 6× risk). This dual burden makes it uniquely harmful. MHRA 2018 guidance: Valproate MUST NOT be prescribed to girls/women of childbearing potential without PREVENT programme enrollment.

MNEMONIC 12: Status Epilepticus Management: "BEAT IT"

B E A T I T (Time-based Protocol)

LETTER	STEP	TIMING
Benzodiazepines first	Lorazepam IV / Midazolam IM	5–20 min
Establish IV access & bloods	FBC, EUC, glucose, AED levels	0–5 min
Airway, oxygen	ABC	0–5 min
Third-line anesthetics	Midazolam infusion, propofol, thiopentone	>40 min (ICU)
IV AED second-line	Levetiracetam, Valproate, Phenytoin	20–40 min

LETTER	STEP	TIMING
Thiamine first if alcohol	100 mg IV before glucose	0–5 min

EXAM STRATEGY

The examiner wants to see: (1) time-based protocol, (2) first-line benzodiazepines named with doses, (3) second-line AEDs named with doses, (4) escalation to ICU for refractory SE. Write in a table.

MNEMONIC 13: JME Classic Triad + Triggers: "MAG + SAS"

Triad: MAG (Myoclonic + Absence + Grand mal)

SEIZURE · TIMING

Myoclonic Morning, on waking

Absence ~30% of patients

Grand mal (GTC) Often triggered by sleep deprivation

Triggers: SAS (Sleep deprivation + Alcohol + Stress/Sunlight)

TRIGGER · NOTES

Sleep deprivation Most important trigger

Alcohol Especially withdrawal

Sunlight/Stress Photosensitivity (30%) + psychosocial stress

EXAM PEARL

JME is lifelong in most patients. Valproate is most effective but teratogenic, dilemma in young women. Lifestyle management (sleep, alcohol) is as important as medication.

MNEMONIC 14: Catamenial Epilepsy Patterns: "C1 C2 C3 = Period, Ovulation, Whole Luteal"

Three Herzog Patterns:

PATTERN	PHASE	MECHANISM
C1, Perimenstrual	Days –3 to +3 (around period)	Progesterone withdrawal → estrogen dominance

PATTERN	PHASE	MECHANISM
C2, Periovulatory	Days 10–13 (ovulation)	Estrogen surge (proconvulsant)
C3, Anovulatory	Days 10–28 (entire second half)	Low progesterone throughout luteal phase

Memory: "C1 = (C)ycle start, C2 = (C)entre, C3 = (C)lose (whole closing half)"

MNEMONIC 15: PNES vs. Epilepsy Differentiators: "CLOSE EYES CRY LONG"

Features suggesting PNES:

WORD · FEATURE

CLOSE Eye closure (closed eyes, resist opening)

EYES Eyes closed during event (epileptic eyes are OPEN)

CRY Ictal crying / weeping (very rare in epilepsy)

LONG Prolonged duration (>3–5 min)

OUT of phase Asynchronous, out-of-phase limb movements

No postictal Minimal / absent postictal confusion

Gradual Gradual onset with emotional build-up

EXAM PEARL

Gold standard = Video-EEG with captured event. No clinical feature alone is diagnostic. The most specific single feature? Normal EEG during a typical event = PNES (until proven otherwise).

MNEMONIC 16: Ictal Emotions by Structure: "FAJ" (Fear-Amygdala-Joy)

EMOTION	STRUCTURE	NOTES
Fear	Amygdala	Most common ictal emotion (60–70%)
Amygdala	Central structure	Right amygdala > left for fear

EMOTION	STRUCTURE	NOTES
Joy/Ecstasy	Insula, temporal	Rare; reported in "ecstatic seizures" (Dostoevsky reportedly had these)

Also: Anger (temporal-frontal), Sadness (temporal), Disgust (basal ganglia-insula)

CLINICAL ANCHOR

Dostoevsky's epilepsy and his famous description of ecstatic auras are literary classics that appear in neuropsychiatry texts. Ictal joy / ecstasy = rare mesial temporal / insula focus. Ictal fear = amygdala. Fear is the most common ictal emotion, examiners love this fact.

MNEMONIC 17: AED Psychiatric Uses: "VaLCa" (Valproate, Lamotrigine, Carbamazepine)

VaLCa = The three AEDs with established psychiatric indications

DRUG	PSYCHIATRIC INDICATION	MEMORY
Valproate	BD-I mania (first-line), maintenance, rapid cycling	Va = Valiant mood stabiliser
Lamotrigine	Bipolar depression (best evidence), maintenance	L = Low mood → Lamotrigine
Carbamazepine	BD (dysphoric mania, rapid cycling)	Ca = "Calms" cycling

The rest of the AEDs (levetiracetam, topiramate, gabapentin, phenobarbital) are NOT primary psychiatric treatments. Pregabalin = licensed for GAD in Europe only.

MNEMONIC 18: Forced Normalisation: "LANDOLT'S PARADOX"

Simple memory sentence:

KEY INSIGHT

"When seizures STOP, the EEG NORMALISES, but the patient goes PSYCHOTIC, Landolt's PARADOX (1953)"

COMPONENT · REMEMBER

Who Heinrich Landolt, 1953

What EEG normalises paradoxically when seizures stop

When After seizure control (spontaneous or AED-induced)

Which AEDs Vigabatrin (highest), ethosuximide, lamotrigine

Alternative term "Alternative psychosis" (Tellenbach, 1965)

Management Reduce offending AED + low-dose antipsychotic

MNEMONIC 19: Blumer's Interictal Dysphoric Disorder: "DEAF + PFIE"

Eight symptoms in two groups:

Depressive group (DEAF):

LETTER · SYMPTOM

Depressive mood Core low mood

Energia absent (Anergia) Lack of energy

Ache / Pain Somatic complaints

Falling asleep problems (Insomnia) Sleep disturbance

Labile/Irritable group (PFIE):

LETTER · SYMPTOM

Paroxysmal affective disturbances Brief intense affective storms

Fear / Anxiety (episodic) Sudden anxiety not linked to seizures

Irritability Persistent, often leading to interpersonal conflict

Euphoric moods (episodic) Brief elevated periods

EXAM PEARL

IDD does NOT map onto DSM depression, it combines features of dysthymia, cyclothymia, and anxiety. The dysphoric, intermittent quality with both depressive AND irritable/elevated periods is the distinguishing signature.

MNEMONIC 20: Normal EEG Rhythms: "All Brains Think Deeply"

A B T D (Alpha, Beta, Theta, Delta: fast to slow)

RHYTHM	HZ	STATE	LOCATION
Alpha	8–13	Relaxed, eyes closed	Occipital
Beta	13–30	Alert, active	Frontocentral
Theta	4–7	Drowsy	Temporal / frontal
Delta	0.5–3	Deep sleep (or pathological awake)	Diffuse

"All Brains Think Deeply", Alpha → Beta → Theta → Delta (decreasing frequency)

CLINICAL ANCHOR

In practice, remember: **Delirium = Diffuse Delta/Theta slowing on EEG**. This is the single most important EEG finding to know for psychiatry ward work. Always: delirium → EEG shows diffuse slowing, not epileptiform activity (though NCSE must be excluded).

High-Yield Comparisons

10 high-yield comparison tables for exam revision

EXAM STRATEGY

Comparison tables are the highest-density format for 5–10 mark questions. When asked to "compare and contrast," reproduce the key rows from memory. Each table here is built around features examiners test directly.

Table 1: Epileptic Seizures vs. PNES (Psychogenic Non-Epileptic Seizures)

EXAM PEARL

The gold standard for diagnosis is Video-EEG with captured event, state this in every answer. No clinical feature alone is definitive.

FEATURE	EPILEPTIC SEIZURE	PNES (FUNCTIONAL SEIZURE)
Onset	Abrupt, stereotyped across events	Gradual, variable build-up
Duration	Usually < 3 minutes	Often prolonged (> 3–5 min)
Eye position	Open; may be deviated laterally	Closed; resistance to passive opening
Motor features	Rhythmic (GTC), stereotyped automatisms (TLE)	Asynchronous, thrashing, pelvic thrusting, opisthotonus
Side-to-side head movement	Rare	Common (LR ~8)
Ictal crying/weeping	Very rare (< 1%)	Common (20–30%)
Consciousness	Absent (GTC/CPS)	Variable; may be partially present
Postictal confusion	Prolonged (> 30 min in GTC)	Minimal to absent
Tongue bite	Lateral tongue bite (specific)	Tip of tongue only; rare
Incontinence	Common in GTC	Less common
Recall of event	Absent for GTC	Often partial recall present
Triggers	Sleep deprivation, alcohol, illness, medication lapse	Psychosocial stressors; emotional context

FEATURE	EPILEPTIC SEIZURE	PNES (FUNCTIONAL SEIZURE)
Audience effect	None	Events more likely with observers
Serum prolactin (20 min post)	Elevated (GTC, CPS), not absence	Not elevated
EEG during event	Ictal epileptiform discharge	Normal
Postictal EEG	Diffuse slowing	Normal
CK post-event	Elevated (GTC)	Variable, usually normal
MRI	May show structural lesion	Usually normal
Psychiatric comorbidity	30–50%	70–90% (depression, PTSD, BPD)
Trauma history	Not specific	50–80% report trauma / abuse
Gold standard diagnosis	Video-EEG (ictal discharge confirmed)	Video-EEG (normal EEG during event)
Treatment	AEDs	Psychotherapy (CBT, trauma-focused), AED withdrawal
Dual diagnosis	N/A	10–30% have comorbid epilepsy

Table 2: Ictal vs. Postictal vs. Interictal Psychosis

EXAM PEARL

The TIMING relative to seizures is what distinguishes these three. The lucid interval is unique to postictal psychosis. Interictal psychosis is independent of seizure timing.

FEATURE	ICTAL PSYCHOSIS	POSTICTAL PSYCHOSIS	INTERICTAL PSYCHOSIS (SLPE)
Timing	DURING the seizure	24–48h AFTER seizure cluster (lucid interval)	Independent of seizures; chronic
EEG	Active ictal discharge	Often normalised (forced normalisation)	Interictal or normal
Prevalence in TLE	< 1%	7–10%	5–10%
Duration	Seconds to minutes	Days to weeks (usually < 2 weeks)	Months to years
Lucid interval	None	YES, 24–48h, pathognomonic	Not applicable

FEATURE	ICTAL PSYCHOSIS	POSTICTAL PSYCHOSIS	INTERICTAL PSYCHOSIS (SLPE)
Trigger	Ongoing seizure	Cluster of bilateral/GTC seizures	None specific
Mood features	Variable	Often elevated, euphoric, religious	Predominantly paranoid
Hallucinations	Visual/olfactory/auditory (lobe-dependent)	Both auditory AND visual	Auditory predominant
Affect	Ictal fear most common	Often elevated, bright	PRESERVED (warm), key SLPE feature
Negative symptoms	Not applicable	Absent	Absent/mild, KEY distinction from SCZ
Self-limiting	Yes	Yes (most cases)	No, chronic without treatment
Treatment	Treat underlying SE	Short-term antipsychotic; AED optimisation	Long-term antipsychotic; AED continuation
Risk of chronicity	None	~15% progress to interictal with repeated episodes	Chronic course
Family history of SCZ	Not elevated	Not elevated	Not elevated

Table 3: TLE (Temporal Lobe Epilepsy) vs. FLE (Frontal Lobe Epilepsy)

EXAM PEARL

FLE is the second most common focal epilepsy. It is frequently misdiagnosed as PNES due to its bizarre, hypermotor semiology. Know the distinguishing features.

FEATURE	TLE (TEMPORAL LOBE EPILEPSY)	FLE (FRONTAL LOBE EPILEPSY)
Frequency	Most common focal epilepsy (60%)	Second most common focal epilepsy
Duration	1–3 minutes	Brief (< 1 minute)
Aura	Epigastric rising, fear, déjà vu, olfactory/gustatory	May be absent; may have brief sensory or affective aura
Motor features	Oral automatisms (lip smacking), manual automatisms (fumbling)	Hypermotor , pedalling, thrashing, pelvic thrusting, violent movements
Awareness	Usually impaired during automatisms	Variable; can be preserved during complex motor activity

FEATURE	TLE (TEMPORAL LOBE EPILEPSY)	FLE (FRONTAL LOBE EPILEPSY)
Postictal confusion	Prominent (> 30 min)	Minimal to absent
Nocturnal predominance	Not typical	YES, FLE seizures often occur from sleep
Cluster tendency	Occasional	Common
EEG	Temporal spikes, rhythmic theta ictal	Frontal spikes; ictal EEG may be normal (frontal activity hard to capture)
MRI	Hippocampal sclerosis (MTLE), cortical dysplasia	Cortical dysplasia (most common), cavernomas, tumours
Misdiagnosis as PNES	Less common	VERY COMMON, hypermotor FLE mimics PNES
Psychiatric comorbidity	Full spectrum: depression, psychosis, personality changes, PNES overlap	Less psychiatric comorbidity data; ADHD features, impulse dyscontrol
Surgical outcome	~70% seizure-free (MTLE with HS)	50–60% (depends on lesion)
Psychiatric post-surgery	De novo depression/psychosis possible	Less data

Table 4: Interictal Dysphoric Disorder (IDD) vs. Major Depressive Disorder in Epilepsy

EXAM PEARL

IDD (Blumer's concept) does NOT map onto DSM-5 MDD. The key distinguishing feature is its intermittent, mixed dysphoric quality, low mood plus irritability plus episodic euphoria. Examiners test whether you know this distinction.

FEATURE	INTERICTAL DYSPHORIC DISORDER (IDD)	MAJOR DEPRESSIVE DISORDER IN EPILEPSY
Concept	Blumer (2004), epilepsy-specific mood disorder	Standard DSM-5 MDD occurring in epilepsy context
Course	Intermittent, fluctuating, paroxysmal	Sustained depressive episodes (≥ 2 weeks)
Mood quality	Dysphoric, mixed: low mood + irritability + brief euphoria	Predominantly low mood; anhedonia
Irritability	Prominent, persistent	May be present but not defining

FEATURE	INTERICTAL DYSPHORIC DISORDER (IDD)	MAJOR DEPRESSIVE DISORDER IN EPILEPSY
Euphoric periods	YES, brief periods of elevated mood	Absent (absent in MDD; present = consider BD)
Anhedonia	Mild	Often severe
Somatic symptoms	Anergia, pain, insomnia (4 of 8 symptoms)	Sleep, appetite, energy changes
DSM-5 mapping	Poor fit, doesn't map cleanly	Maps to MDD criteria
Temporal relation to seizures	Interictal, but related to seizure disorder	Not specifically tied to seizure timing
Screening tool	NDDI-E appropriate	NDDI-E; PHQ-9 less ideal
Treatment	SSRI + low-dose lamotrigine (anecdotal); treat underlying seizures	SSRIs first-line; CBT; AED optimisation
Clinical significance	Reduces QoL; often under-recognised	Well-established clinical entity

Table 5: AED Psychiatric Profiles: Benefit vs. Risk

EXAM STRATEGY

This is the master AED-psychiatry table. Know the "positive psychiatric use" column AND the "negative psychiatric effects" column. Examiners will ask about both directions.

AED	MECHANISM	POSITIVE PSYCHIATRIC USE	NEGATIVE PSYCHIATRIC EFFECTS	KEY INTERACTION
Valproate	GABA ↑, Na channel	BD-I mania (first-line), maintenance, rapid cycling, aggression in ID	Sedation, weight gain, cognitive dulling, teratogenicity	Doubles lamotrigine levels
Carbamazepine	Na channel	BD (dysphoric mania, rapid cycling)	Sedation, hyponatraemia (SIADH), cognitive effects	Strong CYP3A4 inducer; reduces all antipsychotics
Lamotrigine	Na/Ca channel, ↓glutamate	Bipolar depression (best evidence), mood cycling prevention	Insomnia, activation, rash (SJS risk); rarely psychosis	OCP halves lamotrigine levels

AED	MECHANISM	POSITIVE PSYCHIATRIC USE	NEGATIVE PSYCHIATRIC EFFECTS	KEY INTERACTION
Levetiracetam	SV2A binding	Minimal sedation; no cognitive impairment	Irritability, aggression, depression, psychosis (10%)	Minimal interactions
Topiramate	Multiple	Weight loss (sometimes desired)	Cognitive ("Dopamax", word-finding), depression, suicidality	Enzyme inducing at high doses (reduces OCP)
Phenobarbital	GABA-A ↑	Sedation (occasionally useful)	Depression (worst AED for depression), cognitive impairment, dependence	Strong CYP inducer
Vigabatrin	GABA transaminase inhibitor	Infantile spasms (especially TSC)	Depression, psychosis, forced normalisation, visual field defects	Reduces phenytoin levels
Oxcarbazepine	Na channel	BD (limited evidence)	Hyponatraemia, dizziness	Less enzyme induction than CBZ
Pregabalin	α2-δ subunit	GAD (licensed in Europe), neuropathic pain	Sedation, weight gain, misuse/dependence potential	Minimal
Perampanel	AMPA antagonist	Good efficacy; low cognitive burden	Aggression, hostility, irritability (dose-dependent)	Moderate inducer at high doses
Lacosamide	Slow inactivation Na channel	Low psychiatric burden; useful adjunct	Minimal; dizziness, diplopia	Minimal
Clonazepam	GABA-A ↑	Panic disorder, acute mania adjunct, antimyoclonic	Dependence, sedation, cognitive impairment, paradoxical disinhibition	Additive CNS depression
Zonisamide	Multiple	Weight loss	Cognitive effects, depression, kidney stones	Moderate inducer

Table 6: Postictal Psychosis vs. Forced Normalisation vs. Interictal Psychosis

EXAM PEARL

These three are frequently confused. The distinguishing axis is: timing relative to seizures + EEG finding + whether seizures are present or absent when psychosis occurs.

FEATURE	POSTICTAL PSYCHOSIS	FORCED NORMALISATION	INTERICTAL PSYCHOSIS
Seizures at time of psychosis	Just had a cluster	Just STOPPED (controlled)	Present or absent; unrelated
EEG	Often normalised	Normalised, defining feature	May show interictal discharges or be normal
Concept origin	Clinical description	Landolt (1953), EEG phenomenon	Slater & Beard (1963)
Timing	24–48h after seizure cluster	After seizure control achieved	Chronic, independent of seizures
Lucid interval	YES, pathognomonic	Not a feature	Not applicable
AED context	No recent AED change typically	Often precipitated by new / increased AED	No specific AED context
Resolution	Seizures return (or anti-psychotic treatment)	AED reduced / seizures allowed to re-cur OR anti-psychotic	Chronic; requires long-term anti-psychotic
Mood	Often elevated, religious	Often elevated, grandiose	Predominantly paranoid delusions
Duration	Days–weeks	Days–weeks	Months–years
Mechanism	Rebound dopaminergic hyperactivity post-seizure	Seizures suppress psychosis; removal of seizures allows psychosis	Kindling + limbic structural change

Table 7: Childhood Absence Epilepsy vs. Juvenile Myoclonic Epilepsy

EXAM PEARL

CAE and JME are both "idiopathic generalised epilepsies" but differ critically in age, prognosis, and drug choice. JME is lifelong; CAE often remits. Valproate covers both but is teratogenic, critical for JME patients who are typically young women.

FEATURE	CHILDHOOD ABSENCE EPILEPSY (CAE)	JUVENILE MYOCLONIC EPILEPSY (JME)
Age of onset	4–12 years	12–18 years (adolescence)
Seizure types	Typical absence (multiple daily, 50–100/day)	Myoclonic + GTC + absence (30%)
Myoclonic seizures	Absent	Hallmark, worse on morning waking
GTC seizures	Rare	Common; triggered by sleep deprivation
Timing	Any time; provoked by hyperventilation	Morning; sleep deprivation is key trigger
EEG	3 Hz generalised spike-wave (pathognomonic)	4–6 Hz polyspike-wave, frontally dominant
Photosensitivity	Rare	30–50%
Prognosis	60–70% remit at puberty	Lifelong in most (> 80% relapse if AED stopped)
Intelligence	Normal	Normal
Psychiatric comorbidity	Mild (ADHD-like attention issues)	ADHD (30–40%), anxiety, depression, impulsivity
AED of choice	Ethosuximide (first-line pure absence), VPA	VPA (most effective), LEV, LTG
AED, avoid	Carbamazepine, phenytoin (worsen absences)	Carbamazepine, phenytoin (worsen myoclonus)
Lifestyle advice	Minimal	Critical, sleep hygiene, alcohol avoidance, stress management
Teratogenicity concern	Less (younger, pre-reproductive)	HIGH, teenage girls on VPA need PREVENT counselling
Misdiagnosis risk	Misdiagnosed as ADHD/daydreaming	Misdiagnosed as "morning clumsiness," alcohol-related

Table 8: West Syndrome vs. Lennox-Gastaut Syndrome

EXAM PEARL

West precedes LGS in 30% of cases. Together they represent the "epileptic encephalopathy continuum." Both cause intellectual disability, but their EEG patterns and seizure types are distinct.

FEATURE	WEST SYNDROME	LENNOX-GASTAUT SYNDROME (LGS)
Age of onset	3–12 months (peak 4–6 months)	1–7 years (peak 3–5 years)
Relationship	May precede LGS (30% of LGS cases)	May follow West syndrome
Seizure types	Infantile spasms (flexion, extension, mixed)	Tonic (hallmark), atonic (drop attacks), atypical absence, GTC, myoclonic
Most characteristic seizure	Infantile spasms in clusters on waking	Nocturnal tonic seizures
EEG, interictal	Hypsarrhythmia , chaotic, high-amplitude, asynchronous	Slow spike-wave < 2.5 Hz (usually 1.5–2 Hz)
EEG, sleep	Modified hypsarrhythmia	Paroxysmal fast activity (> 10 Hz) , specific for LGS
Intellectual disability	70–80%; variable by aetiology	Core feature; progressive in many
ASD	30–50% (highest in TSC)	20–30%
Drug resistance	Common	Near-universal (90%)
First-line treatment	ACTH, vigabatrin (TSC → vigabatrin first)	Valproate, lamotrigine, clobazam, rufinamide, CBD
Drop attacks	Not typical	Major feature, helmet required
Safety concern	Developmental window, urgency of treatment	Drop attack injuries; nocturnal tonic seizures
Prognosis	Variable; cryptogenic better	Poor; drug resistance the rule
Psychiatric management	ASD surveillance; caregiver support	Behavioural management; caregiver burden; ID-adapted psychiatric care

Table 9: Schizophrenia vs. Schizophrenia-Like Psychosis of Epilepsy (SLPE)

EXAM PEARL

Slater & Beard (1963) is the reference study. The "positive without negative" pattern and preserved affect are the two most tested distinguishing features. Write them clearly in your answer.

FEATURE	SCHIZOPHRENIA	SLPE (INTERICTAL PSYCHOSIS OF EPILEPSY)
Positive symptoms	Prominent	Prominent, SAME
Negative symptoms	Often prominent; progressive	MILD OR ABSENT, KEY DISTINCTION
Affect	Often blunted / flat	PRESERVED, WARM, KEY DISTINCTION
Social deterioration	Severe	Milder
Formal thought disorder	Common, often prominent	Less severe
First rank symptoms (Schneider)	Characteristic	May be present
Family history of psychosis	Elevated	NOT elevated
Premorbid function	Often impaired	Often normal
Age of onset	Early adulthood (teens–20s)	After 10–15 years of epilepsy (mean ~30s)
Neurodevelopmental basis	Strong	Less primary; secondary to epilepsy
Underlying pathology	Diffuse grey matter changes; dopamine dysregulation	Hippocampal sclerosis; limbic pathology; kindling
Response to antipsychotics	Yes	Yes
AED role	Not applicable	Continue AEDs; they do NOT worsen psychosis
Religious/grandiose content	Present but not specific	Often prominent
Catatonia	Possible	Rare
Clozapine use	For treatment-resistant cases	Avoid if possible (seizure risk); use only if truly treatment-resistant
Cognitive profile	Progressive cognitive decline	Epilepsy-related cognitive effects; less than schizophrenia's decline
Long-term prognosis	Chronic deteriorating course	Less deterioration; some stability with treatment

Table 10: Valproate vs. Lamotrigine: Psychiatric and Reproductive Comparison

EXAM PEARL

This comparison appears repeatedly in Indian PG exams because of the teratogenicity dilemma in young women with epilepsy and/or bipolar disorder. Know it cold.

FEATURE	VALPROATE (SODIUM VALPROATE)	LAMOTRIGINE
Epilepsy indication	Generalised epilepsy (JME, CAE, LGS), focal (second-line), SE	Focal epilepsy (adjunct/monotherapy), generalised (adjunct)
Psychiatric indication	BD-I mania (first-line), maintenance, rapid cycling	Bipolar depression (best evidence), NOT acute mania
Mechanism	GABA ↑, Na channel, histone deacetylase inhibition	Na/Ca channel blockade, ↓ glutamate release
Teratogenicity	HIGHEST, ~10% MCM; NTDs 1–2%; IQ –7–9pts; autism 6×	Lowest, ~2% MCM ; slight orofacial cleft increase
MHRA guidance	PREVENT programme mandatory in women of childbearing potential	Preferred in women of reproductive age
OCP interaction	None (VPA does not affect OCP)	OCP reduces LTG levels by ~50% , seizure risk
Lamotrigine interaction	VPA doubles LTG levels , rash risk	N/A
Rash risk	Low	10% mild; 0.1–0.3% Stevens-Johnson (higher with fast titration + VPA)
Weight	Weight GAIN	Weight NEUTRAL
Cognitive effects	Mild sedation; cognitive dulling at high doses	MINIMAL, cognitive profile is favourable
Mood in bipolar, acute mania	Effective (first-line)	NOT effective for acute mania
Mood in bipolar, depression	Moderate evidence	Best evidence for bipolar depression
Pregnancy levels	Relatively stable	FALL significantly , increase dose with monitoring in pregnancy
Breastfeeding	Low milk levels, generally safe	Moderate milk levels, monitor infant

FEATURE	VALPROATE (SODIUM VALPROATE)	LAMOTRIGINE
Drug interactions	Inhibits CYP2C9/UGT, increases LTG, phenobarbital	Affected by enzyme inducers (CBZ, PHT → halve levels) and VPA (double levels)
Monitoring	LFTs, FBC, drug levels, weight	Drug levels (especially in pregnancy); rash watch
Suicide risk	FDA black box (class warning)	FDA black box (class warning)
Bottom line for young woman with epilepsy	Avoid if possible , if essential: PREVENT, folic acid 5mg, minimum dose	Preferred , lowest teratogenicity; adjust for OCP interaction

PYQ Frequency Analysis

Analysis based on PG exams MD Psychiatry Paper IV question patterns, PG theory papers, and PG exams PG entrance patterns. Covers 17+ years of available data.

EXAM STRATEGY

This chapter identifies WHERE to spend your time. High-frequency topics in bold. If a topic has appeared 3+ times, it is near-certain to appear again. Focus 70% of revision time on Tier 1 and Tier 2 topics.

SECTION 1: Master Frequency Table

TOPIC	ESTIMATED FREQUENCY	TIER	QUESTION TYPE	MARKS
Postictal psychosis	★★★★★ Very High	1	Long answer, short note	10, 5
PNES / Pseudoseizures	★★★★★ Very High	1	Long answer, differentiation	10, 5
AEDs as mood stabilisers (VPA, CBZ, LTG)	★★★★★ Very High	1	Long answer, short note	10, 5
Psychiatric effects of AEDs	★★★★★ Very High	1	Long answer, table	10, 5
Depression in epilepsy	★★★★☆ High	1	Short note, long answer	5, 10
Schizophrenia-like psychosis of epilepsy	★★★★☆ High	1	Long answer, short note	10, 5
Seizure classification (ILAE)	★★★★☆ High	1	Short note, part of long answer	5
Forced normalisation / Landolt	★★★★☆ High	1	Short note	5
Temporal lobe epilepsy & psychiatry	★★★★☆ High	1	Long answer	10
Geschwind syndrome	★★★☆☆ Moderate	2	Short note	5

TOPIC	ESTIMATED FREQUENCY	TIER	QUESTION TYPE	MARKS
NDDI-E	★★★☆☆ Moderate	2	Short note, MCQ	5
EEG in psychiatry	★★★☆☆ Moderate	2	Short note	5
West syndrome	★★★☆☆ Moderate	2	Short note	5
Lennox-Gastaut syndrome	★★★☆☆ Moderate	2	Short note	5
JME	★★★☆☆ Moderate	2	Short note	5
Women with epilepsy / teratogenicity	★★★☆☆ Moderate	2	Short note, long answer	5, 10
Status epilepticus management	★★★☆☆ Moderate	2	Short note, protocol	5
Interictal dysphoric disorder	★★☆☆☆ Lower	3	Short note	5
Catamenial epilepsy	★★☆☆☆ Lower	3	Short note	5
Epilepsy surgery & psychiatric outcomes	★★☆☆☆ Lower	3	Short note	5
Ictal fear	★★☆☆☆ Lower	3	Part of larger answer	
Driving and epilepsy	★★☆☆☆ Lower	3	Short note	5
Anti-NMDAR encephalitis	★★☆☆☆ Lower	3	Short note	5
Childhood absence epilepsy	★★☆☆☆ Lower	3	Short note	5

SECTION 2: Tier 1 Topics: Highest Priority

Topic 1: Postictal Psychosis

Estimated appearances: 4–6 times in 17 years

Why it's Tier 1: Combines clinical psychiatry (psychosis management), neuropsychiatry (peri-ictal phenomena), and pharmacology (antipsychotics in epilepsy). Examiners love it

because it tests integration.

How it's been asked:

- "Describe postictal psychosis. Discuss its management." (10 marks)
- "Write a short note on postictal psychosis." (5 marks)
- "What is the lucid interval? Discuss its clinical significance." (5 marks)
- Part of: "Classify psychiatric phenomena in epilepsy."

What the marking key expects:

1. Definition with lucid interval prominently stated
2. Epidemiology (7–10% TLE)
3. Clinical features table (mood, hallucinations, EEG, duration)
4. Risk factors (bilateral foci, prior PIP)
5. Pathophysiology (forced normalisation / dopamine)
6. Management (antipsychotic choice, aripiprazole / olanzapine, avoid clozapine; AED optimisation; psychoeducation)
7. Prognosis (15% risk of chronic interictal psychosis with recurrence)

EXAM PEARL

The examiner wants to see "lucid interval 24–48 hours" in the FIRST paragraph. If you don't mention it early, marks bleed.

Topic 2: PNES / Psychogenic Non-Epileptic Seizures

Estimated appearances: 4–6 times in 17 years

Why it's Tier 1: Tests clinical differentiation skill, psychiatric formulation, and management of a medically complex patient. Also tests awareness of FND framework.

How it's been asked:

- "Compare epileptic seizures with pseudoseizures." (10 marks)
- "Discuss the management of PNES." (10 marks)
- "What is the gold standard for diagnosing PNES? Discuss clinical features." (5–10 marks)
- "Write a short note on psychogenic non-epileptic seizures." (5 marks)

What the marking key expects:

1. Definition and preferred terminology (PNES, functional seizures, not pseudoseizures)
2. Epidemiology (20–30% of EMU referrals; 7-year diagnostic delay)
3. Clinical differentiation table (semiology, EEG, postictal, eye position)
4. Gold standard = Video-EEG with captured event

5. Psychiatric comorbidity profile (depression, PTSD, BPD)
6. Disclosure framework (what to say, what NOT to say)
7. Management (CBT first-line; treat comorbidities; AED withdrawal)
8. Prognosis

EXAM STRATEGY

Always state gold standard early. Always mention 10–30% dual diagnosis (comorbid epilepsy). Always use the term PNES, not pseudoseizures. These are easy marks that candidates routinely miss.

Topic 3: AEDs as Mood Stabilisers

Estimated appearances: 4–5 times in 17 years

Why it's Tier 1: Bridges neurology and psychiatry pharmacology. Extremely practical. Also connects to teratogenicity and drug interactions.

How it's been asked:

- "Discuss the role of anticonvulsants in psychiatry." (10 marks)
- "Write about valproate as a mood stabiliser." (5–10 marks)
- "Compare valproate and lamotrigine in bipolar disorder." (10 marks)
- "Discuss carbamazepine in psychiatry." (5 marks)

Key content points:

- Valproate: BD-I mania first-line; mechanism; teratogenicity; PREVENT
- Carbamazepine: BD (especially rapid cycling, dysphoric); enzyme induction
- Lamotrigine: Bipolar depression (best evidence); rash; OCP interaction
- The three together: VaLCa (Valproate + Lamotrigine + Carbamazepine)

Topic 4: Psychiatric Side Effects of AEDs

Estimated appearances: 4–5 times in 17 years

Why it's Tier 1: Pure pharmacology with direct clinical application. Every resident will encounter this.

How it's been asked:

- "Discuss the psychiatric side effects of antiepileptic drugs." (10 marks)
- "Write a note on levetiracetam and its psychiatric effects." (5 marks)
- "What are the cognitive effects of topiramate?" (5 marks)
- "Discuss phenobarbital and depression." (5 marks)

The examiner's three key drugs:

1. Levetiracetam, irritability / aggression / psychosis (10%)
2. Topiramate, cognitive impairment ("Dopamax"), word-finding
3. Phenobarbital, depression (worst AED for depression)

Plus: Valproate teratogenicity, vigabatrin forced normalisation, FDA black box for all AEDs.

Topic 5: Depression in Epilepsy

Estimated appearances: 3–4 times in 17 years

How it's been asked:

- "Discuss depression in epilepsy." (10 marks)
- "Write a note on NDDI-E." (5 marks)
- "What is the bidirectional relationship between epilepsy and depression?" (5 marks)

Key content requirements:

- Bidirectional relationship (both increase risk of the other, shared neurobiology)
 - Prevalence 30–50% in TLE
 - NDDI-E (6 items, cutoff ≥ 15 , preferred over PHQ-9 in epilepsy)
 - Antidepressants in epilepsy: SSRIs safe; bupropion contraindicated; TCAs avoid
 - Suicide risk (5× higher)
 - FDA 2008 AED suicidality warning
-

Topic 6: SLPE / Interictal Psychosis

Estimated appearances: 3–4 times in 17 years

How it's been asked:

- "Describe schizophrenia-like psychosis of epilepsy." (10 marks)
- "How does interictal psychosis differ from schizophrenia?" (10 marks)
- "Write a note on Slater and Beard (1963)." (5 marks)

Non-negotiable content:

- Slater & Beard 1963, cite this
 - "Positive without negative" pattern
 - Preserved affect (warmth), most distinctive
 - No family history of schizophrenia
 - Appears 10–15 years after epilepsy onset
-

SECTION 3: Tier 2 Topics: Important, Appear Regularly

Topic 7: Forced Normalisation / Landolt

How asked: "Write a short note on forced normalisation." (5 marks)

Must include: Landolt 1953; EEG normalisation when seizures stop; alternative psychosis (Tellenbach); AEDs implicated (vigabatrin, ethosuximide); management (reduce AED + antipsychotic); clinical implication (do NOT increase AED).

Topic 8: ILAE Seizure Classification

How asked: "Classify seizures according to ILAE 2017." (5 marks, or as part of a 10-mark TLE question)

Must include: Three levels (seizure type, epilepsy type, syndrome); focal (aware/impaired/bilateral), generalised (motor/non-motor), unknown; replace old terms with new.

Topic 9: Temporal Lobe Epilepsy and Psychiatry

How asked: "Discuss the psychiatric relevance of temporal lobe epilepsy." (10 marks)

Must include: MTLE features; aura types; psychiatric comorbidities (depression 30–50%, anxiety 25–40%, psychosis 5–10%); Geschwind syndrome; ictal fear; peri-ictal psychoses; PNES overlap.

Topic 10: Women with Epilepsy / Teratogenicity

How asked: "Discuss management of epilepsy in pregnancy." / "Write about teratogenicity of AEDs." (10 marks, 5 marks)

Must include: Valproate hierarchy; lamotrigine preferred; folic acid 5 mg; OCP interactions; pregnancy AED level monitoring; fetal anomaly scans; breastfeeding guidance.

Topic 11: EEG in Psychiatry

How asked: "Discuss the role of EEG in psychiatric practice." (5–10 marks)

Must include: Normal rhythms (table); epileptiform patterns; delirium (diffuse slowing); NCSE; PNES (video-EEG); clozapine monitoring; CJD (PSWCs); drug effects (benzodiazepine → beta).

Topic 12: Status Epilepticus

How asked: "Outline the management of status epilepticus." (5–10 marks)

Must include: ILAE 2015 definition (≥ 5 min); time-based protocol; benzodiazepines first (doses); second-line (LEV, VPA, phenytoin); refractory (ICU, anaesthetic); psychiatric relevance (NCSE).

Topic 13: West Syndrome and LGS

How asked: Usually "short note" (5 marks each)

West, must include: Triad (spasms + hypsarrhythmia + regression); age (3–12 months); ACTH/vigabatrin; ASD and ID outcomes.

LGS, must include: Triad (multiple seizure types + slow SWD < 2.5 Hz + ID); tonic seizures hallmark; drop attacks; drug resistance; psychiatric burden.

SECTION 4: Tier 3 Topics: Lower Frequency, Include if Time Permits

TOPIC · WHAT TO COVER

Interictal dysphoric disorder Blumer (2004); 8 symptoms (DEAF + PFIE); not DSM; intermittent dysphoric quality

Catamenial epilepsy 3 patterns (C1 / C2 / C3); mechanism (estrogen / progesterone); treatment

Epilepsy surgery outcomes ATL; 70% seizure-free; de novo depression; forced normalisation post-surgery

Driving & epilepsy India: seizure-free 2 years required; document counselling

Anti-NMDAR encephalitis Most common autoimmune encephalitis; ovarian teratoma; sequence; antibody test; treatment

Childhood absence epilepsy 3 Hz SWD; misdiagnosed as ADHD; hyperventilation test; ethosuximide

Ictal fear Most common ictal emotion; amygdala origin; vs. panic disorder

JME Triad (MAG); morning myoclonus; sleep deprivation; lifelong; VPA vs. LTG choice

SECTION 5: Question Pattern Analysis by Year-Type

Common Long Answer (10-mark) Patterns

PATTERN · TOPICS THAT FIT

"Describe X. Discuss its management." Postictal psychosis, PNES, status epilepticus, depression in epilepsy

"Compare X and Y." PNES vs. epileptic seizures; SLPE vs. schizophrenia; VPA vs. LTG

"Discuss the psychiatric aspects of X." TLE, epilepsy broadly, AEDs

"Discuss the role of X in Y." AEDs in psychiatry, EEG in psychiatry

"A patient with epilepsy presents with psychosis. Discuss your approach." Peri-ictal psychoses classification + management

Common Short Note (5-mark) Patterns

PATTERN · LIKELY TOPICS

Eponymous phenomena Geschwind syndrome, Landolt phenomenon, Slater & Beard

Screening tools NDDI-E, GAD-7 in epilepsy

Specific syndromes West, LGS, JME, CAE

Specific AED effects Levetiracetam, topiramate, phenobarbital

Clinical concepts Forced normalisation, catamenial epilepsy, lucid interval

SECTION 6: High-Yield Facts That Appear as MCQs or One-Liners

FACT · ANSWER

Most common ictal emotion Fear

Landolt's phenomenon described in 1953

Gold standard for PNES diagnosis Video-EEG with captured event

NDDI-E cutoff for probable MDD ≥ 15 (out of 24)

Why not PHQ-9 in epilepsy? Somatic items overlap with AED side effects

Most psychiatrically relevant epilepsy syndrome Temporal lobe epilepsy (MTLE)

AED with highest psychiatric side effect burden (newer AEDs) Levetiracetam

Most proconvulsant antidepressant Bupropion

Safest antidepressant class in epilepsy SSRIs (sertraline, escitalopram)

Safest antipsychotic in epilepsy Aripiprazole

Most dangerous antipsychotic in epilepsy Clozapine

Clozapine + carbamazepine, why contraindicated? Both cause agranulocytosis independently

Most teratogenic AED Valproate

Least teratogenic common AED Lamotrigine

Valproate NTD risk 1–2% (vs. 0.05% baseline)

Folic acid dose for WWE on AEDs 5 mg / day (start 3 months pre-conception)

EEG finding in delirium Diffuse slowing (theta / delta)

EEG finding in CJD Periodic sharp wave complexes (PSWCs) 1–2 Hz

EEG finding in childhood absence 3 Hz generalised spike-wave discharge

EEG finding in West syndrome Hypsarrhythmia

EEG finding in LGS Slow spike-wave < 2.5 Hz

Seizure-free period for driving in India 2 years

Lucid interval in postictal psychosis 24–48 hours

"Alternative psychosis", coined by Tellenbach (1965)

Slater & Beard study year 1963

SLPE, key negative symptom feature Negative symptoms ABSENT / MILD

SLPE, key affective feature Affect PRESERVED (warm)

IDD described by Blumer (2004)

Most common structural cause of MTLE Hippocampal sclerosis

First-line treatment for West syndrome (TSC) Vigabatrin

First-line treatment for West syndrome (non-TSC) ACTH

Most common autoimmune encephalitis Anti-NMDAR encephalitis

Anti-NMDAR encephalitis, associated tumour Ovarian teratoma (40%)

LGS treatment for drop attacks specifically Rufinamide, valproate, clobazam

FDA year for AED suicidality warning 2008

JME, most effective AED Valproate

Catamenial pattern most common C1 (perimenstrual)

OCP reduces which AED level by ~50%? Lamotrigine

Valproate doubles levels of which AED? Lamotrigine

Postictal psychosis prevalence in TLE 7–10%

Risk of chronic interictal psychosis after recurrent PIP ~15%

PNES, average diagnostic delay 7 years

Prolactin, elevated after which seizure types? GTC and complex partial (NOT absence, NOT frontal)

SECTION 7: Predicted High-Probability Questions for 2026 Exit Exam

EXAM STRATEGY

These are probabilistic, not guaranteed. Based on recency, clinical relevance, and gap analysis (topics not asked in recent years are due).

PRIORITY	PREDICTED QUESTION	RATIONALE
1	"Discuss postictal psychosis, features, pathophysiology, and management." (10 marks)	Perennial favourite; covers peri-ictal phenomena cleanly
2	"Compare epileptic seizures with PNES. Discuss management of PNES." (10 marks)	Due again; integrates neuropsychiatry + FND
3	"Discuss psychiatric side effects of antiepileptic drugs with special reference to levetiracetam and topiramate." (10 marks)	Newer AEDs increasingly prescribed; examiners track this
4	"Discuss Women with Epilepsy, teratogenicity, contraception, and pregnancy management." (10 marks)	MHRA 2018 valproate guidance makes this highly topical
5	"Write a note on forced normalisation. Describe its clinical implications." (5 marks)	Eponymous, elegant, consistently appears

PRIORITY	PREDICTED QUESTION	RATIONALE
6	"Discuss depression in epilepsy, prevalence, screening, and treatment." (10 marks)	Bidirectional relationship is a strong conceptual question
7	"Describe the schizophrenia-like psychosis of epilepsy. How does it differ from schizophrenia?" (10 marks)	Classic Slater & Beard, never goes out of style
8	"Write a short note on the NDDI-E." (5 marks)	Screening tools increasingly asked; specific to epilepsy
9	"Discuss the role of EEG in psychiatric practice." (10 marks)	Cross-cutting topic; tests neuropsychiatric integration
10	"Discuss Lennox-Gastaut syndrome with its psychiatric implications." (5–10 marks)	Epileptic encephalopathies underasked recently

SECTION 8: Topics to COMBINE in Answers

Some topics appear individually but are better answered together, mentioning them in a related answer earns extra marks.

PRIMARY TOPIC · WHAT TO INCLUDE FROM RELATED TOPICS

TLE and psychiatry ILAE classification + peri-ictal phenomena + Geschwind + SLPE + postictal psychosis + depression

Depression in epilepsy Bidirectional relationship + NDDI-E + IDD + antidepressant safety + suicide + AED contribution

AED psychiatric effects Levetiracetam + topiramate + phenobarbital + forced normalisation + AED-psychotropic interactions

PNES management Diagnosis (video-EEG) + disclosure + CBT + treat comorbidities + AED withdrawal + prognosis

Postictal psychosis Lucid interval + forced normalisation + SLPE (progression) + antipsychotic in epilepsy

Revision note: Cross-reference with D2-ModelAnswers.md for fully written-out versions of the top predicted questions.

Quick Review

30 rapid-fire question-answer pairs covering all high-yield Epilepsy & Psychiatry topics

EXAM STRATEGY

Use this file for active recall, cover the answer column, read the question, attempt the answer from memory, then reveal. Do this 48h before the exam. Each answer is deliberately concise, expand in writing practice using D2-ModelAnswers.md.

RAPID-FIRE Q&A: ALL 30 PAIRS

Q1

What is the pathognomonic feature that distinguishes postictal psychosis from other peri-ictal psychoses?

KEY INSIGHT

A: The **lucid interval**, a clear period of 24–48 hours between the seizure cluster and onset of psychosis. The patient appears recovered, then develops acute psychosis. This feature is unique to postictal psychosis and is the single most testable fact about this condition.

Q2

Slater and Beard (1963) described schizophrenia-like psychosis of epilepsy. What are the **TWO** most important features that distinguish it from schizophrenia?

KEY INSIGHT

A: 1. **Negative symptoms are absent or mild** (schizophrenia typically has prominent negative symptoms) 2. **Affect is preserved and warm** (schizophrenia typically shows blunted / flat affect) Additional distinguishing features: No elevated family history of schizophrenia; premorbid function often normal; onset 10–15 years after epilepsy onset.

Q3

What is forced normalisation? Who described it and when?

KEY INSIGHT

A: Forced normalisation (Heinrich **Landolt, 1953**) is the paradoxical normalisation of EEG coinciding with the emergence of psychiatric symptoms (most commonly psychosis) when epileptic seizure activity is suppressed, either spontaneously or pharmacologically. The EEG, previously showing epileptiform activity, becomes normal while psychosis emerges. Tellenbach (1965) described the clinical counterpart as "alternative psychosis."

Q4

Which AED carries the highest risk of inducing forced normalisation?

KEY INSIGHT

A: Vigabatrin (highest risk), followed by ethosuximide, then lamotrigine. Mechanism: excessive GABAergic enhancement may disrupt limbic networks regulating psychotic threshold.

Q5

What is the gold standard for diagnosing PNES?

KEY INSIGHT

A: Video-EEG telemetry with a captured typical event showing normal EEG during the event. No clinical feature alone is sufficient for diagnosis. The combination of video semiology + simultaneous normal EEG confirms the diagnosis.

Q6

Name the 6 items of the NDDI-E and its cutoff score for probable MDD.

KEY INSIGHT

A: Six items (each scored 1–4, total 6–24): 1. Everything is a struggle 2. Nothing I do is right 3. Feel guilty 4. I'd be better off dead 5. Frustrated 6. Difficulty finding pleasure **Cutoff ≥ 15** = probable MDD (sensitivity 81%, specificity 90%) Memory: **G**DN**F**EP, Guilty, Dead (better off), Nothing right, Frustrated, Everything a struggle, Pleasure difficulty.

Q7

Why is NDDI-E preferred over PHQ-9 for screening depression in epilepsy?

KEY INSIGHT

A: PHQ-9 contains somatic items (fatigue, sleep disturbance, concentration difficulties, appetite changes) that **overlap with AED side effects and postictal effects**, producing false positives. NDDI-E focuses exclusively on cognitive-emotional items, avoiding somatic confounders.

Q8

Describe the bidirectional relationship between epilepsy and depression.

KEY INSIGHT

A: - **Epilepsy → Depression**: TLE causes limbic-serotonergic disruption; AED side effects (phenobarbital, topiramate, LEV); psychosocial burden (stigma, driving restrictions). Depression in ~30–50% of TLE. - **Depression → Epilepsy**: Prior depression is an independent risk factor for developing epilepsy (RR ~1.5–2.0). Shared mechanisms: serotonin dysregulation, HPA axis hyperactivity, hippocampal atrophy, neuroinflammation. - **Shared neurobiology**: Both involve serotonin, GABA, glutamate dysregulation and hippocampal pathology.

Q9

Which antidepressant is contraindicated in epilepsy and why?

KEY INSIGHT

A: **Bupropion**, it is the most proconvulsant antidepressant, with dose-dependent seizure risk. It is contraindicated in patients with epilepsy. TCAs and clomipramine are also high-risk and should be avoided. SSRIs (sertraline, escitalopram) are the safest antidepressants in epilepsy.

Q10

Rank the following antipsychotics from **LOWEST** to **HIGHEST** proconvulsant risk: Clozapine, Risperidone, Aripiprazole, Olanzapine, Quetiapine.

KEY INSIGHT

A: (Low → High) **Aripiprazole < Risperidone < Olanzapine ≈ Quetiapine < Clozapine**
Clozapine: 3–5% seizure risk at high doses, highest of all antipsychotics. Aripiprazole: safest choice when an antipsychotic is needed in epilepsy.

Q11

Why is clozapine + carbamazepine absolutely contraindicated?

KEY INSIGHT

A: Dual agranulocytosis risk. Both clozapine and carbamazepine independently suppress bone marrow and can cause agranulocytosis. The combination dramatically increases this risk and is an absolute contraindication. Additionally, carbamazepine (strong CYP3A4 inducer) reduces clozapine plasma levels by 40–60%, creating a pharmacokinetic problem on top of the safety issue.

Q12

What are the five features of Geschwind syndrome?

KEY INSIGHT

A: The 5 H's: 1. **H**ypergraphia, compulsive excessive writing (most specific feature) 2. **H**yperreligiosity, intense spiritual preoccupation 3. **H**yposexuality, decreased (not increased) sexual interest 4. **H**urts to leave / Viscosity, circumstantial, sticky thinking 5. **H**eightedened / deepened affect, everything feels profound Associated with TLE, particularly MTLE. Existence as a distinct syndrome is debated.

Q13

What is the ILAE 2017 replacement for "complex partial seizure"?

KEY INSIGHT

A: Focal seizure with impaired awareness. The 2017 ILAE classification replaced "complex partial" with this term. "Simple partial" became "focal aware seizure." "Secondary generalised" became "focal to bilateral tonic-clonic seizure."

Q14

Describe the classic triad of West syndrome and its first-line treatments.

KEY INSIGHT

A: Triad: 1. Infantile spasms (brief flexion/extension clusters, worst on waking) 2. Hypsarrhythmia (chaotic, high-amplitude, asynchronous EEG) 3. Developmental regression/arrest **First-line:** - **ACTH**, best overall evidence - **Vigabatrin**, first-line specifically if **tuberous sclerosis complex (TSC)** is the aetiology (superior response in TSC) Age of onset: 3–12 months (peak 4–6 months). Psychiatric outcome: ASD in 30–50%, ID in 70–80%.

Q15

What is the EEG hallmark of Lennox-Gastaut syndrome?

KEY INSIGHT

A: Slow generalised spike-wave complexes at < 2.5 Hz (typically 1.5–2 Hz) on interictal EEG. During NREM sleep: **paroxysmal fast activity** (> 10 Hz, "recruiting rhythm"), highly specific for LGS. Background EEG is diffusely slow. Clinical triad: multiple seizure types (tonic hallmark + atonic drop attacks + atypical absence) + slow SWD EEG + intellectual disability.

Q16

What is the JME classic triad and its most important seizure trigger?

KEY INSIGHT

A: Triad (MAG): - Myoclonic jerks (morning, on waking, most characteristic) - Absence seizures (~30% of patients) - GTC seizures (often triggered by sleep deprivation) **Most important trigger: Sleep deprivation.** Alcohol withdrawal, photosensitivity (30–50%), and stress are secondary triggers. JME is lifelong in >80%, requires long-term AED. Valproate is most effective but teratogenic; levetiracetam and lamotrigine are alternatives for women.

Q17

What is the teratogenic risk profile of valproate?

KEY INSIGHT

A: - **Major congenital malformations:** ~10–11% (vs. 1–2% baseline) - **Neural tube defects:** 1–2% (vs. 0.05% baseline) - **Other structural:** Cardiac defects, orofacial clefts, limb anomalies, hypospadias - **Neurodevelopmental (most important):** IQ reduction ~7–9 points; autism risk 6×; ADHD increased, these effects are dose-dependent and independent of structural malformations **MHRA 2018 / 2024:** Valproate MUST NOT be prescribed to girls/women of childbearing potential without PREVENT programme enrolment and annual review. Folic acid 5 mg/day must be started ≥3 months before conception.

Q18

How does an oral contraceptive pill (OCP) interact with lamotrigine?

KEY INSIGHT

A: The OCP (combined, oestrogen-containing) **reduces lamotrigine plasma levels by approximately 50%** through induction of lamotrigine glucuronidation (UGT enzymes). This can cause **breakthrough seizures** when the OCP is started and **lamotrigine toxicity** (rash, dizziness, diplopia) when it is stopped (e.g., pill-free week). Women on lamotrigine + OCP require dose monitoring and adjustment. Conversely, enzyme-inducing AEDs (carbamazepine, phenytoin, phenobarbital) reduce OCP efficacy, IUD is preferred contraception for women on these AEDs.

Q19

What is the Indian regulatory requirement for driving after epilepsy?

KEY INSIGHT

A: Under the Motor Vehicles Act 1988 and Central Motor Vehicles Rules 1989, a person with epilepsy must be **seizure-free for ≥ 2 years** (on or off medication) to be eligible for a driving licence. This is more stringent than the UK (1 year). Clinical obligation: document driving counselling at every visit, record the advice given, and advise reporting to the licensing authority if the patient refuses to stop driving against medical advice.

Q20

Describe the 3 Hz spike-wave discharge, what condition is it pathognomonic of?

KEY INSIGHT

A: **3 Hz generalised spike-wave discharge (SWD)**, regular, bilaterally synchronous, frontally dominant, is pathognomonic of **Childhood Absence Epilepsy (CAE)**. It occurs in bursts of 3–30 seconds, correlates precisely with clinical absences, is provoked by hyperventilation, and is suppressed by eye opening (photic driving). The regularity and frequency (exactly 3 Hz) distinguish it from the slower, irregular SWD of Lennox-Gastaut (<2.5 Hz) and faster polyspike-wave of JME (4–6 Hz).

Q21

What is the most common form of autoimmune encephalitis and how does it present psychiatrically?

KEY INSIGHT

A: **Anti-NMDAR encephalitis** (antibodies against GluN1 subunit of NMDA receptor).
Psychiatric presentation sequence: 1. Prodrome: Fever, headache, malaise 2. **Psychiatric phase:** Agitation, psychosis, behavioural disturbance, often the presenting complaint to psychiatry 3. Seizures (focal and generalised) 4. Movement disorders (orofacial dyskinesias, choreoathetosis) 5. Autonomic instability 6. Decreased consciousness → coma
Demographics: Young women; 40% associated with ovarian teratoma. Diagnosis: CSF anti-GluN1 antibodies (more sensitive than serum). Treatment: Immunotherapy (steroids, IVIG, plasmapheresis) + tumour removal if present.

Q22

What is the ILAE 2015 operational definition of convulsive status epilepticus?

KEY INSIGHT

A: A seizure lasting ≥ 5 minutes OR two or more seizures without full recovery of consciousness between them. This replaced the older "30-minute" definition. The 30-minute threshold (T2) represents when neuronal injury begins, not the operational threshold for treatment. Clinical implication: treat any seizure still ongoing at 5 minutes as status epilepticus, do not wait for 30 minutes.

Q23

Name the second-line AEDs for status epilepticus with doses.

KEY INSIGHT

A: | Drug | Dose | |-----|-----| | **Levetiracetam IV** | 60 mg/kg (max 4500 mg), preferred: minimal interactions, no cardiac monitoring | | **Valproate IV** | 40 mg/kg (max 3000 mg), avoid in pregnancy, hepatic disease, mitochondrial disorders | | **Phenytoin IV** | 20 mg/kg (max 1500 mg), cardiac monitoring required; slow infusion | | **Lacosamide IV** | 200–400 mg, emerging option | Used at 20–40 minutes if first-line benzodiazepines fail.

Q24

What is Interictal Dysphoric Disorder (IDD)? Name its 8 symptoms.

KEY INSIGHT

A: Described by Blumer (2004), an epilepsy-specific mood disorder characterised by intermittent dysphoria that does not map cleanly onto DSM-5 diagnoses. Distinct from MDD by its paroxysmal, mixed quality. **8 symptoms in 2 groups:** *Depressive (DEAF):* - Depressive mood - Energia absent (anergia) - Ache/pain (somatic) - Falling asleep difficulty (insomnia) *Labile/Irritable (PFIE):* - Paroxysmal affective disturbances - Fear/anxiety (episodic) - Irritability - Euphoric moods (brief, episodic) Key distinction from MDD: The brief euphoric periods and intermittent course.

Q25

What is NCSE and why is it a psychiatric emergency?

KEY INSIGHT

A: Non-Convulsive Status Epilepticus (NCSE), prolonged (≥ 10 minutes) epileptic activity without major motor manifestations, manifesting as altered consciousness, behavioural change, or psychosis. Requires EEG confirmation. **Psychiatric emergency because:** - Can present as **acute psychosis**, confusion, mutism, bizarre behaviour, mimicking primary psychiatric disorders - Missed diagnosis = ongoing neuronal injury - Any patient with known epilepsy presenting with acute psychiatric symptoms + fluctuating consciousness + subtle motor automatisms → **get an EEG immediately** **Diagnostic trial:** IV lorazepam 0.1 mg/kg, if clinical and EEG improvement = confirms NCSE. Treat aggressively as per SE protocol.

Q26

Describe the three patterns of catamenial epilepsy (Herzog classification).

KEY INSIGHT

A: | Pattern | Timing | Mechanism | |-----|-----|-----| | **C1** Perimenstrual | Days -3 to +3 (around menstruation) | Abrupt progesterone withdrawal → relative oestrogen dominance | | **C2** Periovulatory | Days 10-13 (ovulation) | Oestrogen surge (proconvulsant) at mid-cycle | | **C3** Anovulatory | Days 10-28 (entire luteal phase) | Chronically low progesterone throughout the second half | **Mechanism:** Oestrogen is proconvulsant (lowers seizure threshold); progesterone is anticonvulsant (positive allosteric modulator of GABA-A). Treatments: acetazolamide (perimenstrual), progesterone supplementation, continuous OCP.

Q27

What psychiatric sequelae can occur after epilepsy surgery (anterior temporal lobectomy)?

KEY INSIGHT

A: - **De novo depression:** 5-20% develop new depression within the first year post-surgery (most common psychiatric complication) - **De novo psychosis:** 1-5%; higher risk if history of postictal psychosis or bilateral foci - **Forced normalisation:** Can occur post-surgery when seizures stop, psychosis emerges paradoxically - **Anxiety improvement:** Usually improves with seizure freedom - **Quality of life improvement:** Generally positive with Engel I outcome (seizure-free ~70% in MTLE with hippocampal sclerosis) Pre-existing depression is the strongest predictor of poor post-surgical psychiatric outcome.

Q28

What are the psychiatric comorbidities of tuberous sclerosis complex (TSC)?

KEY INSIGHT

A: | Comorbidity | Prevalence in TSC | |-----|-----| | ASD | 40–50% (higher than in West syndrome without TSC) | | Intellectual disability | 50% (varies widely by genotype/tuber burden) | | ADHD | 30–50% | | Anxiety disorders | 30–40% | | OCD features | 20–30% | | Aggression/behavioural problems | Common | TSC is caused by mutations in TSC1 (hamartin) or TSC2 (tuberin), mTOR pathway dysregulation. Everolimus (mTOR inhibitor) reduces subependymal giant cell astrocytomas and may modestly improve cognitive outcomes. Early vigabatrin (even pre-symptomatic) reduces ASD risk in TSC-associated infantile spasms.

Q29

Classify EEG rhythms from fastest to slowest and state one clinical association for each.

KEY INSIGHT

A:

KEY INSIGHT

| Rhythm | Frequency | Key Clinical Association | |-----|-----|-----| | **Gamma** | >30 Hz | Cognitive processing; research | | **Beta** | 13–30 Hz | Alert state; increased by benzodiazepines | | **Alpha** | 8–13 Hz | Relaxed, eyes closed; reduced in depression (frontal asymmetry) | | **Theta** | 4–7 Hz | Drowsiness; temporal theta in TLE interictal | | **Delta** | 0.5–3 Hz | Deep sleep; **diffuse = delirium; focal = structural lesion** | CJD: Periodic sharp wave complexes (PSWCs) at 1–2 Hz, pathognomonic. Hypsarrhythmia: Chaotic, asynchronous delta + multifocal spikes, West syndrome.

Q30

Summarise the management of PNES in 6 steps.

KEY INSIGHT

A: 1. **Establish diagnosis definitively**, video-EEG telemetry with captured event (do not diagnose on clinical grounds alone) 2. **Disclose the diagnosis therapeutically**, lead with what it IS (functional nervous system disorder); acknowledge it is real, disabling, not deliberate; never say "nothing is wrong" or "it's all in your head" 3. **Psychotherapy, primary treatment**, seizure-specific CBT (strongest evidence); trauma-focused CBT or EMDR if PTSD present 4. **Treat psychiatric comorbidities**, SSRIs for depression; trauma-focused therapy for PTSD; DBT skills for BPD 5. **Gradual AED withdrawal** (if no comorbid epilepsy), in collaboration with neurology; prepare patient for possible short-term increase in events (extinction burst) 6. **Prognosis counselling**, 30–40% achieve seizure freedom; 50% substantial improvement; poorer outcomes with longer diagnostic delay, secondary gain, comorbid personality disorder

BONUS: 10 One-Line Facts for Last-Minute Revision

· FACT

- 1 Most common ictal emotion = **fear** (amygdala)
- 2 Postictal psychosis lucid interval = **24–48 hours**
- 3 Landolt described forced normalisation in **1953**
- 4 SLPE: **positive symptoms preserved, negative symptoms absent, affect warm**
- 5 NDDI-E cutoff = **≥ 15** (out of 24)
- 6 Most proconvulsant antidepressant = **bupropion**
- 7 Safest antipsychotic in epilepsy = **aripiprazole**
- 8 Most teratogenic AED = **valproate** (~10% MCM)
- 9 Gold standard for PNES = **video-EEG** with captured event
- 10 Indian driving law: seizure-free **2 years** required

Cross-reference: D1 (Study Notes) for depth · D2 (Model Answers) for written practice · D3 (Mnemonics) for retrieval cues · D4 (Comparisons) for differential tables · PYQ Analysis for question prediction

Dementias

Paper IV · Neurology, Medicine & Recent Advances. Six study modes, from notes to quick review.

Study Notes

Sources: Kaplan & Sadock's Synopsis of Psychiatry (12th Ed), Oxford Textbook of Psychiatry, Cummings' Neuropsychiatry and Behavioral Neuroscience

PART 1: OVERVIEW AND DEFINITIONS

1.1 Definition and Conceptual Evolution

Dementia, from Latin *demens* (without mind), refers to an acquired, persistent impairment in cognition that represents a decline from a previously higher level of functioning and is severe enough to interfere with daily activities.

The term "dementia" has been progressively replaced in formal classification systems:

- **DSM-5 (2013):** Replaced with **Major Neurocognitive Disorder (Major NCD)** and **Mild Neurocognitive Disorder (Mild NCD)**
- **ICD-11 (2022):** Uses **Dementia** as the overarching term but categorizes subtypes using neurocognitive disorder framework
- The shift reflects: (a) destigmatization, (b) inclusion of milder presentations, (c) recognition of early intervention windows

EXAM PEARL

DSM-5 uses "Major/Mild Neurocognitive Disorder", NOT "dementia." But ICD-11 still retains "dementia" as a term. Know both systems. Examiners test this distinction.

1.2 DSM-5 Diagnostic Criteria

MAJOR NEUROCOGNITIVE DISORDER (MAJOR NCD)

A. Evidence of significant cognitive decline from a previous level of performance in one or more cognitive domains:

- Complex attention
- Executive function
- Learning and memory
- Language
- Perceptual-motor
- Social cognition

B. Cognitive deficits interfere with independence in everyday activities (bills, medications, etc.)

C. Not exclusively during delirium

D. Not better explained by another mental disorder (depression, schizophrenia)

MILD NEUROCOGNITIVE DISORDER (MILD NCD)

Same as above but:

- **Modest** (not significant) decline
- Deficits do NOT interfere with independence (may require greater effort or compensatory strategies)

EXAM PEARL

The key distinguishing feature between Major and Mild NCD is **functional impairment**, not severity of cognitive testing scores alone.

1.3 ICD-11 Criteria for Dementia

ICD-11 requires:

1. Decline from a previous level of cognitive functioning
2. Impairment in two or more cognitive domains (memory, executive function, attention, language, visuospatial abilities)
3. Interference with ability to function independently in daily activities
4. Not due to normal ageing, delirium, or another mental/behavioral disorder

ICD-11 Subtypes of Dementia:

- 6D80 Dementia due to Alzheimer disease
- 6D81 Dementia due to cerebrovascular disease
- 6D82 Dementia due to Lewy body disease
- 6D83 Dementia due to frontotemporal lobar degeneration
- 6D84 Dementia due to psychoactive substances
- 6D85 Dementia due to HIV
- 6D86 Dementia due to prion disease
- 6D8Y Other specified dementia

PART 2: EPIDEMIOLOGY

2.1 Global Burden

PARAMETER · FIGURE

Global prevalence ~55 million (2023)

New cases per year ~10 million

Cases expected by 2050 ~139 million

Prevalence doubles with each 5-year age increment after 65 After 65 years

Most common type Alzheimer's disease (60-70%)

Women affected more 2:1 ratio (lifespan + hormonal factors)

2.2 India-Specific Epidemiology

EXAM PEARL

India-specific figures are frequently asked in PG exams and other MD exams. Memorize the 5.3 million figure.

PARAMETER · INDIA DATA

Estimated prevalence (2023) 5.3 million (Alzheimer's & Related Disorders Society of India, ARDSI)

Projected 2050 14+ million

Dementia prevalence (urban, 60+) 3.6-4.1%

Dementia prevalence (rural, 60+) 1.2-2.7% (under-recognized)

Vascular dementia proportion Higher in India (~30%) vs West (~20%)

Key risk factors in India Hypertension, diabetes (prevalence rising), low education, head injury

Awareness <5% of dementia cases formally diagnosed in India

Caregiver burden 85-90% of care provided by family (no formal care infrastructure)

10/66 Study (Prince et al.): Landmark study showing dementia prevalence in India at ~3.4% in those 60+. Important because it used population-based sampling and culturally validated tools.

DEMENTIA INDIA REPORT 2010: Published by ARDSI, foundational document for Indian dementia policy. Estimated 3.7 million affected (now revised upward to 5.3 million with updated data).

2.3 Risk Factors

NON-MODIFIABLE

- Age (strongest risk factor)
- Female sex
- Family history / genetics
- Down syndrome (almost universal AD by 40s)

MODIFIABLE (LANCET COMMISSION 2020: 12 MODIFIABLE RISK FACTORS)

RISK FACTOR · PAF (POPULATION ATTRIBUTABLE FRACTION)

Low education (early life) 7%

Hearing loss (midlife) 8%

Hypertension (midlife) 2%

Obesity (midlife) 1%

Smoking 5%

Depression 4%

Physical inactivity 2%

Social isolation 4%

Diabetes 1%

Excessive alcohol 1%

Air pollution 2%

Head injury 3%

Total potentially modifiable: ~40% of dementia cases

EXAM PEARL

Lancet Commission 2020 added air pollution, head injury, and excessive alcohol to the original 2017 list of 9. The combined PAF is ~40%.

PART 3: MILD COGNITIVE IMPAIRMENT (MCI)

3.1 Definition and Criteria (Petersen 2004, updated)

MCI represents the transitional zone between normal ageing and dementia.

Petersen Criteria for MCI:

1. Subjective cognitive complaint (preferably corroborated by informant)
2. Objective cognitive impairment (>1.5 SD below age/education norms on standardized tests)
3. Preserved general cognitive function
4. Intact or minimally impaired activities of daily living (ADLs)
5. Does not meet criteria for dementia

3.2 Types of MCI

TYPE	DESCRIPTION	MOST LIKELY PROGRESSION
Amnestic MCI (single domain)	Memory impairment only	Alzheimer's disease
Amnestic MCI (multiple domain)	Memory + other domains	Alzheimer's disease
Non-amnestic MCI (single domain)	One non-memory domain	Frontotemporal, DLB, or VaD
Non-amnestic MCI (multiple domain)	Multiple non-memory domains	Vascular or other

3.3 Conversion Rates

- ~10-15% of MCI cases convert to dementia per year
- After 5 years: ~50% have converted
- 20-30% of MCI revert to normal cognition
- Amnestic MCI has highest conversion risk to AD

3.4 DSM-5 Equivalent

MCI = **Mild Neurocognitive Disorder** in DSM-5

PART 4: ALZHEIMER'S DISEASE (AD)

4.1 Background

First described by Alois Alzheimer in 1906, patient Auguste Deter, 51-year-old woman with progressive memory loss, delusions, and paranoia. Autopsy revealed senile plaques and neurofibrillary tangles.

Most common cause of dementia worldwide (~60-70% of cases).

4.2 Neuropathology

GROSS PATHOLOGY

- Cortical atrophy, most prominent in:
- Hippocampus (earliest)
- Entorhinal cortex
- Parietal and temporal association cortices
- Relative sparing of primary motor and sensory cortices (until late)
- Ventricular enlargement (ex vacuo)
- Weight of brain reduced by 10-15%

MICROSCOPIC PATHOLOGY (TWO HALLMARKS)

1. Senile Plaques (Amyloid/Neuritic Plaques)

- Extracellular deposits of **beta-amyloid (A β)** peptide
- Derived from cleavage of Amyloid Precursor Protein (APP)
- Dense core surrounded by dystrophic neurites
- Two types:
- **Neuritic plaques**, with tau-positive dystrophic neurites (pathological)
- **Diffuse plaques**, less compact, less pathological significance

2. Neurofibrillary Tangles (NFTs)

- Intraneuronal accumulations of **hyperphosphorylated tau protein**
- Normal tau stabilizes microtubules; in AD, abnormal phosphorylation causes tau to aggregate
- **Paired helical filaments (PHFs)**, characteristic ultrastructure
- Stage distribution: Braak & Braak staging (I-VI)
- Stages I-II: Entorhinal cortex
- Stages III-IV: Hippocampus, limbic system
- Stages V-VI: Neocortex (correlates with clinical dementia)

ADDITIONAL PATHOLOGICAL FEATURES

- **Granulovacuolar degeneration**, in hippocampal neurons
- **Hirano bodies**, eosinophilic intraneuronal inclusions
- **Neuronal loss**, estimated 50-75% reduction in nucleus basalis of Meynert (cholinergic neurons)
- **Synaptic loss**, best correlate of cognitive decline
- **Amyloid angiopathy**, A β deposits in vessel walls

EXAM PEARL

SYNAPTIC LOSS is the best histological correlate of cognitive decline in AD, not plaque burden, not tangle count, not neuronal loss per se.

4.3 Neurochemistry

NEUROTRANSMITTER	CHANGE IN AD	CLINICAL RELEVANCE
Acetylcholine	Markedly decreased (50-90%)	Basis for cholinesterase inhibitor therapy
Noradrenaline	Decreased (locus coeruleus degeneration)	Contributes to behavioral symptoms
Serotonin	Decreased (raphe nuclei)	Depression, agitation
Glutamate	Dysregulated (excitotoxicity)	Basis for memantine
Dopamine	Relatively preserved early	Preserved insight and judgment early

4.4 The Amyloid Cascade Hypothesis (Hardy & Selkoe, 1992; revised 2002)

Core Proposition: The central event in AD pathogenesis is the abnormal accumulation of A β peptide, which triggers a cascade leading to neurodegeneration.

Sequence:

1. Imbalance between A β production and clearance
2. A β aggregation $\rightarrow$ oligomers (most toxic form) $\rightarrow$ plaques
3. Synaptic dysfunction and neuronal stress
4. Tau hyperphosphorylation and tangle formation
5. Neuroinflammation (microglial activation, astrogliosis)
6. Widespread neuronal death and synaptic loss
7. Clinical dementia

APP Processing:

- **Non-amyloidogenic pathway:** α -secretase cleaves APP within A β region $\rightarrow$ no A β formed
- **Amyloidogenic pathway:** β -secretase (BACE1) and γ -secretase cleave APP $\rightarrow$ A β 40 and A β 42
- A β 42 is more amyloidogenic and deposits earlier
- γ -secretase complex includes Presenilin-1 (PSEN1) and Presenilin-2 (PSEN2)

EXAM PEARL

A β 42 (not A β 40) is the primary species depositing in plaques. PSEN1/PSEN2 are components of gamma-secretase.

Criticisms of Amyloid Cascade Hypothesis:

- Anti-amyloid therapies (immunotherapy) have had limited clinical success
- Amyloid can be present without clinical dementia
- Tau pathology may correlate better with cognitive symptoms
- "Amyloid accumulation $\neq$ AD", necessary but may not be sufficient

Current revision: Dual-hit model, A β + tau + neuroinflammation all contribute; no single cascade

4.5 Tau Pathology

- Tau is a microtubule-associated protein encoded by **MAPT gene** (chromosome 17)
- In AD: hyperphosphorylated tau dissociates from microtubules and aggregates intraneuronally
- **Braak Staging (I-VI):** Hierarchical spread from entorhinal cortex $\rightarrow$ limbic $\rightarrow$ neocortex
- Tau PET correlates better with cognitive symptoms than amyloid PET
- Tau spreads via connected neural networks (prion-like propagation hypothesis)

4.6 Genetics of Alzheimer's Disease

GENE	CHROMOSOME	ROLE	TYPE OF AD
APP (Amyloid Precursor Protein)	21	Mutations increase A β production	Early-onset familial (~1%)
PSEN1 (Presenilin 1)	14	Most common familial AD mutation; alters γ -secretase cleavage	Early-onset familial (~5%)
PSEN2 (Presenilin 2)	1	Similar to PSEN1; less penetrant	Early-onset familial (<1%)
APOE4	19	Impairs A β clearance; increases aggregation	Late-onset sporadic (risk factor, NOT deterministic)
TREM2	6	Microglial receptor; variants increase risk	Late-onset sporadic (risk modifier)

APOE Alleles:

- APOE2: Protective
- APOE3: Neutral (most common)

- APOE4: Risk allele, 3-4x risk in heterozygotes; 8-12x in homozygotes
- APOE4 does NOT guarantee AD, it is a risk factor, NOT a deterministic mutation
- APOE4 lowers age of onset by ~7-10 years per allele

EXAM PEARL

Down Syndrome (Trisomy 21) → extra copy of APP gene → early amyloid accumulation → AD by the 4th or 5th decade in almost all cases. This is one of the strongest genetic links.

4.7 Clinical Stages of Alzheimer's Disease

NIA-AA 2018 RESEARCH FRAMEWORK (BIOLOGICAL STAGING: A/T/N)

BIOMARKER	MARKER	TEST
A (Amyloid)	A β 42↓ in CSF, amyloid PET positive	CSF, PET
T (Tau)	Phospho-tau↑ in CSF, tau PET positive	CSF, PET
N (Neurodegeneration)	Total tau↑ in CSF, FDG-PET hypometabolism, MRI atrophy	CSF, PET, MRI

Preclinical AD: A+ T- or A+ T+, no symptoms

Prodromal AD (MCI): A+ T+, mild symptoms

Dementia due to AD: A+ T+ N+, significant impairment

CLINICAL STAGING (REISBERG GLOBAL DETERIORATION SCALE / CLINICAL DEMENTIA RATING)

STAGE	GDS	CLINICAL DESCRIPTION	MMSE RANGE
Very mild (MCI)	3	Difficulty recalling names, losing items	24-30
Mild	4	Forgetting recent events, impaired complex tasks	18-23
Moderate	5	Needs help with ADLs, disoriented to time/place	12-17
Moderately severe	6	Needs help dressing, bathing, toileting; personality changes	5-11

STAGE	GDS	CLINICAL DESCRIPTION	MMSE RANGE
Severe	7	Loss of verbal abilities, incontinence, bedridden	0-4

Memory Loss Pattern in AD:

- Earliest: Episodic memory (recent events, new learning)
- Then: Semantic memory (names, facts)
- Relatively preserved until late: Remote (autobiographical) memory, procedural memory, implicit memory

CLINICAL ANCHOR

AD follows a "last in, first out" rule, the most recently learned information is lost first. This is why patients remember their wedding more clearly than what they had for breakfast.

4.8 Biomarkers

CSF BIOMARKERS (LUMBAR PUNCTURE)

BIOMARKER	CHANGE IN AD	INTERPRETATION
A β 42	Decreased	Sequestered in plaques, less in CSF
Phospho-tau (p-tau)	Increased	Active tangle formation
Total tau (t-tau)	Increased	Neurodegeneration/ neuronal injury
A β 42/A β 40 ratio	Decreased	More sensitive than A β 42 alone
p-tau/A β 42 ratio	Increased	Best overall diagnostic ratio

Sensitivity/Specificity of CSF biomarkers: ~90% / 90% for AD vs controls

NEUROIMAGING BIOMARKERS

MRI:

- Medial temporal lobe atrophy (MTA), especially hippocampus and entorhinal cortex
- **Scheltens score** for MTA (0-4): Score ≥ 2 suggests AD
- White matter changes (incidental)
- Global atrophy pattern: posterior > frontal (unlike FTD)

Amyloid PET (Florbetapir/Flutemetamol/Florbetaben):

- Positive scan: diffuse cortical amyloid accumulation

- Normal = white matter signal only
- Sensitivity ~96%, Specificity ~93% for AD pathology
- FDA-approved; expensive, not widely available in India

FDG-PET:

- Measures glucose metabolism
- AD pattern: **temporo-parietal hypometabolism** ± posterior cingulate
- Spares primary motor, sensory, visual cortex until late
- Useful for differentiating AD from FTD (frontal hypometabolism in FTD)

Tau PET (Flortaucipir/AV-1451):

- Newer; directly images tau tangles
- Correlates better with cognitive symptoms than amyloid PET
- Shows hierarchical Braak-stage pattern

BLOOD BIOMARKERS (EMERGING: 2020S)

BIOMARKER · STATUS

Plasma Aβ42/40 ratio Validated; correlates with amyloid PET

Plasma p-tau217 High diagnostic accuracy; game-changer for screening

Plasma p-tau181 Elevated in AD; widely studied

Neurofilament light chain (NfL) Marker of neurodegeneration; not AD-specific

GFAP (Glial Fibrillary Acidic Protein) Astrocytosis; elevated in AD

EXAM PEARL

Plasma p-tau217 has ~90%+ accuracy for AD diagnosis in recent trials (AHEAD, A4 studies).
Blood biomarkers may replace CSF in the next decade.

4.9 Pharmacotherapy for Alzheimer's Disease

CHOLINESTERASE INHIBITORS (CHEIS)

Mechanism: Inhibit acetylcholinesterase (and in some cases butyrylcholinesterase) → increase synaptic acetylcholine → compensate for cholinergic deficit

DRUG	TYPE	DOSE	HALF-LIFE	KEY POINTS
Donepezil (Aricept)	Selective AChE inhibitor	5mg OD → 10mg → 23mg	70 hours	Once daily; best tolerated; approved all stages

DRUG	TYPE	DOSE	HALF-LIFE	KEY POINTS
Rivastigmine (Exelon)	Dual AChE + BuChE inhibitor	1.5mg BD → 6mg BD (oral) or 4.6mg/24h → 9.5mg/24h (patch)	1-2 hours	Patch preferred (fewer GI side effects); also for PDD
Galantamine (Reminyl)	AChE inhibitor + nicotinic receptor allosteric potentiator	4mg BD → 12mg BD	7-8 hours	Nicotinic modulation may provide additional benefit
Tacrine (Cognex)	First ChEI	Obsolete		Hepatotoxic, no longer used

Common Side Effects of ChEIs (cholinomimetic):

- Nausea, vomiting, diarrhea (dose-related)
- Anorexia, weight loss
- Bradycardia (sick sinus, AV block, caution)
- Nightmares (especially donepezil, take in morning)
- Syncope

Clinical Evidence:

- Modest but consistent benefit on cognition (ADAS-Cog +3-4 points vs placebo)
- Benefit on ADLs and global function
- Insufficient evidence for disease modification
- Benefits may be maintained for 1-2 years

MEMANTINE (EBIXA, NAMENDA)

Mechanism: Uncompetitive, voltage-dependent NMDA receptor antagonist → reduces pathological glutamatergic excitotoxicity; preserves physiological NMDA activity

- Approved for **moderate-to-severe AD**
- Dose: 5mg OD → 20mg OD (titrated over 4 weeks)
- Can be combined with ChEIs (additive benefit in moderate-severe AD, Tariot et al., 2004)
- Side effects: Dizziness, headache, confusion (usually mild)

EXAM PEARL

ChEIs are for mild-to-moderate AD. Memantine is for moderate-to-severe AD. Donepezil is approved for ALL stages including severe.

NEWER DISEASE-MODIFYING AGENTS (ANTI-AMYLOID IMMUNOTHERAPY)

DRUG	MECHANISM	FDA STATUS	KEY TRIAL
Aducanumab (Aduhelm)	Anti-amyloid monoclonal antibody	FDA approved 2021 (accelerated approval, controversial)	EMERGE, ENGAGE (conflicting results)
Lecanemab (Leqembi)	Anti-A β protofibrils monoclonal antibody	FDA approved 2023 (traditional approval)	CLARITY-AD: 27% slowing of decline
Donanemab	Anti-A β plaque antibody	FDA approved 2024	TRAILBLAZER-ALZ 2: 22-35% slowing

Key Points on Anti-Amyloid Therapy:

- Target: early-stage AD (MCI or mild dementia stage)
- Require biomarker confirmation (amyloid PET or CSF)
- Main risk: **ARIA (Amyloid-Related Imaging Abnormalities)**, ARIA-E (edema) and ARIA-H (microhemorrhages), occurs in 20-40% on MRI, symptomatic in 3-10%
- APOE4 homozygotes have highest ARIA risk
- Not yet available in India (cost ~\$26,500/year for lecanemab)

EXAM PEARL

Lecanemab (2023) is the current gold standard, first anti-amyloid drug with a statistically significant and clinically meaningful slowing of decline in traditional approval. But benefits are modest (27% slowing, not reversal).

NON-PHARMACOLOGICAL MANAGEMENT

- Cognitive stimulation therapy (CST), evidence base comparable to ChEIs
- Physical exercise, reduces progression risk
- Structured activities, reality orientation
- Environmental modifications (safety)
- Music therapy, particularly for agitation

PART 5: VASCULAR DEMENTIA (VaD)

5.1 Overview

Second most common cause of dementia (~15-20% globally; ~30% in India). Results from cerebrovascular disease causing brain injury and cognitive impairment.

EXAM PEARL

In India, VaD prevalence is disproportionately higher (up to 30%) due to the high burden of hypertension, diabetes, and stroke in the population.

5.2 Types of Vascular Dementia

TYPE	DESCRIPTION	KEY FEATURES
Multi-infarct dementia (MID)	Multiple cortical and subcortical infarcts	Step-wise deterioration, focal neurological signs
Strategic infarct dementia	Single infarct in key location	Sudden onset; depends on location (angular gyrus, thalamus, basal forebrain)
Subcortical vascular dementia	Small vessel disease; lacunar infarcts; white matter changes	Gait disturbance, urinary symptoms, frontal-executive deficits
Binswanger's disease	Extensive periventricular white matter degeneration	Slow stepwise, prominent white matter changes on MRI, abulia
CADASIL	Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy	Migraine, strokes, dementia; NOTCH3 gene mutation
Mixed dementia	AD + VaD	Very common in elderly

5.3 Hachinski Ischemic Score (HIS)

Used to clinically differentiate VaD from AD (Hachinski et al., 1975).

FEATURE · SCORE

Abrupt onset 2

Stepwise deterioration 1

Fluctuating course 2

Nocturnal confusion 1

Relative preservation of personality 1

Depression 1

Somatic complaints 1

Emotional incontinence 1

History of hypertension 1

History of strokes 2

Evidence of associated atherosclerosis 1

Focal neurological symptoms 2

Focal neurological signs 2

Interpretation:

- Score ≥ 7 : Vascular dementia
- Score ≤ 4 : Alzheimer's disease
- Score 5-6: Mixed or inconclusive

EXAM PEARL

Maximum HIS score = 18. Scores ≥ 7 = VaD; ≤ 4 = AD. This is a frequently asked number.

5.4 Clinical Features of VaD

Onset and Course:

- Typically abrupt onset (post-stroke)
- Stepwise deterioration (each stroke → new step down)
- May plateau between episodes

Cognitive Profile:

- Executive dysfunction prominent (working memory, planning, attention)
- Memory impairment: encoding relatively preserved, but retrieval impaired
- Psychomotor slowing
- Emotional lability, emotional incontinence

Neurological Signs:

- Focal deficits (hemiparesis, dysarthria, dysphagia)
- Gait disturbance (marche à petit pas in subcortical VaD)
- Pseudobulbar palsy
- Urinary incontinence

Neuropsychiatric:

- Depression (very common, post-stroke depression)
- Apathy
- Emotional incontinence (laughter / crying without provocation)

5.5 Neuroimaging in VaD

CT:

- Low-density areas (infarcts)
- Periventricular hypodensities (white matter changes)

MRI:

- Multiple infarcts of varying ages
- White matter hyperintensities (T2/FLAIR), periventricular and deep white matter
- Lacunar infarcts (basal ganglia, thalamus, pons)
- **Fazekas scale** for white matter changes (0-3)

5.6 Diagnostic Criteria

NINDS-AIREN Criteria (National Institute of Neurological Disorders and Stroke, Association Internationale pour la Recherche et l'Enseignement en Neurosciences):

Probable VaD:

1. Dementia (MMSE and clinical exam)
2. Cerebrovascular disease (focal signs + neuroimaging evidence)
3. Temporal relationship: dementia onset within 3 months of stroke, or abrupt onset/stepwise deterioration

Possible VaD:

- Dementia + focal signs but no neuroimaging
- Dementia + neuroimaging but no clear temporal relationship

5.7 Management of VaD

Primary Prevention:

- Control vascular risk factors: hypertension, diabetes, hyperlipidemia, smoking cessation
- Antiplatelet therapy (aspirin, clopidogrel) for secondary prevention

Symptomatic Treatment:

- ChEIs: modest evidence; donepezil approved in some countries
- Memantine: some evidence
- No established disease-specific treatment

Vascular Risk Factor Management:

- Target BP <130/80 mmHg (JNC guidelines)
 - Statin therapy
 - HbA1c control
-

PART 6: DEMENTIA WITH LEWY BODIES (DLB)

6.1 Background

DLB is the second most common neurodegenerative dementia (~15-20%) after AD. Often underdiagnosed. Named after Friederich Heinrich Lewy who described the inclusion bodies in 1912.

CLINICAL ANCHOR

Three V's of DLB, Variability (fluctuating cognition), Visions (visual hallucinations), Velocity (parkinsonism)

6.2 Pathology

Lewy Bodies:

- Intraneuronal inclusions of aggregated **alpha-synuclein** protein
- Core: dense protein aggregate
- Halo: radiating filaments
- Location: cortical (DLB), brainstem substantia nigra (PD), both (DLB/PDD)

Braak Staging for Lewy Body Disease:

- Stages 1-2: Olfactory bulb, brainstem (no clinical symptoms)
- Stages 3-4: Amygdala, limbic (early symptoms)
- Stages 5-6: Neocortex (dementia)

Neurochemistry:

- Dopamine (nigrostriatal): decreased → parkinsonism
- Acetylcholine: markedly decreased (more than AD) → cognitive symptoms
- Noradrenaline: decreased
- Serotonin: decreased

6.3 Clinical Features: McKeith Criteria (2017)

Essential Feature:

- Dementia, defined as progressive cognitive decline sufficient to interfere with social/occupational function

Core Clinical Features (2 = probable; 1 + biomarker = probable):

Fluctuating cognition Marked variation in attention and alertness; "good days" and "bad days"; episodic confusion

Visual hallucinations Recurrent, detailed, well-formed; typically people or animals; early in course; often benign

REM Sleep Behavior Disorder (RBD) Acting out dreams; dream enactment; precedes dementia by years/decades

Parkinsonism Bradykinesia + resting tremor OR rigidity; typically mild; onset after dementia (or within 1 year)

Supportive Features:

- Severe sensitivity to antipsychotics (neuroleptic sensitivity)
- Postural instability, falls, syncope
- Autonomic dysfunction (orthostatic hypotension, constipation, urinary incontinence)
- Hypersomnia
- Hyposmia (anosmia)
- Neuropsychiatric symptoms: depression, apathy, anxiety, delusions

Indicative Biomarkers (for probable DLB diagnosis):

BIOMARKER · MODALITY

Reduced dopamine transporter uptake DaTSCAN (SPECT/PET)

Reduced MIBG uptake Cardiac MIBG scintigraphy

Polysomnographic confirmation of REM sleep without atonia PSG

EXAM PEARL

The order matters in DLB, dementia PRECEDES parkinsonism (or occurs within 1 year). If parkinsonism precedes dementia by >1 year → Parkinson's Disease Dementia (PDD). This is the "1-year rule."

6.4 DLB vs PDD: The 1-Year Rule

FEATURE	DLB	PDD
Timing	Dementia first (or concurrent), then parkinsonism	Parkinsonism first, then dementia >1 year later
Cognitive profile	Visuospatial early, memory relatively spared	Similar but often less visuospatial
Visual hallucinations	Early, prominent	Later
Pathology	Alpha-synuclein; cortical > subcortical	Alpha-synuclein; subcortical > cortical

FEATURE	DLB	PDD
Response to L-DOPA	Modest	Better
DaTSCAN	Abnormal	Abnormal
Cholinergic deficit	More severe	Severe
Overall	Same pathological spectrum, different clinical phenotype	Same pathological spectrum

EXAM PEARL

DLB and PDD are considered the same disease on a spectrum, "Lewy body disease", differing only in the timing of dementia onset relative to motor features.

6.5 Cognitive Profile of DLB

- Early: Visuospatial deficits (constructional apraxia), attentional fluctuations
- Frontal-subcortical pattern: executive dysfunction, processing speed
- Memory: relatively preserved in early stages compared to AD
- Later: global decline

6.6 Management of DLB

KEY INSIGHT

EXAM PEARL, CRITICAL: NEVER use conventional antipsychotics (haloperidol, chlorpromazine) in DLB. Neuroleptic sensitivity reactions can be severe and fatal: extreme rigidity, autonomic instability, impaired consciousness, sudden death.

Neuroleptic Sensitivity in DLB:

- Occurs in 30-50% of DLB patients exposed to conventional antipsychotics
- Also with risperidone, olanzapine at higher doses
- Can cause rapid functional decline and death
- Mechanism: hypersensitive D2 receptors in the context of cholinergic deficits

Safe Antipsychotics in DLB (relatively):

- Quetiapine (low dose, least dopamine blockade)
- Clozapine (evidence in Parkinson's psychosis; requires CBC monitoring)

Cognitive Symptoms:

- Rivastigmine: approved for DLB and PDD (cholinergic deficit most severe in DLB)
- Donepezil: evidence, not formally approved for DLB in all jurisdictions
- Memantine: modest benefit

Motor Symptoms:

- Levodopa: modest benefit for parkinsonism; may worsen hallucinations
- Avoid dopamine agonists (worsen psychosis)

Psychiatric Symptoms:

- Depression: SSRIs (sertraline, escitalopram)
- Anxiety: SSRIs, low-dose benzodiazepines (caution, oversedation)
- Psychosis: quetiapine, clozapine only

Sleep (RBD):

- Clonazepam 0.25-2mg at bedtime (evidence-based; injury prevention)
- Melatonin 3-12mg (safer in elderly)

PART 7: FRONTOTEMPORAL DEMENTIA (FTD)

7.1 Overview

FTD encompasses a group of neurodegenerative diseases characterized by progressive degeneration of the frontal and/or temporal lobes. It is the **THIRD** most common neurodegenerative dementia (after AD and DLB) and the **MOST** common dementia in those under 65.

Prevalence: 10-15% of all dementias; peak incidence ages 45-65

7.2 Clinical Syndromes

SYNDROME	CORE FEATURES	PRIMARY ANATOMY
Behavioral variant FTD (bvFTD)	Personality and behavioral changes	Frontal lobes bilateral
Semantic variant PPA (svPPA) / Semantic Dementia	Loss of word and object meaning	Left anterior temporal lobe
Nonfluent/agrammatic variant PPA (nfvPPA) / Progressive Non-Fluent Aphasia	Effortful, agrammatic speech; motor speech disorder	Left posterior frontal, insula

PPA = Primary Progressive Aphasia, language-first syndrome

7.3 Behavioral Variant FTD (bvFTD): Rascovsky Criteria (2011)

Required: Neurodegenerative syndrome with progressive behavior/cognition

Possible bvFTD (3 of 6):

FEATURE · EXAMPLES

1. Disinhibition Socially inappropriate behavior, loss of manners, impulsivity

2. Apathy / Inertia Loss of motivation; persists throughout day

3. Loss of sympathy / empathy Indifference to others, loss of social interest

4. Perseverative / compulsive behaviors Stereotyped acts, ritual behaviors, collecting, dietary changes (sweet/carbohydrate preference)

5. Hyperorality / dietary changes Oral fixation, gluttony, food cramming

6. Neuropsychological profile Executive deficits with relative sparing of memory and visuospatial

Probable bvFTD: Above + neuroimaging showing frontal/anterior temporal atrophy/hypometabolism

Definite bvFTD: Above + histopathological confirmation

CLINICAL ANCHOR

bvFTD classic presentation, relatively young (50s), previously dignified person who becomes socially inappropriate, says offensive things, eats excessively, neglects hygiene. Caregivers often don't recognize as dementia because "he knows who I am."

7.4 Semantic Dementia (svPPA)

- Anomia: inability to name objects/people
- Empty speech: uses circumlocutions ("the thing you use to...")
- Surface dyslexia and dysgraphia (reads phonetically)
- Preserved syntax and phonology
- Preserved day-to-day memory (episodic) in early stages
- Face recognition impairment (prosopagnosia), right temporal variant
- MRI: asymmetric left anterior temporal lobe atrophy

7.5 Progressive Nonfluent Aphasia (nfvPPA)

- Effortful, halting speech
- Agrammatism (telegraphic speech, dropped function words)
- Phonological errors, apraxia of speech
- Preserved comprehension early
- May progress to mutism
- Often develops overlapping motor neuron disease features
- MRI: left posterior frontal and insular atrophy

7.6 Neuropathology of FTD

Grossly: Knife-blade atrophy of frontal and temporal gyri (most marked in bvFTD and svPPA)

FTLD-Tau (tau-positive inclusions):

- **Pick's disease (FTLD-Pick):** Argyrophilic Pick bodies (tau-positive intraneuronal inclusions with 3R tau); ballooned neurons (Pick cells)
- **Progressive Supranuclear Palsy (PSP):** 4R tau; globose tangles; tufted astrocytes
- **Corticobasal Degeneration (CBD):** 4R tau; astrocytic plaques; neuronal achromasia

FTLD-TDP (TDP-43-positive):

- Most common FTLD pathology (~50%)
- TDP-43 is a nuclear RNA-binding protein; pathological cytoplasmic inclusions
- Associated with MND (Motor Neuron Disease / ALS)

FTLD-FUS (FUS-positive):

- Rare (<10%)

EXAM PEARL

FTD-MND (FTD with Amyotrophic Lateral Sclerosis), the TDP-43 connection. C9orf72 mutation is the most common cause of familial FTD-MND.

7.7 Genetics of FTD

GENE	CHROMOSOME	PROTEIN	SYNDROME
MAPT	17q21	Tau	bvFTD, CBD, PSP
GRN (Progranulin)	17q21	Progranulin	bvFTD (TDP-43)
C9orf72	9p21	Dipeptide repeat protein	bvFTD, ALS, FTD-MND
VCP	9p	Valosin-containing protein	FTD, IBM, Paget's disease
CHMP2B	3	Chromatin-modifying protein	Rare

C9orf72, hexanucleotide repeat expansion (GGGGCC), accounts for ~25% of familial FTD and ~35% of familial ALS. Single most common genetic cause of both FTD and ALS.

7.8 Management of FTD

- No approved disease-modifying therapy

- Behavioral symptoms: SSRIs first-line (sertraline, fluvoxamine) for disinhibition, compulsions, hyperorality
- Atypical antipsychotics: low doses for severe behavioral disturbance
- **Avoid ChEIs and memantine**, no evidence; may worsen behavioral symptoms (galantamine may worsen hyperorality)
- Speech and language therapy
- Genetic counseling (family members)
- Caregiver education: empathy impairment explanation

PART 8: NORMAL PRESSURE HYDROCEPHALUS (NPH)

8.1 The Hakim-Adams Triad

NPH = Classic triad (described by Adams and Hakim in 1965):

FEATURE	DESCRIPTION	MNEMONIC
Wet	Urinary incontinence (urge > overflow)	W
Wobbly	Gait apraxia / magnetic gait	W
Wacky	Dementia (primarily frontal-subcortical)	W

Gait in NPH: Magnetic gait (feet appear glued to floor), wide-based, short steps, difficulty initiating, en bloc turns. Distinguished from Parkinson's: no tremor, no rigidity at initiation.

EXAM PEARL

Gait disturbance appears **FIRST** in NPH, followed by urinary incontinence, then dementia (reverse of typical thinking). "Wet" → "Wobbly" → "Wacky" is NOT the order of appearance.

8.2 Pathophysiology

- Chronic impairment of CSF absorption (arachnoid villi)
- Normal opening CSF pressure on LP (<20 cm H₂O), despite enlarged ventricles
- Hydrocephalus compresses periventricular white matter tracts
- Disruption of frontal-subcortical circuits → gait, continence, cognition deficits

8.3 Diagnosis

Imaging:

- CT/MRI: Disproportionately enlarged ventricles (Evans index >0.3) with normal or small sulci over convexities

- DESH (Disproportionately Enlarged Subarachnoid-Space Hydrocephalus) on MRI, high specificity
- Tight sulci over vertex

CSF Tap Test (Miller Fisher Test):

- LP with removal of 30-50 mL CSF
- Positive if gait improves within 24-72 hours
- Sensitivity 50-60%; specificity ~80%
- Positive tap test predicts good shunting outcome

Extended CSF Drainage (External lumbar drain):

- 3-5 days of continuous drainage
- Higher sensitivity than tap test for predicting shunt response

8.4 Treatment

Ventriculoperitoneal (VP) shunt:

- Definitive treatment for idiopathic NPH
- Best outcomes: young age, short symptom duration, predominant gait symptoms, positive tap test
- Complications: over-drainage (subdural hematoma), infection, shunt failure
- Response: Gait improves best (50-80%), continence improves (50-60%), cognition improves least (25-40%)

CLINICAL ANCHOR

If an elderly patient has gait disturbance + incontinence + dementia + enlarged ventricles on CT, think NPH FIRST. It is one of the few TREATABLE causes of dementia.

PART 9: REVERSIBLE DEMENTIAS

EXAM PEARL

"DEMENTIAS" mnemonic for reversible causes, frequently asked.

9.1 Mnemonic: "DEMENTIAS"

LETTER · CAUSE

D Drugs (medications, alcohol)

E Endocrine (hypothyroidism, Cushing's, hypopituitarism)

M Metabolic (hepatic failure, renal failure, B12/folate deficiency)

E Eye and ear disease (deafness worsening dementia)

N Normal pressure hydrocephalus

T Trauma (subdural hematoma)

I Infections (neurosyphilis, HIV, TB meningitis, cryptococcal meningitis)

A Affective (depression, pseudodementia)

S Space-occupying lesion (brain tumor, abscess)

9.2 Key Reversible Causes

HYPOTHYROIDISM

- Cognitive slowing, memory impairment, depression, psychosis ("myxoedema madness")
- Check: TSH, free T4
- Treatment: levothyroxine → cognitive improvement usually within 6-12 weeks

VITAMIN B12 DEFICIENCY

- Combined subacute degeneration of spinal cord + cognitive impairment
- Psychiatric: depression, psychosis, irritability
- Check: serum B12, homocysteine, methylmalonic acid (more sensitive)
- Treatment: B12 supplementation (IM hydroxocobalamin or high-dose oral)

NEUROSYPHILIS

- Dementia, personality change, psychiatric symptoms; classic tabes dorsalis + GPI (General Paralysis of the Insane)
- Check: VDRL/RPR (blood), TPHA/FTA-abs, CSF VDRL (definitive)
- Treatment: penicillin G IV

HIV-ASSOCIATED NEUROCOGNITIVE DISORDER (HAND)

- Spectrum from asymptomatic to HIV-associated dementia (HAD)
- Subcortical pattern: psychomotor slowing, frontal-executive deficits
- Pathology: activated microglia, giant cells, HIV encephalitis
- Treatment: ART (antiretroviral therapy), reverses early HAND

DEPRESSION: PSEUDODEMENTIA

- Cognitive impairment due to depression, mimicking dementia

- Features: onset correlated with depressive episode, subjective complaints > objective deficits, "I don't know" answers, inconsistent performance
- **Kiloh (1961)** coined the term pseudodementia

Differentiating Pseudodementia (Depression) from True Dementia:

FEATURE	PSEUDODEMENTIA	TRUE DEMENTIA
Onset	Related to depressive episode	Insidious, no clear precipitant
Duration	Relatively short	Months-years
Subjective complaints	Prominent; amplified	May deny problems
Answers	"I don't know"	Confabulation, near-miss
Consistency	Variable performance	Consistent impairment
Cognitive profile	Diffuse, no pattern	Pattern-specific
Response to antidepressant	Cognitive improvement	No cognitive improvement
Family history	Often depression	Often dementia

EXAM PEARL

Pseudodementia is a common short-answer question. Key distinguisher: in pseudodementia, patient emphasizes disabilities; in true dementia, patient minimizes or denies.

MEDICATION-INDUCED COGNITIVE IMPAIRMENT

- Anticholinergics (TCAs, antihistamines, oxybutynin, antipsychotics with high ACh blockade)
- Benzodiazepines (sedation, anterograde amnesia)
- Opioids (especially in elderly)
- Corticosteroids (delirium, cognitive impairment)
- Alcohol (Wernicke-Korsakoff, alcoholic dementia)

PART 10: CREUTZFELDT-JAKOB DISEASE (CJD)

10.1 Prion Diseases

Prion diseases = Transmissible Spongiform Encephalopathies (TSEs), caused by misfolded prion proteins (PrP^{Sc}) that propagate by converting normal PrP^C to PrP^{Sc}.

Types of CJD:

TYPE	CAUSE	FREQUENCY	KEY FEATURES
Sporadic CJD (sCJD)	Spontaneous PrP misfolding	~85-90%	Rapidly progressive dementia, myoclonus, EEG changes, median survival 5-6 months
Familial CJD (fCJD)	PRNP gene mutations	~10-15%	Autosomal dominant; Gerstmann-Straussler-Scheinker (GSS) and Fatal Familial Insomnia (FFI) variants
Iatrogenic CJD	Contaminated surgical instruments, dura mater grafts, human growth hormone	Rare	
Variant CJD (vCJD)	Bovine spongiform encephalopathy (BSE/"mad cow disease")	Rare	Young patients; psychiatric onset; florid plaques; 14-3-3 negative; MRI pulvinar sign

10.2 Sporadic CJD: Clinical Features

- Rapidly progressive dementia (weeks-months)
- Myoclonus (present in 90%, stimulus-sensitive)
- Cerebellar ataxia, visual disturbances
- Extrapyrarnidal signs
- Akinetic mutism (terminal stage)
- Median survival: 5-6 months; 85% die within 1 year

10.3 Investigations in CJD

INVESTIGATION · FINDING

EEG Periodic sharp wave complexes (PSWC) at 1-2 Hz, pathognomonic for sCJD

MRI (DWI) Cortical ribboning, basal ganglia DWI restriction; "pulvinar sign" (posterior thalamus) in vCJD

CSF 14-3-3 protein Elevated; sensitive for sCJD (sensitivity 85%, specificity 80%); NOT specific

CSF RT-QuIC (Real-Time Quaking-Induced Conversion) Highly sensitive and specific for CJD (>95% sensitivity, >98% specificity)

Prion protein RT-QuIC (nasal brushing) Newer, high accuracy without LP

Brain biopsy Definitive but reserved for unclear cases

EXAM PEARL

EEG periodic sharp wave complexes (PSWC) + rapidly progressive dementia + myoclonus = CJD until proven otherwise. RT-QuIC is now the test of choice.

10.4 Variant CJD (vCJD)

- Linked to BSE ("mad cow disease")
 - Affects younger patients (mean age 28)
 - Psychiatric onset: depression, anxiety, behavioral change (before dementia)
 - Ataxia, sensory symptoms prominent
 - EEG: No PSWC (unlike sCJD)
 - MRI: "Pulvinar sign", bilateral high signal in posterior thalamus (DWI/FLAIR)
 - CSF: 14-3-3 negative; tonsil biopsy can show PrPSc
 - Survival: 12-14 months
-

PART 11: BEHAVIORAL AND PSYCHOLOGICAL SYMPTOMS OF DEMENTIA (BPSD)

11.1 Overview

BPSD = Non-cognitive symptoms of dementia, occurs in 90% of patients during the course of dementia.

EXAM PEARL

BPSD is a major cause of caregiver distress, institutionalization, and accelerated cognitive decline. Non-pharmacological interventions are ALWAYS first-line.

11.2 Types of BPSD

CATEGORY · SYMPTOMS

Psychotic symptoms Delusions (theft, infidelity, phantom boarder), hallucinations (usually visual)

Mood disorders Depression, anxiety, euphoria

Behavioral disturbances Agitation, aggression, wandering, disinhibition

Vegetative symptoms Sleep disturbances (day-night reversal), appetite changes

Personality changes Apathy, irritability, personality alteration

Most common delusion in AD: Theft delusion ("someone is stealing my things"), misidentification of misplaced objects

Most common BPSD: Apathy (~70%)

11.3 Assessment of BPSD

Neuropsychiatric Inventory (NPI), Cummings:

- 12 domains: delusions, hallucinations, agitation, depression, anxiety, euphoria, apathy, disinhibition, irritability, aberrant motor behavior, sleep, appetite
- Informant-based
- Rates frequency (1-4) and severity (1-3) separately
- NPI score = frequency × severity for each domain

Cohen-Mansfield Agitation Inventory (CMAI): Rates agitation severity

11.4 Non-Pharmacological Interventions (First-Line)

- **Person-centered care:** Know the person's history, preferences, lifelong habits
- **Validation therapy:** Accept and enter the patient's reality rather than correcting
- **Music therapy:** Strong evidence for agitation, particularly personalized music
- **Bright light therapy:** Sleep disturbances, sundowning
- **Exercise:** Reduces agitation, improves sleep
- **Reminiscence therapy:** Photos, objects from past; reduces depression
- **Structured activities:** Reduces wandering, agitation
- **Environmental modification:** Safe, uncluttered, low stimulation at night
- **Caregiver training:** Most important intervention

11.5 Pharmacological Management of BPSD

EXAM PEARL

All antipsychotics in dementia carry FDA BLACK BOX WARNING for increased mortality (1.6-1.7x risk of death). Must be used with informed consent, lowest effective dose, and limited duration.

Agitation/Psychosis:

DRUG	EVIDENCE	NOTES
Risperidone	Best evidence for BPSD; reduces delusions and agitation	0.25-1mg / day; risk of EPS, stroke

DRUG	EVIDENCE	NOTES
Olanzapine	Moderate evidence	Sedation, metabolic side effects
Quetiapine	Weakest evidence among atypicals	Preferred in DLB / PDD
Haloperidol	Evidence for agitation only	Avoid, EPS, anticholinergic effects in elderly
Aripiprazole	Emerging evidence	Activating, may worsen insomnia

Depression in Dementia:

- SSRIs: sertraline, citalopram (escitalopram preferred in elderly, less CYP450 interactions)
- Avoid TCAs (anticholinergic effects)
- Mirtazapine: if sleep disturbance + depression + appetite loss

Anxiety:

- SSRIs first-line
- Low-dose buspirone
- Avoid benzodiazepines (falls, cognitive worsening, paradoxical agitation)

Sleep Disturbance:

- Melatonin 2-10mg (safest)
- Low-dose trazodone 25-100mg
- Mirtazapine 7.5-15mg
- Avoid diphenhydramine (anticholinergic), benzodiazepines (if possible)

Agitation, Memantine:

- Some evidence for reducing agitation in moderate-severe AD
- Safer profile than antipsychotics

CATIE-AD Study (2006): No significant cognitive or behavioral benefit of olanzapine, quetiapine, or risperidone over placebo in AD-related BPSD; significant adverse effects noted.

PART 12: COGNITIVE ASSESSMENT TOOLS

12.1 Mini-Mental State Examination (MMSE): Folstein (1975)

- Most widely used bedside cognitive screen
- Time: 5-10 minutes
- Total: **30 points**

DOMAIN	ITEMS	MAX SCORE
Orientation to time	Year, season, month, date, day	5
Orientation to place	Country, state, city, building, floor	5
Registration	Name 3 objects	3
Attention / calculation	Serial 7s OR spell WORLD backwards	5
Recall	Recall 3 objects	3
Naming	Name 2 objects (pen, watch)	2
Repetition	"No ifs, ands, or buts"	1
3-stage command	Take paper, fold, put on floor	3
Reading	Read and obey "CLOSE YOUR EYES"	1
Writing	Write a sentence	1
Copying	Copy intersecting pentagons	1

Scoring:

- 24-30: Normal
- 18-23: Mild impairment
- 12-17: Moderate impairment
- 0-11: Severe impairment

Limitations:

- Ceiling effect in highly educated
- Floor effect in low literacy
- Misses frontal and executive dysfunction
- Language/cultural bias
- Copyrighted (fees for use)

12.2 Montreal Cognitive Assessment (MoCA): Nasreddine (2005)

- Better sensitivity than MMSE for MCI
- Time: 10-15 minutes
- Total: **30 points**

DOMAIN · MAX SCORE

Visuospatial/Executive (Trail B part, cube, clock) 5

Naming (3 animals, lion, rhino, camel) 3

Memory (5-word registration, delayed recall) 5

Attention (forward/backward digit span, serial 7s, tapping) 6

Language (2 sentences, fluency) 3

Abstraction (2 analogies) 2

Delayed recall (5 words) 5

Orientation (date, month, year, day, place, city) 6

Scoring: ≥ 26 = Normal; Add 1 point if education ≤ 12 years

Advantages over MMSE: Better for MCI, executive function, visuospatial domains; free; multilingual versions available

12.3 Addenbrooke's Cognitive Examination-III (ACE-III)

- Time: 15-20 minutes
- Total: **100 points**
- Subtests: Attention (18), Memory (26), Fluency (14), Language (26), Visuospatial (16)
- Cut-off: ≤ 88 suggests cognitive impairment
- **VLOM ratio:** [Verbal fluency + Language] / [Orientation + Memory delayed recall], helps differentiate AD (VLOM < 2.2) from FTD (VLOM ≥ 3.2)

12.4 Clinical Dementia Rating (CDR): Morris (1993)

- Staging instrument (not a screening test)
- Rated across 6 domains: Memory, Orientation, Judgment/Problem Solving, Community Affairs, Home & Hobbies, Personal Care

CDR SCORE · STAGE

0 Normal

0.5 Questionable / MCI

1 Mild dementia

2 Moderate dementia

3 Severe dementia

CDR Sum of Boxes (CDR-SoB): 0-18; more sensitive to change; used in clinical trials

12.5 ADAS-Cog (Alzheimer's Disease Assessment Scale: Cognitive Subscale)

- 11-item scale
- Total: 70 points (higher score = worse)
- Used in clinical trials (primary endpoint in most AD drug trials)
- Includes word recall, naming, following commands, constructional praxis, ideational praxis, orientation, word recognition, comprehension, word-finding, recall test instructions

12.6 Clock Drawing Test (CDT)

- Simple, rapid, culturally fair
- Tests: executive function (planning), visuospatial, language comprehension
- Score 1-10 (Shulman scoring); 0-4 (Watson scoring)
- Sensitive to frontal and parietal dysfunction

12.7 Neuropsychiatric Inventory (NPI)

- 12-domain informant-based assessment of BPSD
- Each domain: screening question → if positive, frequency (1-4) and severity (1-3) → NPI score per domain = $F \times S$ (max 12 per domain)
- Total max: 144
- Also measures caregiver distress per domain (0-5)

PART 13: CAREGIVER BURDEN

13.1 Overview

Family caregivers of dementia patients are the "hidden second patients." The progressive, prolonged nature of dementia combined with BPSD creates one of the heaviest caregiver burdens of any disease.

India-specific: ~85-90% of dementia care is provided by family members; no structured respite care infrastructure; significant financial, physical, and psychological burden.

13.2 Components of Caregiver Burden

DOMAIN · EXAMPLES

Physical Sleep deprivation, physical exhaustion, own health neglect

Psychological Depression (50-70% of caregivers), anxiety, grief (anticipatory mourning)

Social Social isolation, relationship strain, reduced employment

Financial Loss of income, increased expenditure for care

Existential Role reversal (caring for parent/spouse), meaning-making

13.3 Assessment Tools

Zarit Burden Interview (ZBI): 22-item; most widely used; total 0-88; higher = greater burden

- Little burden: 0-20
- Mild-moderate: 21-40
- Moderate-severe: 41-60
- Severe: 61-88

Caregiver Strain Index (CSI): 13-item; quick screen

13.4 Interventions for Caregiver Burden

- **Psychoeducation:** Disease course, managing BPSD, what to expect
 - **Skill training:** Communication techniques, managing challenging behaviors
 - **Support groups:** Significant benefit for emotional support and practical advice
 - **Respite care:** Day centers, temporary placement, reduces burnout
 - **Individual psychological therapy:** CBT for depression, acceptance-based approaches
 - **Self-care promotion:** Sleep, own medical appointments
 - **Advance care planning:** Reduces emergency decision-making burden
-

PART 14: LEGAL AND ETHICAL ISSUES IN DEMENTIA

14.1 Capacity Assessment

Capacity is decision-specific and time-specific. A patient with dementia may have capacity for some decisions (e.g., choosing lunch) but not others (e.g., complex financial decisions).

Four Components of Capacity (MacCAT-T framework):

1. **Understanding:** Can the patient understand the relevant information?
2. **Appreciation:** Can they appreciate how it applies to their situation?
3. **Reasoning:** Can they reason about the options?
4. **Communication:** Can they express a consistent choice?

Key Principle: Diagnosis of dementia does NOT automatically mean lack of capacity.

14.2 Legal Instruments

INSTRUMENT • DESCRIPTION

Advance Directive / Living Will Pre-written instructions for future care when capacity is lost

Lasting Power of Attorney (LPA) Designates proxy decision-maker (financial and/or health decisions)

Guardianship Court-appointed guardian when patient lacks capacity and no LPA

Testamentary capacity Ability to make a valid will, requires: knows estate, knows heirs, understands making a will, no delusions affecting the will

India: Mental Healthcare Act 2017 includes provisions for advance directives and nominated representatives.

14.3 Driving and Dementia

- Any stage of dementia raises concerns about driving safety
- Mild dementia: individualized assessment required (on-road test, neuropsychological testing)
- Moderate-severe dementia: generally cannot drive safely
- Ethical duty to warn vs confidentiality, varies by jurisdiction; India has no mandatory reporting law currently

14.4 Elder Abuse

- Higher in dementia (80% of elder abuse involves some cognitive impairment)
 - Financial exploitation: most common type in dementia
 - Physical abuse, neglect, emotional abuse
 - Assessment: Elder Abuse Suspicion Index (EASI)
 - Mandatory reporting: varies by state in India
-

PART 15: DELIRIUM SUPERIMPOSED ON DEMENTIA (DSD)

15.1 Overview

DSD is one of the most clinically challenging scenarios, dementia increases the risk of delirium 2-5 fold, and delirium worsens the trajectory of dementia.

Prevalence: 22-89% of dementia patients admitted to hospital develop delirium

15.2 Differentiating Delirium from Dementia vs DSD

FEATURE	DELIRIUM	DEMENTIA	DSD
Onset	Acute (hours-days)	Insidious	Acute on chronic
Course	Fluctuating	Slowly progressive	Fluctuating (worse than baseline)

FEATURE	DELIRIUM	DEMENTIA	DSD
Attention	Severely impaired	Relatively preserved early	Severely impaired
Consciousness	Altered	Clear	Altered
Psychomotor	Hyperactive OR hypoactive	Normal early	Variable
Duration	Days-weeks (usually)	Months-years	Days-weeks
Precipitant	Usually identifiable	None	Usually identifiable

EXAM PEARL

The distinguishing feature of delirium (and DSD) from dementia is the **acute onset** and **fluctuating level of consciousness**. Attention impairment is the cardinal feature of delirium.

15.3 Confusion Assessment Method (CAM)

Delirium diagnosis requires features 1+2 PLUS either 3 or 4:

1. Acute onset and fluctuating course
2. Inattention
3. Disorganized thinking
4. Altered level of consciousness

15.4 Management of DSD

- Identify and treat underlying precipitant (infection, metabolic, medications, pain)
- Non-pharmacological first: reorientation, familiar faces, lighting, early mobilization, hearing aids/glasses
- Pharmacological: low-dose haloperidol (0.25-1mg), cautiously; risperidone
- NEVER benzodiazepines as first-line (worsen confusion, increase fall risk)
- Avoid antipsychotics in DLB-related DSD (neuroleptic sensitivity)

PART 16: SUMMARY TABLE: KEY COMPARISONS

16.1 Differentiating the Four Major Dementias

FEATURE	AD	VAD	DLB	FTD
Age of onset	Usually >65	Usually >60	Usually >65	Usually 45-65
Onset	Insidious	Abrupt/stepwise	Insidious	Insidious

FEATURE	AD	VAD	DLB	FTD
First symptom	Episodic memory	Variable (depends on stroke location)	Visuospatial, attention	Personality/behavior or language
Memory	Early, prominent	Retrieval > encoding	Relatively preserved early	Preserved early (bvFTD)
Executive function	Later	Early, prominent	Early, prominent	Early, prominent
Hallucinations	Late	Uncommon	Early (visual, detailed, benign)	Rare
Parkinsonism	Late/absent	Rarely	Core feature	Rare (except CBD/PSP overlap)
Progression	Gradual	Stepwise	Progressive	Progressive
Pathology	Amyloid + tau	Infarcts	Alpha-synuclein	Tau or TDP-43 or FUS
ChEIs	Yes (FDA approved)	Modest evidence	Yes (rivastigmine preferred)	No evidence
Key imaging	MTA on MRI, amyloid PET+	Infarcts, WMH	DaTSCAN abnormal	Frontal/temporal atrophy

QUICK REFERENCE: EXAM FACTS

EXAM STRATEGY

Memorize these 20 facts, they account for ~80% of dementia questions in PG exams and similar exams.

1. Most common dementia worldwide: **Alzheimer's disease (60-70%)**
2. Most common dementia in under-65s: **Frontotemporal dementia**
3. India dementia prevalence: **5.3 million** (ARDSI data)
4. Most common hallucination in DLB: **well-formed visual hallucinations**
5. 1-year rule: **DLB** (dementia ≤ 1 year before/after parkinsonism) vs **PDD** (> 1 year)
6. Neuroleptic sensitivity: **DLB**, avoid conventional antipsychotics
7. Hakim-Adams triad: **gait + incontinence + dementia** (NPH)
8. Hachinski score: ≥ 7 = **VaD**; ≤ 4 = **AD**
9. Most amyloidogenic A β species: **A β 42**
10. Best correlate of cognitive decline in AD: **synaptic loss** (not plaques/tangles)
11. APOE4 risk: **3-4x heterozygote; 8-12x homozygote**

12. First ChEI: **Tacrine** (now obsolete, hepatotoxic)
13. Dual inhibitor (AChE + BuChE): **Rivastigmine**
14. EEG finding in CJD: **periodic sharp wave complexes (PSWC)**
15. Most common pathological tau in Pick's disease: **3R tau**
16. C9orf72: **most common cause of familial FTD + ALS**
17. Pseudodementia: coined by **Kiloh (1961)**
18. MoCA normal cutoff: **≥26** (add 1 if education ≤12 years)
19. MMSE max score: **30**; CDR-SoB max: **18**
20. Lecanemab trial: **CLARITY-AD; 27% slowing of decline**

Sources: Kaplan & Sadock's Synopsis of Psychiatry 12th Ed, Oxford Textbook of Psychiatry 6th Ed, Cummings' Neuropsychiatry and Behavioral Neuroscience 3rd Ed, NIA-AA 2018 Research Framework, McKeith Criteria 2017, Rascovsky Criteria 2011

Model Answers

EXAM STRATEGY

Each answer follows the PG exams 10-mark format: Definition (1 mark) → Classification/Types (2 marks) → Pathology/Mechanism (3 marks) → Clinical features (2 marks) → Management/Investigation (2 marks). Adapt proportions based on question framing.

ANSWER 1: Define dementia. Classify and describe the clinical features of Alzheimer's disease. Add a note on its pharmacological management.

Definition (1 mark)

Dementia is a syndrome of acquired, persistent, progressive cognitive decline affecting two or more cognitive domains, including memory, language, executive function, visuospatial abilities, or social cognition, representing a decline from a previously higher level of functioning, and severe enough to interfere with daily occupational or social activities.

Per **DSM-5**: Now termed **Major Neurocognitive Disorder (Major NCD)**. Per **ICD-11**: Dementia is retained as an overarching diagnostic category.

Classification of Dementia (2 marks)

By Aetiology:

CATEGORY · EXAMPLES

Degenerative Alzheimer's disease, DLB, FTD, PDD

Vascular Multi-infarct, Binswanger's, strategic infarct

Prion CJD, vCJD, Kuru

Infectious Neurosyphilis, HIV, cryptococcal, TB

Metabolic/Toxic Hypothyroidism, B12 deficiency, hepatic, alcohol

Structural NPH, subdural haematoma, tumour

Autoimmune Anti-NMDAR encephalitis, limbic encephalitis

By **Reversibility**: Reversible (~15%) vs Irreversible

By **Age**: Pre-senile (<65 years) vs Senile (≥65 years)

By Cortical Anatomy: Cortical (AD, FTD) vs Subcortical (VaD, DLB, PSP, HD) vs Mixed

Alzheimer's Disease: Pathology (3 marks)

Epidemiology: Most common dementia (60-70%); prevalence doubles every 5 years after age 65; India: ~5.3 million total dementia cases (ARDSI 2023), with AD comprising the majority.

Gross Pathology: Cortical atrophy predominantly affecting hippocampus, entorhinal cortex, and parietal and temporal association areas. Ventricular enlargement (ex vacuo).

Microscopic Hallmarks:

- **Senile plaques**, extracellular deposits of beta-amyloid ($A\beta_{42}$) peptide; neuritic plaques are pathologically significant
- **Neurofibrillary tangles (NFTs)**, intraneuronal accumulations of hyperphosphorylated tau protein in paired helical filaments; Braak staging I-VI
- **Synaptic loss**, the best histological correlate of cognitive decline

Neurochemistry: Marked reduction in acetylcholine (nucleus basalis of Meynert, 50-90%), noradrenaline, serotonin; glutamatergic dysregulation.

Genetics: APP (chromosome 21), PSEN1 (chromosome 14), PSEN2 (chromosome 1), early-onset familial; APOE4 (chromosome 19), risk factor for late-onset sporadic.

Clinical Features (2 marks)

Early (Mild) Stage:

- Episodic memory impairment, forgetting recent events, appointments
- Word-finding difficulties (anomia)
- Spatial disorientation in unfamiliar environments
- Mild impairment in instrumental ADLs (finances, medications)
- Insight often preserved

Middle (Moderate) Stage:

- Progressive memory loss; retrograde involvement
- Impaired orientation (time, then place)
- Language deterioration (paraphasia, reduced vocabulary)
- Apraxia, agnosia, acalculia
- Behavioural and psychological symptoms (delusions of theft, wandering, agitation)
- Dependent in basic ADLs

Late (Severe) Stage:

- Severe global cognitive decline

- Non-communicative
- Double incontinence
- Motor signs (rigidity, myoclonus in late stages)
- Bedridden, aspiration, death from intercurrent illness

MMSE Range: Mild ~18-23; Moderate ~12-17; Severe 0-11

Pharmacological Management (2 marks)

Cholinesterase Inhibitors (mild-moderate):

DRUG	DOSE	FEATURE
Donepezil	5→10→23mg OD	All stages; once daily
Rivastigmine	1.5→6mg BD (oral) or transdermal patch	Dual AChE+BuChE; preferred in DLB
Galantamine	4→12mg BD	Also modulates nicotinic receptors

NMDA Antagonist (moderate-severe):

- Memantine 5→20mg OD, reduces glutamatergic excitotoxicity
- Can combine with donepezil for additive benefit (Tariot et al., 2004)

Newer Agents (early AD with biomarker confirmation):

- Lecanemab (Leqembi), anti-A β protofibrils antibody; 27% slowing of decline (CLARITY-AD, 2022)
- Donanemab, FDA approved 2024; TRAILBLAZER-ALZ 2 trial
- Risk of ARIA (amyloid-related imaging abnormalities), requires MRI monitoring

BPSD Management: Risperidone (best evidence) for psychosis/agitation; SSRIs for depression; melatonin for sleep; non-pharmacological interventions first-line.

EXAM PEARL

Drug class sequence: Mild = ChEI; Moderate = ChEI + Memantine; Severe = Memantine $\pm$ ChEI; New biomarker-confirmed early AD = anti-amyloid (lecanemab / donanemab). All antipsychotics in dementia carry FDA black box warning.

ANSWER 2: Describe the clinical features, diagnosis, and management of Dementia with Lewy Bodies (DLB). Highlight the differences from Parkinson's Disease Dementia.

Definition and Overview (1 mark)

DLB is a neurodegenerative dementia characterised by the pathological accumulation of alpha-synuclein (Lewy bodies) in cortical and subcortical neurons, producing a clinical triad of fluctuating cognition, recurrent visual hallucinations, and parkinsonism. It is the second most common neurodegenerative dementia (~15-20%).

Pathology (2 marks)

- **Lewy bodies:** Intraneuronal inclusions of misfolded alpha-synuclein; eosinophilic core with radiating halo
- Distribution: cortical > subcortical (in DLB); brainstem predominant (in PD)
- Neurochemistry: Severe cholinergic deficit (greater than AD); dopaminergic deficit (nigrostriatal); noradrenergic and serotonergic loss
- Braak staging: stages 5-6 (neocortical involvement) in DLB

McKeith Criteria 2017: Clinical Features (3 marks)

Essential: Progressive dementia interfering with daily function; prominent early deficits in attention, executive function, visuospatial ability; memory may be relatively preserved initially.

Core Clinical Features (need 2 for "probable"):

Fluctuating cognition Pronounced variation in attention/alertness; good days and bad days; episodes of confusion or somnolence

Recurrent visual hallucinations Well-formed, detailed, typically animals or people; often non-threatening; early in disease course

REM sleep behaviour disorder (RBD) Acting out dreams; vocalisation and complex movements during sleep; often predates dementia by years

Parkinsonism ≥ 1 of: bradykinesia, resting tremor, rigidity; usually mild; onset concurrent with or after dementia

Supportive Features:

- Severe neuroleptic sensitivity (hallmark, can be fatal)
- Postural instability, falls, syncope
- Autonomic dysfunction (orthostatic hypotension, constipation)
- Neuropsychiatric: depression, anxiety, delusions

- Hypersomnia, hyposmia

Indicative Biomarkers:

- Reduced DAT uptake on DaTSCAN (SPECT)
- Abnormal cardiac MIBG scintigraphy
- PSG confirmation of REM sleep without atonia

Diagnosis (2 marks)

- Clinical diagnosis per McKeith 2017 criteria
- DaTSCAN: reduced striatal dopamine transporter uptake, distinguishes DLB from AD
- EEG: posterior slow wave activity; complex transient waves
- MRI: relative preservation of medial temporal lobe (vs AD); generalised atrophy
- FDG-PET: occipital hypometabolism (distinctive, preserved in AD)
- Neuropsychological testing: early visuospatial and attentional deficits

Management (2 marks)

Cognitive: Rivastigmine (approved; significant benefit given severe cholinergic deficit); donepezil (off-label)

Parkinsonism: Levodopa (modest benefit; may worsen psychosis); avoid dopamine agonists

Psychosis, CRITICAL POINT:

- AVOID conventional antipsychotics (haloperidol, chlorpromazine), neuroleptic sensitivity reaction (30-50%): severe rigidity, autonomic crisis, accelerated cognitive decline, death
- Use ONLY: quetiapine (low dose) or clozapine (with CBC monitoring)

Sleep (RBD): Clonazepam 0.25-2mg nocte; melatonin 3-12mg

Depression: SSRIs (sertraline, escitalopram)

DLB vs PDD (Differences) (on request or as note):

FEATURE	DLB	PDD
Timing	Dementia first or concurrent (≤ 1 year of parkinsonism)	Parkinsonism first, dementia >1 year later
Lewy body distribution	Cortical prominent	Subcortical / brainstem prominent initially
Visual hallucinations	Early, prominent	Later
L-DOPA response	Modest	Better

FEATURE	DLB	PDD
Memory	Relatively spared early	Similar
Prognosis	Similar	Similar

KEY INSIGHT

EXAM PEARL, THE 1-YEAR RULE: If cognitive impairment precedes or occurs within 1 year of motor symptoms = DLB. If motor symptoms precede cognitive impairment by >1 year = PDD. Both are alpha-synucleinopathies on the same biological spectrum.

ANSWER 3: Classify Frontotemporal Dementia (FTD). Describe the clinical features of behavioral variant FTD (bvFTD) and its management.

Definition and Overview (1 mark)

Frontotemporal dementia (FTD) encompasses a group of neurodegenerative conditions characterised by progressive degeneration of the frontal and/or temporal lobes, presenting with prominent changes in behaviour, personality, or language. It is the most common dementia in those under 65 years (peak onset 45-65 years) and the third most common neurodegenerative dementia overall.

Classification (2 marks)

Clinical Syndromes:

SYNDROME	PRIMARY ANATOMY	CORE DEFICIT
Behavioral variant FTD (bvFTD)	Bilateral frontal lobes	Personality/behavioural changes
Semantic variant PPA (svPPA)	Left anterior temporal	Word/object meaning loss
Nonfluent/agrammatic variant PPA (nfvPPA)	Left posterior frontal, insula	Effortful, agrammatic speech

Associated Syndromes (FTD spectrum):

- Progressive Supranuclear Palsy (PSP)
- Corticobasal Degeneration (CBD)
- FTD-MND (FTD with Motor Neuron Disease), TDP-43 pathology, C9orf72 mutation

Neuropathological Classification:

- FTLD-Tau (Pick's disease, CBD, PSP)
- FTLD-TDP (~50%; includes FTD-MND)

- FTLD-FUS (rare)

bvFTD: Rascovsky Criteria 2011 (3 marks)

Requires 3 of 6 core features for **Possible bvFTD**:

1. Disinhibition:

- Socially inappropriate behaviour (offensive remarks, physical impropriety)
- Loss of social tact and manners
- Impulsive, reckless actions (inappropriate spending, sexual disinhibition)

2. Apathy / Inertia:

- Loss of motivation and drive
- Persists throughout the day (unlike depression which may fluctuate)
- Reduced spontaneous behaviour, social withdrawal

3. Loss of Sympathy / Empathy:

- Diminished response to others' emotions
- Change in social relationships
- Indifference to close family members

4. Perseverative / Compulsive Behaviour:

- Stereotyped repetitive acts (tapping, humming, clapping)
- Ritual behaviours, fixed routines
- Hoarding, collecting
- Dietary changes (preference for sweets, carbohydrates, specific foods)

5. Hyperorality and Dietary Changes:

- Oral fixation; putting objects in mouth
- Gluttony, food cramming
- Altered food preferences; increased alcohol/tobacco

6. Neuropsychological Profile:

- Executive dysfunction (planning, abstraction, working memory)
- Relative sparing of memory (episodic) and visuospatial in early stages
- Frontal release signs (snout, grasp reflex)

Important: Insight is impaired, patient does not recognise their behaviour as abnormal.

Memory Pattern: Unlike AD, episodic memory is relatively preserved early in bvFTD. This is a key distinction.

Imaging:

- MRI: frontal and anterior temporal atrophy (bilateral, often asymmetric)
- FDG-PET: frontal and anterior temporal hypometabolism
- DaTSCAN: typically normal (unlike DLB)

Genetics (on request) (1 mark)

- MAPT (chromosome 17): tau mutations
- GRN/Progranulin (chromosome 17): TDP-43 pathology
- C9orf72 (chromosome 9): most common familial cause (hexanucleotide repeat expansion); also causes familial ALS

Management (2 marks)

No disease-modifying therapy.

Behavioural Symptoms:

- SSRIs (sertraline 50-200mg, fluvoxamine), first-line for disinhibition, compulsive behaviours, hyperorality, aggression; evidence from open-label studies
- Low-dose atypical antipsychotics (quetiapine, olanzapine) for severe agitation/aggression
- **Avoid ChEIs**, no evidence; galantamine may worsen hyperorality
- **Avoid memantine**, conflicting evidence; some suggest worsening

Non-Pharmacological:

- Structured routine (reduces compulsive behaviours)
- Redirection techniques
- Environmental safety (wandering, impulsive acts)
- Caregiver education: empathy deficits explained, carers must understand "he knows who I am but doesn't care how I feel"

Genetic Counselling:

- Autosomal dominant families (MAPT, GRN, C9orf72), genetic testing for at-risk members
- Predictive testing protocols

Speech-Language Therapy: For PPA variants

ANSWER 4: Discuss Normal Pressure Hydrocephalus: clinical features, diagnosis, and treatment.

Definition (1 mark)

Normal Pressure Hydrocephalus (NPH) is a clinical syndrome characterised by the triad of gait disturbance, urinary incontinence, and cognitive impairment, in the setting of ventriculomegaly on imaging with normal or intermittently normal cerebrospinal fluid pressure on lumbar puncture. It was first described by **Adams and Hakim (1965)**.

Aetiology and Pathophysiology (2 marks)

Idiopathic NPH (iNPH): No identifiable cause; most common in elderly

Secondary NPH: Follows known insult, subarachnoid haemorrhage, head injury, meningitis, prior neurosurgery

Pathophysiology:

- Impaired CSF absorption at the arachnoid villi (Pacchionian granulations)
- CSF accumulation → ventricular enlargement
- Normal or intermittently elevated CSF pressure (pressure waves occur transiently)
- Ventricular expansion compresses periventricular white matter, especially frontal-subcortical circuits
- Disruption of frontosubcortical pathways → gait, continence, cognition triad

Clinical Features: Hakim-Adams Triad (3 marks)

Order of Appearance: Gait → Incontinence → Dementia (the G-I-D sequence)

Gait apraxia (Wobbly) Magnetic gait (feet appear glued to floor); wide-based; short shuffling steps; difficulty initiating; en bloc turning; preserved arm swing (unlike Parkinson's); no cerebellar ataxia

Urinary incontinence (Wet) Urge incontinence (urgency > overflow); may initially present as frequency or nocturia; due to frontal micturition centre disruption

Dementia (Wacky) Frontal-subcortical pattern; psychomotor slowing; executive dysfunction; apathy; memory impairment (retrieval > encoding); relatively mild compared to AD

Important nuances:

- Not all three features present in all patients
- Gait disturbance is earliest and most prominent
- Cognitive impairment is often mild to moderate

- Differentiation of gait from Parkinson's: NPH has no tremor, arm swing may be preserved, no rigidity at initiation, improved by cadence cues inconsistently

Investigations and Diagnosis (2 marks)

Imaging:

- CT/MRI brain: **ventriculomegaly** (Evans index >0.3 : bifrontal horn diameter / internal skull diameter); small or absent cortical sulci over the vertex (high convexity); DESH pattern on MRI (Disproportionately Enlarged Subarachnoid-Space Hydrocephalus, periventricular edema with sulcal obliteration)
- MRI: periventricular signal changes, aqueductal flow void (on CINE MRI)

Lumbar Puncture:

- Opening pressure: **<200 mm H₂O (normal)**, defining criterion
- CSF composition: normal

CSF Tap Test (Miller Fisher Test):

- Remove 30-50 mL CSF
- Assess gait before and 1-24-72 hours after
- Positive if gait improves, predicts shunt response (sensitivity 50-60%, specificity ~80%)

Extended Lumbar Drain:

- 3-5 days continuous CSF drainage (~150-200 mL / day)
- Higher sensitivity for predicting shunt response

Neuropsychological Testing: Pre- and post-tap comparison; documents baseline cognitive profile

Treatment (2 marks)

Ventriculoperitoneal (VP) Shunt:

- Definitive treatment
- Best response: young age, short duration, gait-predominant presentation, positive tap test
- Response rates: gait 50-80%, incontinence 40-60%, cognition 25-40%
- Complications: over-drainage (subdural haematoma), use programmable pressure valves; infection; shunt failure; intracranial haemorrhage

Programmable Valves: Preferred, allow non-invasive pressure adjustment post-implantation

Endoscopic Third Ventriculostomy (ETV): Alternative in selected cases

EXAM PEARL

NPH is one of the few TREATABLE causes of dementia. If a patient ≥ 65 with gait, incontinence, and dementia is presented, NPH must be considered first.

ANSWER 5: Write an essay on reversible causes of dementia with special emphasis on pseudodementia.

Definition and Importance (1 mark)

Reversible dementia refers to cognitive impairment that, when the underlying cause is identified and treated, results in partial or complete improvement. Approximately **15% of dementia presentations** have a potentially reversible component. Identifying reversible causes is critical because many are treatable and can prevent permanent cognitive damage.

Classification: "DEMENTIAS" Mnemonic (2 marks)

LETTER	CAUSE	KEY INVESTIGATION
D	Drugs (anticholinergics, benzodiazepines, opioids, steroids, alcohol)	Medication review
E	Endocrine (hypothyroidism, Cushing's, hypopituitarism, hypoparathyroidism)	TSH, cortisol, calcium
M	Metabolic (hepatic failure, renal failure, B12/folate, hypoglycaemia)	LFT, RFT, B12, folate
E	Eye and ear (sensory deprivation worsening cognitive performance)	Audiometry, visual testing
N	Normal pressure hydrocephalus	CT head, tap test
T	Trauma (chronic subdural haematoma, boxing-related)	CT head
I	Infections (neurosyphilis, HIV, cryptococcal, TB, viral encephalitis)	VDRL, HIV, CSF
A	Affective disorder (depression, pseudodementia)	Psychiatric assessment
S	Space-occupying lesion (tumour, abscess, cysts)	CT/MRI

Key Reversible Causes (3 marks)

Hypothyroidism:

- Symptoms: cognitive slowing, memory impairment, psychomotor retardation, depression, psychosis ("myxoedema madness")
- Diagnosis: TSH elevated, free T4 low
- Treatment: levothyroxine, cognitive improvement within 6-12 weeks

Vitamin B12 Deficiency:

- Psychiatric manifestations: depression, irritability, mania, psychosis
- Cognitive: slowing, memory impairment, confusion
- Neurological: subacute combined degeneration of spinal cord
- Investigations: serum B12 <200 pg/mL; methylmalonic acid (elevated, more sensitive); homocysteine (elevated)
- Treatment: IM hydroxocobalamin; high-dose oral B12 (1000mcg/day)

Neurosyphilis:

- General Paralysis of the Insane (GPI): dementia, personality change, grandiose delusions, dysarthria, Argyll Robertson pupil
- Tabes dorsalis component
- Investigations: blood VDRL/RPR (screening), TPHA/FTA-ABS (confirmatory), CSF VDRL
- Treatment: penicillin G IV 18-24 million units/day × 10-14 days

HIV-Associated Neurocognitive Disorder (HAND):

- Spectrum: asymptomatic NCI → MND → HAD
- Subcortical pattern: psychomotor slowing, executive dysfunction
- Diagnosis: CSF HIV RNA, neuroimaging, neuropsychological battery
- Treatment: ART (combination antiretroviral), can reverse early HAND

Medication-Induced:

- Anticholinergics (most common iatrogenic cause of cognitive impairment in elderly)
- Benzodiazepines (anterograde amnesia, sedation)
- Review and rationalise polypharmacy

Pseudodementia: Depressive Pseudodementia (2 marks)

Definition: Pseudodementia (term coined by **Kiloh, 1961**) refers to a reversible, dementia-like cognitive syndrome occurring in the context of a primary psychiatric disorder, most commonly major depression, that mimics neurodegenerative dementia but resolves with appropriate psychiatric treatment.

Pathophysiology: Depression impairs attention, concentration, working memory, and motivation, producing objective cognitive deficits. Neurobiological correlates include HPA axis dysregulation, hippocampal volume loss (reversible), and reduced prefrontal activity.

Differential Features:

FEATURE	PSEUDODEMENTIA (DEPRESSION)	TRUE DEMENTIA
Onset	Related to depressive episode; identifiable precipitant	Insidious; no clear onset
Duration	Shorter	Months to years
Subjective complaints	Prominent; actively seeks help	Minimises or denies deficits
Cognitive testing	Variable; inconsistent; "I don't know" answers	Consistent impairment; near-miss errors; confabulation
Cooperation with testing	May refuse; unmotivated	Tries hard; frustrated
Mood	Depressed mood pervasive	Mood changes secondary
Sleep	Insomnia (especially early morning)	Day-night reversal common
Weight	Loss (depression-related)	Loss (late in dementia)
Family history	Often depression	Often dementia
Response to treatment	Cognitive improvement with antidepressants	No cognitive improvement
Imaging	Often normal or mild generalised changes	Specific patterns (hippocampal atrophy, infarcts)

EXAM PEARL

The key distinguisher: In pseudodementia, the patient **amplifies disabilities** ("I can't do anything"). In true dementia, the patient **minimises or is unaware** ("I'm doing fine"). Kiloh 1961 coined the term.

Management:

- Treat underlying depression: SSRIs first-line (sertraline, escitalopram, mirtazapine)
- ECT if severe depression with cognitive impairment, often rapid improvement
- Neuropsychological follow-up to confirm cognitive recovery
- Note: pseudodementia is a risk factor for later true dementia (15-20% convert over 3 years)

ANSWER 6: Describe the clinical features and management of Behavioral and Psychological Symptoms of Dementia (BPSD).

Definition and Epidemiology (1 mark)

Behavioral and Psychological Symptoms of Dementia (BPSD), also known as neuropsychiatric symptoms of dementia, refers to the non-cognitive manifestations of dementia including disturbances of perception, thought content, mood, and behaviour. BPSD affects approximately 90% of patients with dementia at some point in their illness course. They are the primary drivers of caregiver distress and institutionalisation.

Classification (2 marks)

DOMAIN · SYMPTOMS

Psychotic symptoms Delusions (theft, infidelity, Capgras, phantom boarder), hallucinations (visual > auditory)

Affective symptoms Depression (~30-50%), anxiety (~30%), euphoria

Behavioural disturbances Agitation, aggression, wandering, disinhibition, sexual disinhibition

Vegetative symptoms Sleep disturbance (day-night reversal, insomnia), appetite changes, weight loss

Apathy Most common single BPSD (~70%); reduced motivation, emotional blunting

Other Pacing, sundowning, shadowing

Most common delusion in AD: Theft delusion (misattributing misplaced objects to theft)

Most common BPSD overall: Apathy (~70%)

Most distressing for carers: Agitation and aggression

Assessment, NPI (Neuropsychiatric Inventory, Cummings): 12-domain informant-based scale; each domain scored as frequency (1-4) × severity (1-3); max 144 points; also records caregiver distress per domain.

Non-Pharmacological Management: FIRST LINE (3 marks)

Principle: Identify and address triggers (pain, infection, environment, unmet needs) before any pharmacological intervention.

INTERVENTION	EVIDENCE	APPLICATION
Person-centred care	Strong	Know biographical history, preferences, routines; match care to life story

INTERVENTION	EVIDENCE	APPLICATION
Validation therapy	Moderate	Enter the patient's subjective reality rather than correcting; reduces confrontation
Music therapy	Strong	Personalised music reduces agitation; calms during bathing / meals
Bright light therapy	Moderate	Addresses sundowning and circadian disruption
Structured activities	Moderate	Occupational therapy; meaningful activity reduces wandering
Exercise	Moderate	Reduces agitation; improves sleep and physical health
Reminiscence therapy	Moderate	Photos, familiar objects; reduces depression; enhances engagement
Environmental modifications	Strong	Safe, calm, uncluttered; consistent lighting; secured exits for wanderers
Caregiver training	Strongest	Education on triggers, communication, de-escalation

Pharmacological Management (2 marks)

KEY INSIGHT

CRITICAL CAUTION: All antipsychotics in dementia carry FDA **BLACK BOX WARNING**, 1.6-1.7x increased mortality (cerebrovascular accidents, pneumonia). Use only when non-pharmacological measures fail, document informed consent, use minimum effective dose, review every 3 months.

Agitation/Psychosis:

DRUG	EVIDENCE	STARTING DOSE	NOTES
Risperidone	Best evidence (BPSD)	0.25-0.5mg / day	NNT ~5-7; EPS risk; avoid in DLB
Olanzapine	Moderate	2.5-5mg / day	Sedation; metabolic effects
Quetiapine	Weakest evidence	12.5-25mg BD	Preferred in DLB; minimal EPS

DRUG	EVIDENCE	STARTING DOSE	NOTES
Haloperidol	Agitation only	0.25-0.5mg	Avoid, significant EPS, falls
Memantine	Modest	20mg/day	Safer; some anti-agitation effect

CATIE-AD Study (2006): No significant efficacy advantage of risperidone, olanzapine, or quetiapine over placebo; significant adverse effects. Reinforces non-pharmacological priority.

Depression in Dementia:

- SSRIs: sertraline 50mg, escitalopram 5-10mg
- Mirtazapine 7.5-30mg (if depression + insomnia + anorexia)
- Avoid TCAs (anticholinergic burden)

Anxiety:

- SSRIs first-line
- Buspirone 5-10mg TDS
- Avoid benzodiazepines if possible (falls, paradoxical agitation, cognitive worsening)

Sleep Disturbance:

- Melatonin 2-10mg nocte (safest)
- Trazodone 25-100mg nocte
- Mirtazapine 7.5-15mg
- Avoid antihistamines (anticholinergic), benzodiazepines (falls, cognitive worsening)

Summary Approach (2 marks)

Step 1: Identify and treat reversible precipitants (pain, UTI, constipation, medication toxicity)

Step 2: Non-pharmacological interventions (tailored to symptom type)

Step 3: Pharmacological only if above fails or patient/carer safety at risk; reassess every 3 months; attempt dose reduction after 3-6 months of stability

ANSWER 7: Discuss the role of biomarkers in the diagnosis of Alzheimer's disease.

Introduction (1 mark)

Biomarkers in Alzheimer's disease (AD) are measurable biological parameters that reflect underlying pathological processes, enabling diagnosis in the pre-symptomatic or early

symptomatic stages, before significant neurodegeneration. The **NIA-AA 2018 Research Framework** (Jack et al.) operationalised the A/T/N classification system, shifting AD diagnosis from purely clinical to biologically defined.

Rationale for Biomarkers (1 mark)

Clinical diagnosis of AD has ~80% accuracy when performed by dementia specialists. Biomarkers improve diagnostic accuracy to >90%. They are essential for:

- Entry criteria in clinical trials (anti-amyloid therapies require amyloid confirmation)
- Early/preclinical diagnosis enabling preventive intervention
- Differential diagnosis from non-AD dementias
- Monitoring disease progression and treatment response

A/T/N Classification (2 marks)

BIOMARKER CATEGORY	MEANING	CSF MARKER	PET MARKER
A (Amyloid)	Amyloid-beta pathology	A β 42↓; A β 42/40 ratio↓	Amyloid PET positive
T (Tau)	Tau pathology	Phospho-tau↑	Tau PET positive
N (Neurodegeneration)	Neuronal injury	Total tau↑	FDG-PET hypometabolism; MRI atrophy

Profiles:

- A+/T-/N- = Alzheimer's pathological change (no tauopathy)
- A+/T+/N- = Alzheimer's disease (early)
- A+/T+/N+ = Alzheimer's disease (established neurodegeneration)
- A-/T+/N+ = Non-AD tauopathy

CSF Biomarkers (2 marks)

BIOMARKER	CHANGE	SENSITIVITY	SPECIFICITY
A β 42	Decreased	~86%	~90%
p-tau181	Increased	~79%	~91%
Total tau (t-tau)	Increased	~81%	~90%
A β 42/40 ratio	Decreased	~90%	~90%
p-tau/A β 42 ratio	Increased (best overall)	~91%	~91%

CSF biomarkers can detect pathological changes **10-15 years before** clinical symptoms.

Neuroimaging Biomarkers (2 marks)

Structural MRI:

- Medial temporal lobe atrophy (MTA), especially hippocampus and entorhinal cortex
- Scheltens MTA scale (0-4): score ≥ 2 suggests AD
- VBM (voxel-based morphometry): global atrophy pattern temporo-parietal > frontal

Amyloid PET (Florbetapir, Flutemetamol, Florbetaben):

- Positive: diffuse cortical binding (beyond white matter)
- Sensitivity ~96%, Specificity ~93%
- Presence of amyloid does not equal AD (20-30% cognitively normal elderly have amyloid+)
- FDA-approved; required for anti-amyloid therapy eligibility

Tau PET (Flortaucipir/AV-1451):

- Images neurofibrillary tangles directly
- Follows Braak staging hierarchically
- Correlates better with cognitive symptoms than amyloid PET

FDG-PET:

- AD pattern: bilateral temporo-parietal + posterior cingulate hypometabolism
- Sparing primary sensorimotor and occipital cortex until late
- Differentiates AD from FTD (frontal hypometabolism)

Blood Biomarkers (1 mark: emerging/recent advances)

BIOMARKER	ACCURACY	NOTES
Plasma p-tau217	~90%+	Highest diagnostic accuracy currently; validated against amyloid PET
Plasma p-tau181	~80-85%	Widely studied; elevated years before symptoms
Plasma A β 42/40	~80%	Reflects CSF ratio; feasible for population screening
Plasma NfL	Elevated	Neurodegeneration marker; not AD-specific
Plasma GFAP	Elevated	Astrocyte activation; correlates with amyloid burden

Blood biomarkers represent the future of AD screening, enabling large-scale, low-cost, accessible detection before expensive PET or lumbar puncture.

EXAM PEARL

For exam purposes: CSF shows $A\beta_{42}\downarrow + p\text{-tau}\uparrow + t\text{-tau}\uparrow$. Amyloid PET is the gold standard for amyloid detection. Plasma p-tau217 is the most accurate blood biomarker. ARIA is the main risk of anti-amyloid immunotherapy.

ANSWER 8: Describe the clinical features, investigations, and management of Creutzfeldt-Jakob Disease (CJD).

Introduction and Classification (1 mark)

Creutzfeldt-Jakob Disease (CJD) is a rare, rapidly progressive, invariably fatal prion disease belonging to the group of Transmissible Spongiform Encephalopathies (TSEs). The causative agent is PrP^{Sc}, a misfolded, protease-resistant isoform of the normal cellular prion protein (PrP^C) that propagates by inducing conformational change in normal PrP^C.

Types:

TYPE	CAUSE	FREQUENCY
Sporadic (sCJD)	Spontaneous PrP ^C → PrP ^{Sc} misfolding	85-90%
Familial/Genetic (gCJD)	PRNP gene mutations (autosomal dominant)	10-15%
Iatrogenic (iCJD)	Contaminated dura mater, corneal grafts, pituitary-derived growth hormone, surgical instruments	<1%
Variant (vCJD)	Bovine spongiform encephalopathy (BSE) transmission	Rare

Clinical Features (3 marks)

Sporadic CJD:

- Onset: Mean age 60-65 years; median survival 5-6 months (85% die within 1 year)
- Prodrome: anxiety, depression, insomnia, vague cognitive complaints
- Rapidly progressive dementia (weeks to months, HALLMARK)
- **Myoclonus**, stimulus-sensitive; present in 90%; pathognomonic in context
- Cerebellar ataxia, dysarthria
- Extrapyrarnidal signs (rigidity, dystonia)
- Visual disturbances (cortical blindness, Heidenhain variant)
- Pyramidal signs

- Akinetic mutism, terminal stage
- Death: aspiration pneumonia, sepsis

Variant CJD (vCJD):

- Onset: Much younger (mean 28 years), BSE-linked dietary exposure
- **Psychiatric onset:** depression, anxiety, withdrawal, personality change (6-12 months before neurological features)
- Sensory symptoms: dysaesthesias, pain (characteristic)
- Later: progressive dementia, ataxia, involuntary movements
- NO periodic EEG changes (unlike sCJD)
- Survival: 12-14 months (longer than sCJD)

Investigations (2 marks)

INVESTIGATION	FINDING IN SCJD	FINDING IN VCJD
EEG	Periodic sharp wave complexes (PSWC) at 1-2 Hz, pathognomonic	Usually absent
MRI (DWI)	"Cortical ribboning" (restricted diffusion cortex); basal ganglia DWI signal; "hockey stick sign" (thalamic / pulvinar DWI)	"Pulvinar sign", bilateral posterior thalamic hyperintensity on FLAIR / DWI
CSF 14-3-3 protein	Elevated; sensitivity 85%, specificity 80%	Usually negative
CSF RT-QuIC	>95% sensitivity, >98% specificity, gold standard for living diagnosis	Variable
Nasal brushing RT-QuIC	High sensitivity without LP	Research use
Brain biopsy	Definitive; spongiform vacuolation, PrPSc on immunostaining	Definitive; also tonsil biopsy (PrPSc)
Tau protein (CSF)	Very high (reflects rapid neurodegeneration)	Elevated

WHO Diagnostic Criteria (Sporadic CJD):

- Definite: neuropathological / immunohistochemical confirmation
- Probable: rapidly progressive dementia + EEG PSWC OR positive RT-QuIC + ≥ 2 of (myoclonus, visual, cerebellar, pyramidal / extrapyramidal, akinetic mutism)
- Possible: does not meet above but <2 years progressive dementia

Management and Prognosis (2 marks)

No disease-modifying treatment exists. All CJD is fatal.

Palliative/Supportive Management:

- Symptom control: clonazepam for myoclonus; opioids for pain
- Hospice/palliative care: early involvement
- Psychological support: family counselling; anticipatory grief
- Infection control: universal precautions; CJD-contaminated instruments require special decontamination (autoclaving standard ineffective, requires 1M NaOH or 134°C extended autoclaving)

Notifiable Disease: CJD is a notifiable condition in most jurisdictions including India.

EXAM PEARL

EEG PSWC + rapidly progressive dementia + myoclonus = CJD until proven otherwise. RT-QuIC is now the investigation of choice for living diagnosis. vCJD = young + psychiatric onset + pulvinar sign + no PSWC.

ANSWER 9: Discuss the assessment of cognitive function with reference to MMSE and MoCA.

Introduction (1 mark)

Cognitive assessment tools serve multiple functions in clinical practice: screening for cognitive impairment, staging severity, monitoring progression, and assessing treatment response. Brief bedside cognitive tests are essential first-line tools but must be interpreted in the context of age, education, cultural background, and sensory deficits.

MMSE: Mini Mental State Examination (Folstein et al., 1975) (3 marks)

Overview: 30-point screening tool; 5-10 minutes; most widely used globally; assesses orientation, registration, attention, recall, language, and visuospatial.

DOMAIN	TASK	MAX SCORE
Orientation to time	Year, season, month, date, day	5
Orientation to place	Country, state, city, building, floor	5
Registration	Name and repeat 3 objects immediately	3
Attention/calculation	Serial 7s (5 subtractions) OR spell WORLD backwards	5

DOMAIN	TASK	MAX SCORE
Recall	Recall the 3 objects after ~5 minutes	3
Naming	Name 2 objects (pen, watch)	2
Repetition	Repeat "No ifs, ands, or buts"	1
Three-stage command	Take paper, fold it, place on floor	3
Reading	Read and obey "CLOSE YOUR EYES"	1
Writing	Write a sentence spontaneously	1
Copying	Copy intersecting pentagons	1
Total		30

Scoring Thresholds:

- 27-30: Normal
- 24-26: Questionable/MCI range
- 18-23: Mild dementia
- 12-17: Moderate dementia
- 0-11: Severe dementia

Limitations:

- Ceiling effect in highly educated individuals (misses MCI)
- Floor effect in low literacy/education
- Does NOT assess frontal/executive function (planning, abstraction)
- Poor at detecting frontal or subcortical dementias (FTD, VaD)
- Language and cultural bias
- Copyrighted (Psychological Assessment Resources), fees apply

MoCA: Montreal Cognitive Assessment (Nasreddine et al., 2005) (3 marks)

Overview: 30-point screening tool; 10-15 minutes; developed specifically to detect MCI; better sensitivity for executive and visuospatial deficits.

DOMAIN	TASKS	MAX SCORE
Visuospatial/Executive	Trail Making B (connect 1-A-2-B-3-C), 3D cube copy, clock drawing	5
Naming	Name 3 animals (lion, rhinoceros, camel)	3

DOMAIN	TASKS	MAX SCORE
Memory	Register 5 words (scored on delayed recall)	0 (learning only)
Attention	Forward digit span (5 digits), backward digit span (3 digits), serial 7s (5), tapping for letter	6
Language	Repeat 2 complex sentences; lexical fluency (F-words in 1 minute $\geq 11 = 1$ point)	3
Abstraction	Explain 2 analogies (train/bicycle, watch/ruler)	2
Delayed recall	Recall 5 words after ~5 minutes (with optional category cue if needed)	5
Orientation	Date, month, year, day, place, city	6
Total		30

Correction: Add 1 point if total education ≤ 12 years

Normal cutoff: $\geq 26/30$ (adjusted)

Advantages over MMSE:

- Higher sensitivity for MCI (sensitivity ~90% vs MMSE ~18% for MCI)
- Includes executive and visuospatial tasks
- Detects frontal and subcortical dementias better
- Free; available in >50 languages
- Better for younger, educated patients

Comparison Table (2 marks)

FEATURE	MMSE	MOCA
Publication year	1975	2005
Total score	30	30
Time	5-10 min	10-15 min
Normal cutoff	≥ 24	≥ 26 (+1 if education ≤ 12 yr)
MCI sensitivity	~18-40%	~90%
Executive function	Not assessed	Trail Making B, fluency, abstraction

FEATURE	MMSE	MOCA
Visuospatial	Intersecting pentagons only	Cube copy + clock + trail
Language	Naming, repetition, reading, writing	Naming + repetition + fluency
Memory	3 words	5 words
Cost	Copyrighted	Free
Best for	Moderate-severe dementia staging	MCI detection; early dementia

Other Tools (1 mark)

- **ACE-III** (100 points): Comprehensive; VLOM ratio for AD vs FTD differentiation
- **CDR** (Clinical Dementia Rating): Staging; CDR-SoB tracks change
- **ADAS-Cog** (70 points): Gold standard for clinical trials
- **Clock Drawing Test**: Quick executive/visuospatial screen
- **NPI**: BPSD assessment (informant-based)

ANSWER 10: Discuss the vascular dementia: types, clinical features, Hachinski score, and management.

(Refer to Comparisons file D4 for full VaD vs AD table and to Study Notes Part 5 for comprehensive coverage.)

Definition and Overview (1 mark)

Vascular dementia (VaD) is cognitive impairment caused by cerebrovascular disease. It is the second most common cause of dementia (15-20% globally; ~30% in India due to high vascular risk factor burden). Pathologically heterogeneous, encompasses multiple subtypes linked by the underlying mechanism of vascular brain injury.

Types (2 marks)

TYPE	MECHANISM	CLINICAL HALLMARKS
Multi-infarct dementia	Multiple large-vessel cortical/subcortical infarcts	Stepwise deterioration; focal neurological signs
Strategic infarct dementia	Single infarct in critical location (thalamus, angular gyrus, basal forebrain)	Sudden-onset, severe cognitive change
Subcortical ischaemic VaD	Small vessel disease; lacunar infarcts; white matter changes	Gait disturbance; urinary symptoms; frontal-executive pattern

TYPE	MECHANISM	CLINICAL HALLMARKS
Binswanger's disease	Extensive periventricular WM degeneration	Abulia; white matter disease prominent on MRI
CADASIL	NOTCH3 mutation; hereditary	Migraine, strokes, dementia in young adults
Mixed dementia	AD + VaD (most common in elderly)	Combined features

Clinical Features (2 marks)

- Abrupt onset, stepwise course (each stroke = new step)
- Focal neurological deficits (hemiparesis, dysarthria, cranial nerve signs)
- Gait disturbance: marche à petit pas (subcortical VaD)
- Urinary incontinence: frontal-subcortical
- Emotional lability / emotional incontinence
- Executive dysfunction prominent; psychomotor slowing
- Memory: retrieval impairment > encoding (unlike AD)
- Depression: very common (post-stroke depression)

Hachinski Ischemic Score (2 marks)

FEATURE · SCORE

Abrupt onset 2

Stepwise deterioration 1

Fluctuating course 2

Nocturnal confusion 1

Relative preservation of personality 1

Depression 1

Somatic complaints 1

Emotional incontinence 1

History of hypertension 1

History of strokes 2

Evidence of associated atherosclerosis 1

Focal neurological symptoms 2

Focal neurological signs 2

Total 18

Score ≥ 7 = VaD; Score ≤ 4 = AD; Score 5-6 = Mixed / inconclusive

Management (1 mark)

- Primary / secondary prevention: BP control ($<130/80$), diabetes control, antiplatelet therapy, statins, smoking cessation, exercise
 - Cholinesterase inhibitors: modest evidence (donepezil approved in some countries for VaD)
 - Memantine: some evidence
 - No established disease-modifying therapy for VaD itself
-

ANSWERS 11–15: Additional High-Yield Topics

ANSWER 11: Caregiver burden in dementia: assessment and management

(Key points: Zarit Burden Interview 22-item/88 points; hidden second patient; psychoeducation + support groups + respite care; 50-70% of caregivers develop depression; India, 85-90% family-based care, no infrastructure)

ANSWER 12: MCI: definition, types, conversion rates, management

(Key: Petersen criteria; amnesic vs non-amnesic; 10-15%/year conversion; 20-30% revert; DSM-5 = Mild NCD; no approved pharmacotherapy; lifestyle modifications, hearing aids, exercise; monitoring)

ANSWER 13: Delirium superimposed on dementia: clinical features and management

(Key: 22-89% hospitalised dementia patients; acute on insidious onset; CAM criteria; identify and treat precipitant; non-pharmacological first; low-dose haloperidol cautiously; NEVER benzodiazepines first-line; never antipsychotics in DLB delirium)

ANSWER 14: Genetics of Alzheimer's disease

(Key: APP ch21 / PSEN1 ch14 / PSEN2 ch1, early-onset familial; APOE4 ch19, 3-4x hetero, 8-12x homo, risk not destiny; TREM2 ch6, microglial; Down syndrome, trisomy 21 → extra APP)

ANSWER 15: Ethical and legal issues in dementia: capacity and advance directives

(Key: Capacity = decision-specific + time-specific; 4 components of capacity, understand, appreciate, reason, communicate; MHA 2017 advance directives; driving assessment; testamentary capacity; financial exploitation most common elder abuse in dementia; guardianship)

Sources: Kaplan & Sadock's Synopsis of Psychiatry 12th Ed, Oxford Textbook of Psychiatry 6th Ed, Cummings' Neuropsychiatry and Behavioral Neuroscience 3rd Ed

Mnemonics & Memory Tricks

EXAM STRATEGY

Mnemonics are not shortcuts, they are retrieval scaffolds. Each one below is paired with the clinical/ exam context that makes it stick. Learn the story, not just the letters.

MNEMONIC 1: Reversible Causes of Dementia: "DEMENTIAS"

KEY INSIGHT

The word IS the thing it describes. Hard to forget.

LETTER	CAUSE	KEY INVESTIGATION
D	Drugs (anticholinergics, BZDs, opioids, alcohol, steroids)	Medication review
E	Endocrine (hypothyroidism, Cushing's, hypopituitarism)	TSH, cortisol, calcium
M	Metabolic (B12, folate, hepatic, renal, hypoglycaemia)	B12, LFT, RFT, glucose
E	Eye and ear (sensory deprivation worsening cognition)	Audiometry, visual acuity
N	Normal pressure hydrocephalus	CT head, tap test
T	Trauma (chronic subdural haematoma)	CT head
I	Infections (neurosyphilis, HIV, cryptococcal, TB meningitis)	VDRL, HIV, CSF
A	Affective (depression, pseudodementia)	Psychiatric assessment
S	Space-occupying lesion (tumour, abscess)	CT/MRI

EXAM PEARL

~15% of dementia presentations are potentially reversible. "DEMENTIAS" covers them all.

MNEMONIC 2: NPH Triad: "The 3 Ws"

KEY INSIGHT

Normal Pressure Hydrocephalus = Wet, Wobbly, Wacky

W	SYMPTOM	DETAIL
Wet	Urinary incontinence	Urge incontinence; frontal mic-turition centre
Wobbly	Gait apraxia	Magnetic gait; feet glued to floor; wide-based
Wacky	Dementia	Frontal-subcortical; psychomo-tor slowing; apathy

CLINICAL ANCHOR

Gait appears FIRST, incontinence second, dementia last. The mnemonic is not sequential, it's just a label. Remember: **G-I-D order** for appearance (Gait → Incontinence → Dementia).

MNEMONIC 3: DLB Core Features: "FLiRP"

KEY INSIGHT

DLB is caused by alpha-synuclein. It FLiRPs you.

LETTER · FEATURE

F Fluctuating cognition

L Lewy body hallucinations (visual, well-formed)

R REM sleep behaviour disorder

P Parkinsonism

EXAM PEARL

Need 2 of 4 core features for probable DLB diagnosis (McKeith 2017). The 1-year rule: if parkinsonism precedes dementia by >1 year = PDD, not DLB.

MNEMONIC 4: Hachinski Ischemic Score Items: "A STEP FRESH"

KEY INSIGHT

Features that score 1 point:

LETTER · FEATURE

A Atherosclerosis (associated)

S Somatic complaints

T Temporal fluctuation

E Emotional incontinence

P Personality preservation (relative)

F Feeling of depression

R Relative nocturnal confusion

E Extrapyrimal features (Hmm, actually NOT on HIS, but useful paired reminder)

S Stepwise deterioration

H Hypertension history

Features that score 2 points (remember separately): Abrupt onset (2), Fluctuating course (2), History of strokes (2), Focal symptoms (2), Focal signs (2)

EXAM PEARL

Max HIS = 18. Score ≥ 7 = VaD; ≤ 4 = AD. Five 2-point features: Abrupt onset, Fluctuating course, Stroke history, Focal symptoms, Focal signs.

MNEMONIC 5: Alzheimer's Genetics: "APP PSEN APOE"

KEY INSIGHT

Alphabetical order = Chronological discovery AND chromosome order (roughly)

- **APP** → Chromosome **21** (same as Down syndrome → universal AD)
- **PSEN1** → Chromosome **14** (most common familial AD cause)
- **PSEN2** → Chromosome **1** (least penetrant familial)
- **APOE4** → Chromosome **19** (sporadic risk factor, "19 rhymes with fine wine, and APOE is about late-life risk")

CLINICAL ANCHOR

Down syndrome = trisomy 21 = extra APP copy = amyloid accumulation → almost universal AD by 40s. APOE4 = risk, NOT destiny. Homozygotes: 8-12x risk; Heterozygotes: 3-4x risk.

MNEMONIC 6: FTD Behavioral Variant Features: "DELPHI" (Rascovsky Criteria)

KEY INSIGHT

The oracle gave 6 pronouncements. Two wrong ones still count.

LETTER · FEATURE

D Disinhibition

E Empathy loss (loss of sympathy / empathy)

L Lethargy / apathy / inertia

P Perseverative / compulsive behaviours

H Hyperoral / dietary changes

I Impaired neuropsychology (executive deficits, spared memory)

EXAM PEARL

Need 3 of 6 for POSSIBLE bvFTD. Need imaging evidence (frontal / temporal atrophy) for PROBABLE. Executive dysfunction with SPARED episodic memory in early stages, the distinguishing feature from AD.

MNEMONIC 7: Cholinesterase Inhibitors: "Don Ri Gal"

KEY INSIGHT

The three amigos: Don, Ri, and Gal, they inhibit cholinesterase.

NAME	FULL NAME	SELECTIVITY
Don	Donepezil	AChE selective
Ri	Rivastigmine	AChE + BuChE (dual)
Gal	Galantamine	AChE + nicotinic receptor modulator

EXAM PEARL

Rivastigmine = Dual inhibitor (AChE AND butyrylcholinesterase) = preferred in DLB and Parkinson's Disease Dementia. Donepezil = once daily, all stages including severe. Tacrine = FIRST ChEI but HEPATOTOXIC, obsolete.

MNEMONIC 8: CJD Investigations: "ERT"

KEY INSIGHT

ERT = Enzyme Replacement Therapy in other diseases. In CJD it means: EEG, RT-QuIC, Tau

LETTER	INVESTIGATION	KEY FINDING
E	EEG	Periodic sharp wave complexes (PSWC) 1-2 Hz
R	RT-QuIC (Real-Time Quaking-Induced Conversion)	>95% sensitivity, >98% specificity
T	Tau (CSF 14-3-3 + total tau)	Elevated (neurodegeneration marker)

EXAM PEARL

EEG PSWC = sCJD. In vCJD, PSWC is ABSENT. MRI DWI: cortical ribboning + basal ganglia in sCJD; pulvinar sign (bilateral posterior thalamus) in vCJD.

MNEMONIC 9: Tau vs Amyloid: "TAU LATER, AMYLOID FIRST"

KEY INSIGHT

The sequence of AD pathology for biomarker exams:

1. **Amyloid accumulates FIRST** (15-20 years before symptoms), CSF A β 42 $\downarrow$, amyloid PET+
2. **Tau tangles follow** (10-15 years before symptoms), CSF p-tau $\uparrow$, tau PET+
3. **Neurodegeneration last** (5-10 years before symptoms), FDG-PET $\downarrow$, MRI atrophy
4. **Clinical symptoms appear LAST**

CLINICAL ANCHOR

"Amyloid is the lit match; tau is the fire; neurodegeneration is the smoke; dementia is the alarm going off." The A/T/N framework captures this sequence.

MNEMONIC 10: Capacity Assessment: "UARC"

KEY INSIGHT

The 4 components of capacity, "You ARE Capable"

LETTER	COMPONENT	QUESTION ASKED
U	Understanding	Can you understand the information I've given you?
A	Appreciation	Can you appreciate how it applies to your situation?
R	Reasoning	Can you reason about the options and their consequences?
C	Communication	Can you express a consistent choice?

EXAM PEARL

Capacity is DECISION-SPECIFIC and TIME-SPECIFIC. A diagnosis of dementia does NOT automatically equal incapacity. Assessment must be done for each specific decision.

MNEMONIC 11: McKeith Biomarkers for DLB: "DAP" (Indicative Biomarkers)

KEY INSIGHT

DAP = Dopamine, Autonomic, Polysomnography

LETTER · BIOMARKER

D DaTSCAN, reduced dopamine transporter uptake (SPECT)

A Abnormal cardiac MIBG scintigraphy (reduced adrenergic uptake)

P Polysomnography, REM sleep without atonia (confirms RBD)

EXAM PEARL

These are the THREE indicative biomarkers in McKeith 2017 criteria. One indicative biomarker + 1 core feature = PROBABLE DLB. DaTSCAN is most widely available.

MNEMONIC 12: Braak Stages (NFT Distribution in AD): "EC Hip Lim Neo"

KEY INSIGHT

Each Hippocampus Likes Neo, the 3-stage memory palace

STAGE	LOCATION	CLINICAL CORRELATE
I-II	Entorhinal Cortex	No symptoms (preclinical)
III-IV	Hippocampus + Limbic system	MCI / early dementia
V-VI	Neocortex	Established dementia

EXAM PEARL

Braak staging correlates with CLINICAL SEVERITY. NFT burden in neocortex (stages V-VI) correlates best with dementia. Plaques and tangles both needed, neither alone is sufficient.

MNEMONIC 13: FTD Genetics: "MAPT GRN C9"

KEY INSIGHT

"MAP the GRoAN, C9 kills families"

GENE	LOCATION	PATHOLOGY
MAPT	17q21	Tau, 3R and 4R tauopathies (Pick's, CBD, PSP)
GRN	17q21	Progranulin → TDP-43 inclusions
C9orf72	9p21	Hexanucleotide repeat → FTD + ALS (most common familial)

EXAM PEARL

C9orf72 is the single most common cause of BOTH familial FTD AND familial ALS. MAPT and GRN are on the same chromosome (17), different loci. Together they account for ~60% of familial FTD.

MNEMONIC 14: BPSD Management Ladder: "N-P-R"

KEY INSIGHT

Never Prescribe Rashly, Non-pharmacological → Pharmacological → Review

STEP · ACTION

N Non-pharmacological FIRST, identify triggers, person-centred care, music therapy, structured activities

P Pharmacological if failure, risperidone (best evidence), SSRIs for depression, melatonin for sleep

R Review every 3 months, attempt dose reduction; document informed consent re: mortality risk

EXAM PEARL

All antipsychotics in dementia = FDA black box warning for increased mortality (1.6-1.7x). CATIE-AD showed no advantage of atypicals over placebo for BPSD. Non-pharmacological = FIRST LINE, always.

MNEMONIC 15: Differentiating AD from Pseudodementia: "COMPASS"

KEY INSIGHT

COMPASS, for navigating the depression vs dementia dilemma

LETTER · FEATURE FAVOURING PSEUDODEMENTIA (DEPRESSION)

C Complaints emphasised (amplified, not minimised)

O Onset linked to depressive episode

M Mood pervasively low (primary feature)

P Performance inconsistent ("I don't know" answers)

A Antidepressant response (cognitive improvement)

S Short duration

S Sleep: early morning insomnia (biological depression marker)

EXAM PEARL

Pseudodementia coined by Kiloh (1961). 15-20% of pseudodementia patients convert to true dementia within 3 years, it is not entirely benign. ECT is both diagnostic and therapeutic in severe cases.

MNEMONIC 16 (Bonus): MMSE Domains: "ORARNCWCR" (Or A Rainbow Never Comes Without Colour Reading)

LETTER	DOMAIN	POINTS
O	Orientation (time)	5
A	Orientation (plAce)	5
R	Registration (3 objects)	3
A	Attention (serial 7s/WORLD)	5
R	Recall (3 objects)	3
N	Naming	2
C	Command (3-stage)	3
W	Writing	1
C	Copying (pentagons)	1
R	Repetition	1

Total = 30

MNEMONIC 17 (Bonus): VaD Types: "MSSBC"

KEY INSIGHT

"More Strokes Should Bother Cerebrum"

LETTER · TYPE

M Multi-infarct dementia

S Strategic infarct dementia

S Subcortical ischaemic VaD

B Binswanger's disease

C CADASIL

QUICK RECALL CARD

MNEMONIC · COVERS

DEMENTIAS Reversible causes

3 Ws NPH triad

FLiRP DLB core features

DELPHI bvFTD features (6)

Don Ri Gal Cholinesterase inhibitors

ERT CJD investigations

UARC Capacity components

DAP DLB indicative biomarkers

EC Hip Lim Neo Braak stages

MAPT GRN C9 FTD genetics

N-P-R BPSD management ladder

COMPASS Pseudodementia vs AD

APP PSEN APOE AD genetics

A STEP FRESH HIS items

TAU LATER AMYLOID FIRST AD biomarker sequence

Sources: Kaplan & Sadock's Synopsis of Psychiatry 12th Ed, Oxford Textbook of Psychiatry 6th Ed, Cummings' Neuropsychiatry and Behavioral Neuroscience 3rd Ed

High-Yield Comparisons

EXAM STRATEGY

Comparison tables are the highest-yield format for short-answer and viva questions. Know which row the examiner will ask about. Starred rows (**) are most commonly asked.

TABLE 1: AD vs VaD vs DLB vs FTD: Master Comparison

FEATURE	ALZHEIMER'S DISEASE	VASCULAR DEMENTIA	DLB	FTD (bvFTD)
Frequency	60-70% of dementia	15-20% (30% in India)	15-20%	10-15% (most common <65)
Age of onset	Usually >65	Usually >60	Usually >65	45-65 (younger)
Sex	F > M	M > F	M ≥ F	M = F
Onset	Insidious	Abrupt/stepwise	Insidious	Insidious
Course	Gradually progressive	Stepwise (plateau between events)	Progressive with fluctuations	Progressive
First symptom	Episodic memory loss	Depends on infarct location	Visuospatial/attention	Personality/behaviour OR language
Memory	Early, severe (encoding deficit)	Retrieval > encoding deficit	Relatively spared early	Preserved early (bvFTD)
Executive function	Impaired later	Early, prominent	Early, prominent	Early, prominent
Visuospatial	Later	Variable	Early (constructional apraxia)	Relatively spared
Language	Anomia, later aphasia	Variable	Preserved early	Language-first variants (PPA)
Insight	Lost early	Often preserved	Variable	Often lost early
Hallucinations	Rare until late	Uncommon	Visual, well-formed, early	Rare
Parkinsonism	Absent/late	Rarely	Core feature	Absent (except CBD/PSP overlap)

FEATURE	ALZHEIMER'S DISEASE	VASCULAR DEMENTIA	DLB	FTD (BVFTD)
Fluctuating cognition	Not characteristic	Not characteristic	Core feature	Not characteristic
Gait disturbance	Late	Early (lacunar/subcortical)	Early	Late
Neurological signs	Absent early	Focal signs, pseudobulbar palsy	Mild parkinsonism	Frontal release signs
Emotional lability	Late	Characteristic	Uncommon	Disinhibition prominent
Depression	Common (30%)	Very common (post-stroke)	Common	Apathy > depression
Pathology	Amyloid plaques + tau tangles	Infarcts, white matter changes	Alpha-synuclein (Lewy bodies)	Tau (Pick) or TDP-43 or FUS
Genetics (key)	APP, PSEN1, PSEN2, APOE4	Vascular risk factors; CADASIL	Alpha-synuclein gene rarely	MAPT, GRN, C9orf72
Key imaging	MTA on MRI; amyloid PET+	Infarcts, WMH on MRI	DaTSCAN abnormal; occipital FDG↓	Frontal/anterior temporal atrophy
DaTSCAN	Normal	Normal	Abnormal	Normal
EEG	Diffuse slowing (late)	Focal changes	Posterior slow waves	Frontal slowing
ChEIs	Yes, approved all stages	Modest evidence	Yes (rivastigmine preferred)	No evidence; may worsen
Memantine	Mod-severe AD	Some evidence	Modest benefit	Conflicting; generally avoid
Key caution	ARIA with anti-amyloid therapy	Bleeding risk (antiplatelets)	NEVER conventional antipsychotics	Avoid ChEIs; avoid memantine
Prognosis (median survival)	8-10 years	Variable	5-8 years	6-8 years

EXAM PEARL

The four key discriminators: (1) Memory first = AD; (2) Stepwise + vascular RF = VaD; (3) Visual hallucinations + RBD + fluctuation = DLB; (4) Personality change in younger person = FTD. Each has a unique neuroimaging and pathological signature.

TABLE 2: MCI vs Mild Dementia (Major vs Mild NCD)

FEATURE	MCI (MILD NCD, DSM-5)	MILD DEMENTIA (MAJOR NCD, DSM-5)
DSM-5 term	Mild Neurocognitive Disorder	Major Neurocognitive Disorder (mild stage)
ICD-11	Mild neurocognitive disorder	Dementia (mild)
Cognitive decline	Modest decline from prior level	Significant decline from prior level
Functional impact	ADLs preserved ; may need extra effort/compensatory strategies	ADLs impaired ; requires assistance
Independence	Maintained	Lost for at least some instrumental ADLs
Cognitive testing	1-1.5 SD below age/education norms	Usually >1.5 SD below norms; dementia range
MMSE	Usually 24-28	Usually <24
MoCA	Usually 18-25	Usually <18
CDR	0.5	1 or above
Annual conversion to dementia	~10-15% per year	Already dementia, progression monitored
Pharmacotherapy	None approved	ChEIs, memantine (AD)
Key Petersen criteria	Memory complaint + objective deficit + preserved ADLs + not dementia	Full dementia criteria met

EXAM PEARL

The SINGLE key distinguishing criterion between MCI and dementia is **functional impairment in ADLs**. Not the cognitive test score, the function. An MMSE of 22 with fully preserved ADLs = MCI; same score with impaired ADLs = mild dementia.

TABLE 3: MMSE vs MoCA: Full Comparison

FEATURE	MMSE (FOLSTEIN, 1975)	MOCA (NASREDDINE, 2005)
Year	1975	2005
Total score	30	30
Administration time	5-10 minutes	10-15 minutes

FEATURE	MMSE (FOLSTEIN, 1975)	MOCA (NASREDDINE, 2005)
Normal cutoff	≥24	≥26 (add 1 if education ≤12 years)
MCI sensitivity	~18-40% (very poor)	~90% (excellent)
MCI specificity	~80-90%	~87%
Executive function	NOT assessed	Trail Making B, fluency, abstraction
Visuospatial	Intersecting pentagons only	Cube copy + clock drawing + trail
Memory (items)	3 words	5 words
Memory (type)	Immediate recall only (also delayed)	Delayed recall with optional cues
Attention	Serial 7s or WORLD	Serial 7s + forward digit span (5) + backward (3) + tapping
Language	Naming (2), repetition, reading, writing	Naming (3 animals) + repetition (2 sentences) + lexical fluency
Orientation	10 points (time + place)	6 points (date, month, year, day, place, city)
Abstract reasoning	Not assessed	2 analogies (2 marks)
Copyright	Copyrighted (PAR Inc.)	Free
Languages available	~30	50+
Best for	Staging moderate-severe dementia; epidemiology	MCI detection; early dementia; frontal dementias
Limitations	Misses MCI; no executive; cultural bias	Longer; floor effect in severe dementia
FTD sensitivity	Poor	Better (executive tasks)
DLB sensitivity	Poor (misses visuospatial)	Better
Indian validation	Multiple studies (Hindi, Kannada, Tamil)	Validated in multiple Indian languages

EXAM PEARL

If a question asks "which test is better for MCI?", the answer is always MoCA. If a question asks which test is most widely used globally, MMSE. MoCA sensitivity for MCI is ~90% vs MMSE ~18%.

TABLE 4: Donepezil vs Rivastigmine vs Galantamine

FEATURE	DONEPEZIL	RIVASTIGMINE	GALANTAMINE
Brand names	Aricept, Donesyn	Exelon	Reminyl, Razadyne
Mechanism	Selective AChE inhibitor	Dual: AChE + BuChE inhibitor	AChE inhibitor + nicotinic receptor allosteric potentiator (APL)
Selectivity	AChE selective	AChE and butyrylcholinesterase	AChE + nAChR modulation
Half-life	~70 hours (longest)	1-2 hours (short; but brain binding sustained)	7-8 hours
Dosing	5mg OD → 10mg OD → 23mg OD	1.5mg BD → 3mg BD → 4.5mg BD → 6mg BD (oral) OR patch 4.6mg → 9.5mg/24h	4mg BD → 8mg BD → 12mg BD
Administration	Once daily (convenience)	BD (oral) or patch (once daily)	BD (with food, reduces GI side effects)
Formulations	Tablet, ODT	Capsule, oral solution, transdermal patch	Tablet, extended-release capsule, oral solution
Patch advantage	No patch formulation	Fewer GI side effects; preferred route	No patch formulation
Approved indications	All stages of AD including severe	Mild-moderate AD; PDD (approved)	Mild-moderate AD
DLB/PDD	Off-label evidence	Preferred, dual inhibition matches pathology	Off-label
Key side effects	Nausea, vomiting, diarrhea; nightmares (take in morning)	Nausea (dose-related; patch reduces this)	Nausea; syncope
Cardiac caution	Yes (bradycardia, AV block, sick sinus)	Yes	Yes
Brain penetration	Good	Good	Good
Evidence level	Strongest overall (most trials)	Strong; patch preferred	Moderate-strong
Cost	Low (generic available)	Patch is costlier	Moderate

EXAM PEARL

Rivastigmine patch = preferred route because it significantly reduces GI side effects (the main reason for discontinuation). Rivastigmine is the only ChEI formally approved for Parkinson's Disease Dementia (PDD). Donepezil is the only ChEI approved for SEVERE AD.

TABLE 5: DLB vs PDD: The 1-Year Rule

FEATURE	DEMENTIA WITH LEWY BODIES (DLB)	PARKINSON'S DISEASE DEMENTIA (PDD)
Timing	Dementia onset ≤ 1 year of parkinsonism	Parkinsonism precedes dementia by >1 year
Parkinsonism onset	After (or concurrent with) dementia	First
Dementia onset	First (or concurrent)	After established PD
Pathological substrate	Alpha-synuclein (Lewy bodies)	Alpha-synuclein (Lewy bodies)
Distribution	Cortical $>$ subcortical	Subcortical $>$ cortical (initially)
Visual hallucinations	Early, prominent	Later in disease course
Cognitive profile	Visuospatial + attentional deficit early	Similar, executive + visuospatial
Memory	Relatively spared early	Relatively spared early
Fluctuations	Prominent	Less prominent
L-DOPA response	Modest	Better
DaTSCAN	Abnormal	Abnormal
Cholinergic deficit	More severe	Severe
ChEI preference	Rivastigmine	Rivastigmine (approved)
Antipsychotic caution	Severe neuroleptic sensitivity	Significant sensitivity
Conceptual relationship	Same disease spectrum, Lewy body disease	Same disease spectrum, Lewy body disease
Diagnostic criterion	McKeith 2017	Standard PD + dementia >1 year

CLINICAL ANCHOR

DLB and PDD are the same pathological process, alpha-synuclein aggregation, differing only in the anatomical trajectory and clinical timing. The "1-year rule" is an arbitrary but clinically necessary distinction. Think of them as two windows into the same building.

TABLE 6: Reversible vs Irreversible Dementias

FEATURE	REVERSIBLE DEMENTIAS	IRREVERSIBLE DEMENTIAS
Proportion	~15% of presentations	~85%
Examples	Hypothyroidism, B12 deficiency, NPH, neurosyphilis, depression, SDH, drug-induced	AD, VaD, DLB, FTD, CJD, HD
Key distinguishing history	Shorter duration; identifiable precipitant; systemic features	Long, insidious, no systemic features
Investigation yield	Bloods: TFT, B12, folate, LFT, RFT, VDRL, HIV	Neuroimaging, CSF biomarkers, genetic testing
Most important reversible cause	Depression (pseudodementia), most common, most easily missed	
Most treatable structural cause	NPH, VP shunt gives 50-80% gait improvement	
Most dangerous missed cause	Chronic subdural haematoma, can be fatal without evacuation	
Most common iatrogenic cause	Anticholinergic medications	
Mnemonic	DEMENTIAS	

EXAM PEARL

Always screen for reversible causes in any new dementia presentation, TFT, B12, folate, FBC, LFT, RFT, glucose, VDRL, HIV, CT head. Cost-effective; potentially curative.

TABLE 7: BPSD Pharmacotherapy Summary

SYMPTOM DOMAIN	FIRST CHOICE	SECOND CHOICE	AVOID	EVIDENCE LEVEL
Psychosis/Delusions	Risperidone 0.25-1mg	Olanzapine 2.5-5mg	Haloperidol, conventional APs	Moderate (RCT evidence)
Agitation	Non-pharm first; Risperidone	Quetiapine 12.5-50mg; Memantine	Benzodiazepines (first-line)	Moderate
Depression	Sertraline 50mg / Escitalopram 5-10mg	Mirtazapine 15-30mg	TCAs (anticholinergic)	Moderate

SYMPTOM DOMAIN	FIRST CHOICE	SECOND CHOICE	AVOID	EVIDENCE LEVEL
Anxiety	SSRIs	Buspirone 5-10mg TDS	Benzodiazepines (falls, cognition)	Low-moderate
Sleep, insomnia	Melatonin 2-10mg	Trazodone 25-100mg	Diphenhydramine; clonazepam first-line	Low-moderate
Sleep, RBD (DLB)	Clonazepam 0.25-2mg	Melatonin 3-12mg		Moderate
Apathy	Non-pharm (structured activity)	Methylphenidate (emerging; for AD)	Antidepressants alone (little evidence)	Low
Psychosis in DLB	Quetiapine (low dose)	Clozapine (with CBC monitoring)	ALL conventional APs; risperidone; olanzapine higher doses	Moderate
Disinhibition (FTD)	Sertraline / Fluvoxamine	Atypical APs (low dose)		Low (open-label)
Compulsive behaviours (FTD)	SSRIs (fluvoxamine evidence)		ChEIs (may worsen)	Low

EXAM PEARL

CATIE-AD (2006) showed no significant advantage of atypical antipsychotics over placebo for BPSD, with significant adverse effects. All antipsychotics in dementia: FDA black box warning for increased mortality. Non-pharmacological = first line, always.

TABLE 8: Cognitive Assessment Tools Comparison

WIDE COMPARISON · LANDSCAPE

TOOL	YEAR	SCORE	TIME	DOMAINS	NORMAL	BEST FOR	KEY LIMITATION
MMSE	1975	/30	5-10 min	Orientation, memory, attention, language, visuospatial	≥24	Staging moderate-severe; epidemiology	Poor MCI sensitivity (~18%); no executive
MoCA	2005	/30	10-15 min	All MMSE + executive, abstraction	≥26 (+1 if edu ≤12yr)	MCI detection; early dementia	Longer; copy-right-free but needs training
ACE-III	2012	/100	15-20 min	Attention (18), Memory (26), Fluency (14), Language (26), Visuospatial (16)	≥88	Comprehensive; AD vs FTD (VLOM ratio)	Long; needs training
ADAS-Cog	1984	/70	30-45 min	Memory, language, praxis, orientation	Lower = better (no normal cutoff)	Clinical trials (primary endpoint)	Too long for clinical use
CDR	1993	0-3 (0.5 increments)	20-30 min (informant interview)	6 domains; staging only	0 = normal	Staging and monitoring	Not a screening test
CDR-SoB	1993	0-18	Same	Sum of box scores	0	Clinical trials (more sensitive to change)	Informant needed
Clock Drawing		Varies (0-10 Shulman)	2-3 min	Visuospatial, executive, planning	≥8/10	Quick screen; frontal-parietal pathology	Not validated as standalone
NPI	1994	0-144	10-15 min (informant)	12 BPSD domains (F×S)	0	BPSD assessment and monitoring	Informant-based only; not cognitive

TOOL	YEAR	SCORE	TIME	DOMAINS	NORMAL	BEST FOR	KEY LIMITATION
RUDAS	2004	/30	10 min	Memory, visu- ospatial, drawing, judgment, language	≥22	Low literacy/edu- cation; culturally fair	Less established

EXAM PEARL

For clinical trials in AD: ADAS-Cog is the gold-standard primary endpoint. For staging in clinical practice: CDR. For MCI detection: MoCA. For BPSD measurement: NPI. For quick bedside screen: MMSE (universal) or MoCA (preferred).

TABLE 9: CJD Types Comparison

FEATURE	SPORADIC CJD	VARIANT CJD	FAMILIAL CJD	IATROGENIC CJD
Frequency	85-90%	Rare (~230 cases total)	10-15%	Very rare
Cause	Spontaneous PrP misfolding	BSE (bovine prion)	PRNP gene mutation	Contaminated tissue/instruments
Age at onset	Mean 60-65 years	Mean 28 years	Variable	Variable
Onset symptoms	Cognitive	Psychiatric (depression, anxiety)	Cognitive/mixed	Cerebellar (pituitary GH); cognitive
EEG	PSWC (1-2 Hz), pathognomonic	Usually absent	Variable	Variable
MRI	Cortical ribboning (DWI); basal ganglia signal	Pulvinar sign (bilateral posterior thalamus)	Variable	Variable
14-3-3 CSF	Elevated	Usually negative	Variable	Variable
Pathology	Spongiform vacuolation + PrPSc	Florid plaques (amyloid core + spongiform halo); PrPSc widespread	Spongiform + PrPSc	Spongiform + PrPSc
Tonsillar biopsy	Not useful	Diagnostic (PrP-Sc in lymphoid tissue)	Not useful	Not useful
Survival	5-6 months (median)	12-14 months	Variable	Variable
PRNP codon 129	Usually MM (methionine/methionine)	All cases VV or MV initially	Gene-specific	Variable
Public health	Notifiable; standard precautions	Notifiable; potential transmission from food	Genetic counselling	Notifiable; instrument decontamination

EXAM PEARL

vCJD = young + psychiatric onset + pulvinar sign + florid plaques + NO PSWC on EEG + tonsil biopsy positive. sCJD = elderly + rapid cognitive decline + myoclonus + PSWC + cortical ribboning on DWI.

TABLE 10: AD Pharmacotherapy: Timeline and Mechanism

WIDE COMPARISON · LANDSCAPE

DRUG	CLASS	FDA APPROVAL YEAR	STAGE	MECHANISM	KEY TRIAL	KEY RISK
Tacrine	ChEI (1st gen)	1993 (withdrawn)	All	AChE inhibitor		Hepatotoxicity, OBSOLETE
Donepezil	ChEI	1996	All stages	Selective AChE	ADAS-Cog trials	Bradycardia; nightmares
Rivastigmine	ChEI	2000	Mild-moderate; PDD	AChE + BuChE	EXPRESS trial (patch)	GI side effects (oral)
Galantamine	ChEI	2001	Mild-moderate	AChE + nAChR APL	Multiple RCTs	GI; syncope
Memantine	NMDA antagonist	2003	Moderate-severe	Uncompetitive NMDA blockade	MEM-MD-02 (Tariot 2004 combo)	Dizziness; confusion (mild)
Aducanumab	Anti-amyloid mAb	2021 (accelerated, controversial)	MCI/mild AD + amyloid+	Clears Aβ aggregates and plaques	EMERGE/ENGAGE (conflicting)	ARIA-E and ARIA-H (30-40%)
Lecanemab	Anti-amyloid mAb	2023 (traditional)	MCI/mild AD + amyloid+	Clears Aβ protofibrils	CLARITY-AD (27% slowing)	ARIA; APOE4 highest risk
Donanemab	Anti-amyloid mAb	2024	Early AD + amyloid+	Clears Aβ plaques (N-terminal Aβ)	TRAILBLAZER-ALZ 2 (22-35% slowing)	ARIA; infusion reactions

EXAM PEARL

The progression: symptomatic ChEIs (1996-2001) → memantine (2003) → 20 years of anti-amyloid failures → lecanemab (2023) first convincing disease modification. All anti-amyloid agents require biomarker confirmation (amyloid PET or CSF). ARIA is the defining side effect.

SUMMARY: Key Numbers to Memorise

PARAMETER · VALUE

India dementia prevalence 5.3 million

AD proportion of dementia 60-70%

Annual MCI→dementia conversion 10-15%

Hachinski ≥ 7 VaD

Hachinski ≤ 4 AD

MMSE max 30; normal ≥ 24

MoCA max 30; normal ≥ 26

ACE-III max 100; impaired ≤ 88

CDR-SoB max 18

ADAS-Cog max 70 (higher = worse)

NPI max 144

Zarit Burden Interview max 88

DLB 1-year rule Parkinsonism within 1 year of dementia = DLB

ChEI efficacy (ADAS-Cog) +3-4 points vs placebo

Lecanemab clinical efficacy 27% slowing of decline

ARIA incidence (lecanemab) ~20-30% on MRI (symptomatic ~3%)

Antipsychotic mortality risk 1.6-1.7x increased

sCJD median survival 5-6 months

vCJD median survival 12-14 months

NPH gait improvement post-shunt 50-80%

Sources: Kaplan & Sadock's Synopsis of Psychiatry 12th Ed, Oxford Textbook of Psychiatry 6th Ed, Cummings' Neuropsychiatry and Behavioral Neuroscience 3rd Ed, McKeith 2017, Rascovsky 2011, NIA-AA 2018

PYQ Frequency Analysis

EXAM STRATEGY

This analysis covers PG exams MD Psychiatry exit exam patterns (17+ years of data), cross-referenced with PG exams, and other Indian PG psychiatry exams. Questions are mapped by topic, format, and frequency. High-frequency topics are starred.

SECTION 1: FREQUENCY HEATMAP

TOPIC	EXAM FREQUENCY	EXAM FREQUENCY	COMBINED PRIORITY
Alzheimer's disease (comprehensive)	★★★★★	★★★★★	Tier 1, Certain
BPSD, management	★★★★★	★★★★★	Tier 1, Certain
Dementia, classification	★★★★★	★★★★★	Tier 1, Certain
DLB, clinical features + management	★★★★★	★★★★★	Tier 1, Certain
Reversible dementias + pseudodementia	★★★★★	★★★★★	Tier 1, Certain
VaD, types + Hachinski score	★★★★★	★★★★★	Tier 1, High
NPH, Hakim-Adams triad + management	★★★★★	★★★★★	Tier 1, High
FTD, behavioral variant	★★★★★	★★★★★	Tier 1, High
MMSE vs MoCA	★★★★★	★★★★★	Tier 1, High
Cognitive assessment tools (general)	★★★★★	★★★★★	Tier 1, High
Amyloid cascade hypothesis	★★★★	★★★★	Tier 2, Medium
Biomarkers in AD	★★★★	★★★★	Tier 2, Medium
CJD, clinical features	★★★★	★★★★	Tier 2, Medium
Caregiver burden, dementia	★★★★	★★★★	Tier 2, Medium

TOPIC	EXAM FREQUENCY	EXAM FREQUENCY	COMBINED PRIORITY
Capacity and legal issues	★★★	★★★	Tier 2, Medium
MCI, definition and criteria	★★★	★★★	Tier 2, Medium
Genetics of AD	★★★	★★★	Tier 2, Medium
DLB vs PDD, differences	★★★	★★★	Tier 2, Medium
Anti-amyloid therapy (lecanemab etc.)	★★	★★★	Tier 3, Emerging
FTD genetics (C9orf72)	★★	★★★	Tier 3, Emerging
Delirium superimposed on dementia	★★	★★	Tier 3, Watch
CADASIL	★★	★★	Tier 3, Watch
Blood biomarkers (p-tau217)	★	★★	Tier 3, Emerging

SECTION 2: QUESTION FORMAT ANALYSIS

10-Mark Long Essay Questions (Most Common for Dementias)

QUESTION PATTERN	FREQUENCY	LIKELY MARKS DISTRIBUTION
"Classify dementia. Describe clinical features and management of Alzheimer's disease."	Very high	Def+Class (3) + Features (4) + Mgmt (3)
"Describe clinical features, diagnosis and management of DLB. Differentiate from PDD."	Very high	CF (3) + Diag (3) + Mgmt (2) + Diff (2)
"Define pseudodementia. Differentiate from true dementia."	Very high	Def+Epidemiology (2) + Differentiation table (5) + Mgmt (3)
"Describe BPSD. Discuss pharmacological and non-pharmacological management."	Very high	Def+Types (3) + Non-pharm (3) + Pharm (4)
"Write about Normal Pressure Hydrocephalus."	High	Triad (3) + Pathophysiology (2) + Investigations (2) + Treatment (3)

QUESTION PATTERN	FREQUENCY	LIKELY MARKS DISTRIBUTION
"Describe behavioral variant FTD, clinical features and management."	High	Overview+Classification (2) + CF (4) + Mgmt (4)
"Write an essay on vascular dementia."	High	Types (3) + CF (2) + HIS (2) + Mgmt (3)
"Describe biomarkers in Alzheimer's disease."	Medium-high	Classification A/T/N (2) + CSF (3) + Imaging (3) + Blood (2)
"Write about CJD."	Medium	Types (2) + CF sCJD (3) + Investigations (3) + Mgmt (2)
"Describe cognitive assessment in dementia, MMSE and MoCA."	Medium-high	MMSE (4) + MoCA (4) + Comparison (2)

5-Mark Short Answer Questions (Frequent)

TOPIC · FREQUENCY

Hachinski Ischemic Score Very high

Amyloid cascade hypothesis High

Cholinesterase inhibitors in dementia High

McKeith criteria for DLB High

Reversible causes of dementia (list + brief) High

Hakim-Adams triad High

CDR (Clinical Dementia Rating) Medium

Neuroleptic sensitivity in DLB Medium

ADAS-Cog Medium

Braak staging Medium

Genetics of early-onset AD Medium

Anti-amyloid therapy, lecanemab Medium (rising)

CSF biomarkers in AD Medium

Caregiver burden, Zarit scale Medium

Viva / Short Note Patterns

TOPIC · LIKELY QUESTION

DaTSCAN "What is DaTSCAN? When is it used?"

ARIA "What is ARIA? What causes it?"

Pick's disease "Pick bodies, describe"

C9orf72 "What is the significance of C9orf72 mutation?"

Evans index "How is NPH diagnosed on CT?"

Pseudodementia "Kiloh's pseudodementia, describe"

EEG in CJD "What EEG pattern is seen in CJD?"

Rivastigmine patch "Why is transdermal rivastigmine preferred?"

Capacity "How do you assess capacity in a dementia patient?"

SECTION 3: TOPIC-WISE QUESTION BANK (Reconstructed)

Alzheimer's Disease

1. Define dementia. Classify dementia and describe the clinical features and management of Alzheimer's disease. (10 marks)
2. Describe the neuropathological changes seen in Alzheimer's disease. (5 marks)
3. Write a note on the amyloid cascade hypothesis. (5 marks)
4. Describe the genetics of Alzheimer's disease. (5 marks)
5. What are the pharmacological options available for the management of Alzheimer's disease? (5 marks)
6. Write a note on biomarkers in the diagnosis of Alzheimer's disease. (5 marks)
7. Classify cholinesterase inhibitors. Describe their mechanism of action, indications, and side effects. (10 marks)
8. What is memantine? Describe its mechanism of action and role in dementia. (5 marks)
9. Write a note on newer disease-modifying therapies in Alzheimer's disease. (5 marks)
10. Describe the neuropsychological changes in Alzheimer's disease and their assessment. (10 marks)
11. What is APOE4? Describe its role in Alzheimer's disease. (5 marks)
12. Describe the A/T/N classification of Alzheimer's disease biomarkers. (5 marks)

Vascular Dementia

1. Classify vascular dementia. Describe the clinical features and Hachinski Ischemic Score. (10 marks)
2. Write a note on Hachinski Ischemic Score. (5 marks)
3. Describe the neuroimaging findings in vascular dementia. (5 marks)
4. Write a note on CADASIL. (5 marks)
5. Compare and contrast Alzheimer's disease and vascular dementia. (10 marks)

Dementia with Lewy Bodies

1. Describe the clinical features, diagnosis and management of Dementia with Lewy Bodies. Differentiate from Parkinson's Disease Dementia. (10 marks)
2. What is neuroleptic sensitivity in DLB? Describe its management. (5 marks)
3. Write a note on REM sleep behaviour disorder in dementia. (5 marks)
4. Describe the McKeith criteria for DLB. (5 marks)
5. What is DaTSCAN? Describe its role in DLB. (5 marks)

Frontotemporal Dementia

1. Classify frontotemporal dementia. Describe the clinical features and management of behavioral variant FTD. (10 marks)
2. Write a note on semantic dementia. (5 marks)
3. Describe the genetics of frontotemporal dementia. (5 marks)
4. Compare Pick's disease with Alzheimer's disease. (5 marks)
5. Write a note on progressive non-fluent aphasia. (5 marks)

NPH and Reversible Dementias

1. Describe Normal Pressure Hydrocephalus, clinical features, investigations and treatment. (10 marks)
2. Write an essay on reversible causes of dementia. (10 marks)
3. Describe pseudodementia, clinical features and differentiation from true dementia. (5 marks)
4. Write a note on the CSF tap test in NPH. (5 marks)
5. What is myxoedema madness? Describe cognitive features of hypothyroidism. (5 marks)
6. Describe the clinical features of neurosyphilis and its management. (5 marks)

BPSD

1. Describe the behavioral and psychological symptoms of dementia. Discuss their pharmacological and non-pharmacological management. (10 marks)
2. Write a note on the Neuropsychiatric Inventory (NPI). (5 marks)

3. Describe the management of agitation in dementia. (5 marks)
4. What are the risks of antipsychotic use in dementia? Discuss evidence-based alternatives. (10 marks)
5. Write a note on CATIE-AD study. (5 marks)

CJD

1. Describe the clinical features, investigations and management of Creutzfeldt-Jakob disease. (10 marks)
2. Compare sporadic CJD with variant CJD. (5 marks)
3. What is RT-QuIC? Describe its significance in CJD diagnosis. (5 marks)
4. Write a note on prion diseases. (5 marks)

Cognitive Assessment

1. Describe the MMSE, components and scoring. What are its limitations? (10 marks)
2. Compare MMSE with MoCA. Which is better for detecting MCI and why? (10 marks)
3. Write a note on the Clinical Dementia Rating (CDR) scale. (5 marks)
4. Describe ADAS-Cog and its role in clinical trials. (5 marks)
5. What is the MoCA? Describe its components and advantages over MMSE. (5 marks)
6. Write a note on clock drawing test. (5 marks)

MCI

1. Define Mild Cognitive Impairment. Classify and describe conversion rates. (10 marks)
2. Differentiate MCI from early Alzheimer's disease. (5 marks)
3. What is Mild Neurocognitive Disorder as per DSM-5? (5 marks)

Legal and Ethical

1. Discuss capacity assessment in a patient with dementia. (10 marks)
2. Write a note on advance directives and dementia. (5 marks)
3. Describe the ethical issues in driving cessation in dementia. (5 marks)

Caregiver

1. Describe caregiver burden in dementia, assessment and management. (10 marks)
 2. Write a note on the Zarit Burden Interview. (5 marks)
-

SECTION 4: EXAMINER'S FAVOURITE TRAPS AND HOW TO AVOID THEM

EXAM STRATEGY

These are the specific errors that cost marks. Memorise the correct answer for each.

TRAP	WRONG ANSWER	CORRECT ANSWER
"Best correlate of cognitive decline in AD"	Plaque count / tangle count	Synaptic loss
"Most common BPSD"	Agitation	Apathy (~70%)
"1-year rule in DLB"	Parkinsonism within 1 year AFTER dementia	Dementia within 1 year of parkinsonism onset (or dementia FIRST)
"Hachinski cutoff for VaD"	>5 or >6	≥7
"MMSE cutoff for MCI"	24	MMSE is POOR for MCI; MoCA ≥26 is the cutoff
"Which ChEI is approved for PDD?"	Donepezil	Rivastigmine (formally approved)
"Dual-mechanism ChEI"	Donepezil	Rivastigmine (AChE + BuChE)
"EEG finding in vCJD"	PSWC	PSWC is ABSENT in vCJD; present in sCJD
"MRI sign in vCJD"	Cortical ribboning	Pulvinar sign (bilateral posterior thalamus)
"Who coined pseudodementia?"	Folstein / Roth	Kiloh (1961)
"First ChEI approved?"	Donepezil	Tacrine (1993, now obsolete, hepatotoxic)
"What chromosome is PSEN1?"	1 or 19	Chromosome 14
"What chromosome is APOE?"	14 or 21	Chromosome 19
"What is trisomy 21's dementia link?"	APOE4	APP gene (extra copy → amyloid)
"Most amyloidogenic Aβ"	Aβ40	Aβ42
"Antipsychotic of choice in DLB psychosis"	Risperidone	Quetiapine (or clozapine); risperidone has neuroleptic sensitivity risk
"Order of NPH symptoms"	Dementia first	Gait → Incontinence → Dementia

TRAP	WRONG ANSWER	CORRECT ANSWER
"Which BPSD delusion is most common in AD?"	Capgras	Theft delusion
"CATIE-AD finding"	Atypicals superior to placebo	No significant advantage; significant adverse effects
"Lecanemab trial name"	ENGAGE / EMERGE	CLARITY-AD

SECTION 5: PREDICTED HIGH-PROBABILITY QUESTIONS (2026 Exam)

EXAM STRATEGY

Based on topic cycles, recent advances, and pattern analysis, these are the most likely questions for the September 2026 sitting.

Almost Certain (prepare as 10-mark essays)

1. Classify dementia. Describe clinical features and management of Alzheimer's disease, include newer disease-modifying therapies.
2. Describe BPSD, classification, assessment (NPI), and evidence-based management.
3. Clinical features, diagnosis and management of DLB, differentiate from PDD.
4. Reversible dementias, with special emphasis on pseudodementia and its differentiation from true dementia.

Very Likely (prepare as 5-mark short answers + be ready for 10)

1. Normal Pressure Hydrocephalus, Hakim-Adams triad, tap test, VP shunt outcomes.
2. Behavioral variant FTD, Rascovsky criteria and management.
3. Compare MMSE and MoCA, with specific focus on MCI detection.
4. Vascular dementia, Hachinski Ischemic Score and management.
5. Biomarkers in AD, A/T/N framework, CSF, PET, blood biomarkers.
6. CJD, sporadic vs variant, EEG findings, RT-QuIC.

Watch These (may appear as short answers or viva)

1. Caregiver burden assessment and management, Zarit scale.
2. Capacity assessment in dementia, components and clinical approach.
3. Lecanemab and donanemab, mechanism, trial results, ARIA.
4. C9orf72, role in FTD and ALS.
5. Delirium superimposed on dementia, CAM criteria, management.

SECTION 6: MARKS ALLOCATION STRATEGY

For a 10-Mark Essay on Dementia

SECTION	MARKS	CONTENT
Definition	1	Concise, accurate, DSM-5 term if asked
Classification	2	Table format; by aetiology AND by reversibility
Pathology / Mechanism	3	Most marks go here, details count
Clinical features	2	Stages if AD; types if VaD; core features if DLB
Management	2	Both pharmacological AND non-pharmacological

For a 5-Mark Short Answer

SECTION	MARKS	CONTENT
Definition/Overview	1	One clear sentence
Core content	3	Table or structured points preferred
Clinical relevance / exam note	1	The distinguishing fact, one pearl

General Rules

- Tables score better than paragraphs, examiners scan for structure
- Start with definition, even if not asked; sets the frame
- End with a clinical pearl or management note, shows applied knowledge
- Never waste space on re-reading the question, jump to content

SECTION 7: TOPIC CROSS-LINKS

These topics frequently appear together in the same question or as sub-parts:

PRIMARY TOPIC · OFTEN COMBINED WITH

AD Cholinesterase inhibitors; amyloid hypothesis; MMSE; MCI

DLB Neuroleptic sensitivity; DaTSCAN; RBD; PDD comparison

VaD Hachinski score; risk factors; stroke management

FTD bvFTD Rascovsky criteria; genetics (C9orf72); PPA

NPH Reversible dementias; tap test; VP shunt

BPSD NPI; antipsychotic risks; CATIE-AD; caregiver burden

Pseudodementia Depression; reversible dementias; Killoh

CJD EEG; prion diseases; RT-QuIC; vCJD

Biomarkers A/T/N; CSF; amyloid PET; lecanemab eligibility

Capacity MHA 2017; advance directives; ethical issues

Analysis based on PG exams MD Psychiatry examination papers 2007-2026, PG theory papers, PG entrance patterns, and published question bank compilations.

Quick Review

EXAM STRATEGY

Vignettes test applied knowledge, not recall alone. For each case: (1) identify the diagnosis from the pattern, (2) know the single most discriminating feature, (3) know the first management step. All names are fictitious.

VIGNETTE 1: The Professor Who Forgot His Lectures

Case:

Mr. Arvind Kulkarni, 72 years old, retired professor, is brought by his wife with a 3-year history of progressive memory difficulty. Initially he began forgetting appointments and students' names. Over the past year, he has been unable to manage his finances, gets lost in familiar neighbourhoods, and repeats the same questions within minutes. He denies any memory problems, "my wife is overreacting." There are no focal neurological signs. MMSE score: 19/30. MRI brain shows bilateral hippocampal and parietal atrophy. He has no vascular risk factors.

Q1. What is the most likely diagnosis? What specific MMSE finding pattern supports this?

Answer: Most likely diagnosis is **Alzheimer's disease (Major Neurocognitive Disorder due to AD)**.

Supporting features: insidious onset, progressive course over 3 years, episodic memory impairment as the dominant early symptom, denial/anosognosia (patient minimises deficits, contrasts with pseudodementia), instrumental ADL impairment (finances, navigation), no vascular risk factors, MMSE 19/30 (mild-moderate range), bilateral hippocampal atrophy on MRI (medial temporal lobe atrophy, hallmark of AD).

MMSE pattern: disproportionate loss on orientation (temporal first: year/month/date before place), registration/recall (3-word recall severely impaired), with relative preservation of language tasks early.

EXAM PEARL

Anosognosia, lack of insight into one's own cognitive deficits, is a characteristic feature of AD. The patient minimises, not amplifies. This is the opposite of pseudodementia.

Q2. What investigations would you order to confirm the diagnosis and exclude reversible causes?

Answer:

First-line bloods (exclude reversible): FBC, ESR, LFT, RFT, TFT (TSH), blood glucose, serum B12, folate, VDRL, HIV serology, serum calcium.

Neuroimaging: MRI brain (already done, shows MTA; Scheltens score ≥ 2 in bilateral hippocampus).

Neuropsychological testing: MoCA (more sensitive than MMSE for documenting profile), ACE-III (VLOM ratio to differentiate AD from FTD).

CSF biomarkers (if available/clinical trial): A β 42 $\downarrow$, phospho-tau $\uparrow$, total-tau $\uparrow$, A β 42/40 ratio $\downarrow$, confirms AD pathology.

Amyloid PET (if available): Positive cortical amyloid uptake, confirms amyloid pathology; required for anti-amyloid therapy eligibility.

FDG-PET (if diagnosis uncertain): Bilateral temporo-parietal + posterior cingulate hypometabolism, AD pattern.

Q3. Outline the pharmacological management. What is the role of lecanemab in this patient?

Answer:

Current stage: Mild-moderate AD (MMSE 19/30), appropriate for cholinesterase inhibitor initiation.

Cholinesterase inhibitor: Donepezil 5mg OD for 4-6 weeks $\rightarrow$ titrate to 10mg OD.
Alternative: rivastigmine (oral or patch) or galantamine.

Add memantine if progresses to moderate-severe stage (MMSE <15) or as combination for added benefit.

Lecanemab eligibility: Requires (a) early AD, MCI or mild dementia stage; (b) amyloid PET positive or CSF amyloid biomarkers confirming amyloid pathology; (c) MMSE ≥ 22 (mild stage) preferred. With MMSE 19, this patient is at the border, may qualify for mild AD criteria. Main risk: ARIA-E and ARIA-H (require baseline and surveillance MRI). APOE4 genotyping recommended pre-treatment (APOE4 homozygotes: highest ARIA risk). Benefit: 27% slowing of clinical decline (CLARITY-AD trial, 2022).

Non-pharmacological: Cognitive stimulation, structured activities, caregiver education, environmental safety modifications, driving assessment.

VIGNETTE 2: The Retired Brigadier with a "Good Day, Bad Day"

Case:

Mr. Dharamveer Singh, 74 years old, retired army officer, is brought by his son with 2-year history of fluctuating memory and attention. His son reports that some days he is

completely lucid, converses normally, and recalls recent events; on other days he seems confused, stares blankly, and cannot recognise his grandchildren. Over the past year, he reports seeing "small children playing in the corner of the room", which he initially found amusing, now frightening. His wife notes he cries out during sleep and has knocked her off the bed twice while "fighting in his dreams." He has mild right-hand tremor and slowness noticed for the past 8 months. MMSE: 23/30.

Q1. What is the most likely diagnosis? Which four features point to this diagnosis?

Answer: Most likely diagnosis: **Dementia with Lewy Bodies (DLB)**.

The four McKeith core features are all present:

1. **Fluctuating cognition**, good days and bad days, episodic confusion, variable alertness
2. **Recurrent visual hallucinations**, well-formed, detailed (small children), early in course
3. **REM sleep behaviour disorder (RBD)**, acting out dreams, vocalisation, injuring bed partner
4. **Parkinsonism**, resting tremor + bradykinesia (right hand, slowness)

Per McKeith 2017 criteria: 2 of 4 core features = Probable DLB. This patient has all 4 = Probable DLB with high confidence.

EXAM PEARL

The 1-year rule, dementia onset and parkinsonism within 1 year of each other (or dementia first) = DLB. If tremor and slowness preceded dementia by >1 year, diagnosis would be PDD.

Q2. His son asks about treating the visual hallucinations with haloperidol. What is your response?

Answer: Haloperidol is **absolutely contraindicated** in DLB.

Neuroleptic sensitivity reaction occurs in 30-50% of DLB patients exposed to conventional antipsychotics (and higher-dose atypicals). Clinical consequences: severe Parkinsonism, autonomic instability, impaired consciousness, accelerated cognitive decline, and **death** in severe cases.

Mechanism: DLB involves severe dopaminergic deficit (nigrostriatal) combined with profound cholinergic deficits. Blocking D2 receptors with haloperidol produces catastrophic extrapyramidal and autonomic decompensation.

Safe options for psychosis in DLB:

- **Quetiapine** (preferred): 12.5-25mg at night; lowest dopamine blockade among atypicals; titrate slowly
- **Clozapine**: 6.25-25mg; evidence from Parkinson's psychosis literature; requires regular CBC (agranulocytosis risk)

- **Rivastigmine:** Treatment of cognitive symptoms also reduces hallucinations (cholinergic restoration); first-line overall

First step before any antipsychotic: Trial of rivastigmine (cholinesterase inhibitor), reduces frequency and distress of hallucinations in DLB without neuroleptic sensitivity risk.

Q3. Describe the investigations you would perform to confirm the diagnosis.

Answer:

Clinical biomarkers (McKeith 2017 indicative biomarkers):

- **DaTSCAN (SPECT):** Reduced dopamine transporter uptake in striatum, expected to be abnormal in DLB; distinguishes DLB from AD (normal DaTSCAN)
- **Cardiac MIBG scintigraphy:** Reduced cardiac adrenergic uptake, abnormal in DLB/PDD; preserved in AD
- **Polysomnography (PSG):** Confirms REM sleep without atonia, objective confirmation of RBD

Neuroimaging:

- **MRI:** relative preservation of medial temporal lobe (unlike AD); generalised atrophy; no significant WMH
- **FDG-PET:** occipital hypometabolism (characteristic of DLB; unlike AD where occipital is spared until late)

Neuropsychological testing: Visuospatial deficits early (constructional apraxia, Rey figure), attentional fluctuation, frontal-executive deficits

EEG: Posterior slow wave activity, transient sharp waves, supportive but not diagnostic

VIGNETTE 3: The CEO Who Became Rude

Case:

Mr. Rakesh Mehta, 57 years old, successful businessman, is brought by his wife with an 18-month history of personality change. She reports that he has become "a completely different person", making offensive comments to clients, spending impulsively on unnecessary purchases, and recently exposing himself in a shopping mall. He has been eating voraciously, particularly craving sweets, and has gained 8 kg. He shows no remorse or awareness of his behaviour. Neuropsychological testing shows executive dysfunction but relatively preserved memory and visuospatial skills. MRI brain: frontal and anterior temporal atrophy bilaterally.

Q1. What is the diagnosis? List the specific diagnostic criteria met.

Answer: Diagnosis: **Behavioral Variant Frontotemporal Dementia (bvFTD)**, Rascovsky Criteria 2011.

Features present (need 3 of 6 for POSSIBLE; neuroimaging evidence = PROBABLE):

RASCOVSKY CRITERION · EVIDENCE IN CASE

1. Early disinhibition Offensive remarks, impulsive spending, public indecent exposure

2. Early apathy/inertia Implied (no remorse, reduced appropriate social behaviour)

3. Early loss of empathy/sympathy No awareness, no remorse, indifference to consequences

4. Perseverative/compulsive behaviours Food craving behaviour, impulsive patterns

5. Hyperorality and dietary changes Voracious eating, sweet craving, 8 kg weight gain

6. Executive neuropsychological profile Executive dysfunction with preserved memory and visuospatial

MRI: frontal and anterior temporal atrophy = **PROBABLE bvFTD**

Age 57 is characteristic, bvFTD is the most common dementia in those under 65.

EXAM PEARL

Unlike AD, episodic memory is relatively preserved in early bvFTD. This patient's wife says "he knows who I am, he knows our history", but he no longer cares. That's the core of FTD, the semantic and procedural self is intact; the social-emotional self is gone.

Q2. What is the role of genetic testing in this patient? Name the three most important genes.

Answer: Genetic testing is indicated because:

- Age of onset <65 years
- Family history (if present), autosomal dominant inheritance in ~30-40% of familial FTD
- FTD-MND co-occurrence raises C9orf72 probability significantly

Three key genes:

GENE	LOCATION	PATHOLOGY	NOTES
C9orf72	9p21	Dipeptide repeat proteins	Most common familial FTD (25%) AND familial ALS (35%); hexanucleotide repeat expansion
MAPT	17q21	3R/4R tau inclusions	Tau-positive FTD; also causes CBS, PSP

GENE	LOCATION	PATHOLOGY	NOTES
GRN (Progranulin)	17q21	TDP-43 inclusions	Haploinsufficiency; variable penetrance; GRN and MAPT are on same chromosome

Process: Genetic counselling before testing; inform about implications for first-degree relatives; predictive testing protocol for at-risk family members.

Q3. Describe the management of this patient, pharmacological and non-pharmacological.

Answer:

No disease-modifying therapy available.

Pharmacological, behavioural symptoms:

- **SSRIs first-line:** Sertraline 50-200mg/day or fluvoxamine 50-300mg/day, evidence for reducing disinhibition, compulsive behaviours, hyperorality, impulsive acts (open-label studies)
- Low-dose atypical antipsychotics (quetiapine 25-50mg) for severe behavioural disturbance unresponsive to SSRIs
- **Avoid:** Cholinesterase inhibitors (no evidence; galantamine may worsen hyperorality); memantine (conflicting, some suggest worsening)

Non-pharmacological:

- Structured daily routine, reduces compulsive behaviours through predictability
- Redirection techniques for disinhibited behaviour
- Environmental safety, financial power of attorney urgently (before capacity is fully lost); remove credit cards, car keys
- Staff and family training: explain empathy impairment; de-personalise the behaviour
- Occupational therapy for meaningful activity

Legal/social urgency: At 57, capacity may still be partially present, urgent advance care planning, lasting power of attorney for finances and health, will review. His business and financial affairs are at high risk from impulsive decisions.

VIGNETTE 4: The Triad That Points to a Treatable Diagnosis

Case:

Mrs. Kamala Iyer, 70 years old, retired teacher, is brought with a 1-year history of progressive gait difficulty, urinary urgency with occasional incontinence, and gradual cognitive decline. Her daughter notes she walks with short, shuffling steps and takes a long time to "get going" from a chair. Neurological examination: wide-based gait, no tremor, no

rigidity at rest, arm swing preserved. She has no history of hypertension, diabetes, or head injury. CT brain shows disproportionately enlarged lateral ventricles with an Evans index of 0.34, and the cortical sulci over the vertex appear effaced. Lumbar puncture opening pressure: 160 mm H₂O.

Q1. What is the diagnosis? What findings confirm it?

Answer: Diagnosis: **Idiopathic Normal Pressure Hydrocephalus (iNPH)**, Hakim-Adams syndrome.

Confirming findings:

- **Clinical triad:** Gait apraxia (magnetic gait, wide-based, short steps, difficulty initiating) + urinary incontinence (urge type) + cognitive decline (frontal-subcortical pattern), appearing in the classic G-I-D sequence
- **CT findings:** Evans index 0.34 (>0.3 confirms ventriculomegaly) + effaced sulci over the vertex (disproportionate, ventricles enlarged but convexity sulci small = DESH pattern)
- **LP opening pressure:** 160 mm H₂O = NORMAL (<200 mm H₂O), defining criterion: large ventricles with normal pressure
- **Gait characteristics:** Magnetic gait with preserved arm swing and no resting tremor, distinguishes from Parkinson's disease

EXAM PEARL

NPH is one of the few TREATABLE causes of dementia. G-I-D = order of symptom appearance (Gait first, then Incontinence, then Dementia). The 3 Ws (Wet, Wobbly, Wacky) are labels, not sequence.

Q2. What is the CSF tap test? How does it help?

Answer: The **CSF Tap Test (Miller Fisher Test)**:

Procedure: Lumbar puncture with removal of 30-50 mL of CSF; gait and cognitive function assessed before and at 1 hour, 24 hours, and 72 hours post-tap.

Positive result: Objective improvement in gait (shorter step time, wider step length, increased gait velocity on timed tests) within 24-72 hours.

Diagnostic value:

- Sensitivity: ~50-60%
- Specificity: ~80-90%
- A positive tap test strongly predicts good shunting outcome (PPV ~75-90%)
- A negative tap test does not exclude NPH (false negative rate ~40-50%)

Extended lumbar drain (if tap test negative but clinical suspicion high):

- 3-5 days continuous CSF drainage via external lumbar drain (~150-200 mL/day)

- Higher sensitivity than single tap test (~70-80%)
- Cumbersome but more predictive

Q3. Describe the surgical treatment and expected outcomes.

Answer:

Ventriculoperitoneal (VP) Shunt:

- Catheter placed in lateral ventricle → peritoneal cavity
- Uses a pressure-adjustable (programmable) valve, allows non-invasive pressure setting post-operatively
- General anaesthesia required

Predictors of good outcome:

- Young age (relative)
- Short symptom duration (<2 years)
- Gait-predominant presentation (vs dementia-predominant)
- Positive CSF tap test
- No significant comorbid white matter disease

Expected response rates:

SYMPTOM · RESPONSE RATE

Gait 50-80% (best response)

Urinary incontinence 40-60%

Cognitive decline 25-40% (least responsive)

Complications:

- Over-drainage → subdural haematoma (use programmable valve to adjust)
 - Shunt infection (~5%)
 - Shunt failure / malfunction (requires revision)
 - Intracranial haemorrhage (insertion-related)
-

VIGNETTE 5: The Widow Who "Can't Remember Anything"

Case:

Mrs. Sujata Patel, 65 years old, retired bank manager, is brought by her son 6 months after her husband's death. She reports severe memory difficulty, inability to concentrate, poor sleep, and loss of appetite. She scores 21 / 30 on MMSE. She volunteers extensively during testing: "I can't do this, I've forgotten everything, I'm useless." On formal testing, her

performance is inconsistent, she scores 0/3 on word recall in one trial but 3/3 in another. She has a previous history of depression 10 years ago, resolved with antidepressants. MRI brain: no significant atrophy.

Q1. What is the most likely diagnosis and how does it differ from true dementia?

Answer: Most likely diagnosis: **Depressive Pseudodementia** (Depressive Pseudodementia, Kiloh 1961), now conceptualised as a major depressive episode with prominent cognitive symptoms.

Features supporting pseudodementia over true dementia:

FEATURE	IN THIS CASE	SIGNIFICANCE
Onset	6 months post-bereavement (identifiable precipitant)	Pseudodementia
Subjective complaints	Prominent, volunteered ("I can't do anything")	Pseudodementia, patients amplify
Cooperation	Engaged but unmotivated ("I'm useless")	Pseudodementia
Consistency	Inconsistent (0/3 then 3/3 on same task)	Pseudodementia
Previous depression	Yes (10 years ago)	Pseudodementia
MRI	Normal	Pseudodementia
Duration	6 months (short)	Pseudodementia
Answers	"I can't remember" (not near-miss)	Pseudodementia

True dementia features absent: no anosognosia, no consistent deficits, no pattern-specific neuropsychological loss, no structural changes.

CLINICAL ANCHOR

Kiloh (1961): pseudodementia coined. Key rule, in pseudodementia, the patient **complains more than they perform badly**. In dementia, the patient **performs worse than they complain**.

Q2. What investigations would help differentiate, and what is your management plan?

Answer:

Investigations to differentiate:

TEST · EXPECTED FINDING

Detailed neuropsychological battery Inconsistent; effort-dependent; no specific dementia pattern

Depression rating scale (HDRS/PHQ-9) High score confirming depressive syndrome

MoCA pre/post-treatment Improvement with antidepressant treatment

MRI brain Normal or only mild age-appropriate changes

TFT, B12, folate To exclude other reversible causes

Biomarkers (CSF/PET) if doubt persists Normal in pseudodementia (A β 42, p-tau not significantly abnormal)

Management:

1. **Antidepressant:** Escitalopram 5-10mg OD (or sertraline 50mg OD), first-line for elderly depression
2. **Mirtazapine 15-30mg** if insomnia + poor appetite prominent (sedating, orexigenic)
3. **Psychotherapy:** Grief-focused CBT; behavioural activation; interpersonal therapy
4. **Monitor cognition:** Formal MoCA at 3 months, should improve with depression remission
5. **ECT:** If severe, refractory, or rapid functional decline, also diagnostically confirmatory if cognitive improvement occurs

Caution: 15-20% of pseudodementia patients convert to true dementia within 3 years, follow-up neuropsychological assessment at 12 months essential.

Q3. What is the significance of this diagnosis for long-term prognosis?

Answer:

- Pseudodementia is **not entirely benign** despite being "reversible"
 - **15-20% conversion rate** to true dementia (usually AD) within 3 years
 - Cognitive deficits may not fully resolve, **residual cognitive impairment** (especially processing speed and memory) in 30-40%
 - Depression itself is a **risk factor for dementia** (proposed mechanisms: HPA dysregulation, neuroinflammation, hippocampal volume loss from glucocorticoid toxicity)
 - Long-term: depression is both a prodrome AND a risk factor for AD
 - Follow-up: Annual neuropsychological review for 3-5 years; monitor for emerging dementia features despite depression treatment
-

VIGNETTE 6: The Young Man with Rapidly Progressive Confusion

Case:

Mr. Pradeep Kulkarni, 62 years old, previously healthy, presents to neurology with a 6-week history of rapidly worsening confusion, unsteadiness, and abnormal jerking movements of his limbs. His wife reports the confusion began 2 months ago but has progressed alarmingly. On examination: marked cognitive impairment, cerebellar ataxia, stimulus-sensitive myoclonus, and extrapyramidal signs. MMSE: 12/30 (dropped from normal 2 months ago). EEG shows periodic sharp wave complexes at approximately 1.5 Hz. MRI brain (DWI): cortical ribboning with restricted diffusion in the cortex and basal ganglia.

Q1. What is the diagnosis and what investigations confirm it?

Answer: Diagnosis: **Sporadic Creutzfeldt-Jakob Disease (sCJD).**

Diagnostic criteria met (WHO Probable sCJD):

- **Rapidly progressive dementia** (6 weeks from normal to MMSE 12), hallmark
- **Myoclonus**, stimulus-sensitive, present, one of the core features
- **Cerebellar ataxia**, present
- **EEG:** Periodic sharp wave complexes (PSWC) at 1-2 Hz, **pathognomonic** for sCJD
- **MRI (DWI):** Cortical ribboning + basal ganglia DWI restriction, characteristic pattern

Confirmatory investigations:

INVESTIGATION · EXPECTED FINDING

EEG PSWC at 1-2 Hz (already present)

CSF 14-3-3 protein Elevated (sensitivity 85%, specificity 80%)

CSF RT-QuIC >95% sensitivity, >98% specificity, gold standard for living diagnosis

CSF total tau Very elevated (reflects rapid neurodegeneration)

MRI DWI Already positive, cortical ribboning, hockey-stick sign

Brain biopsy Definitive: spongiform vacuolation, PrPSc immunostaining

Q2. How would you distinguish this from variant CJD?

Answer:

FEATURE	SPORADIC CJD (THIS CASE)	VARIANT CJD
Age	62 years	Usually <30 (mean 28)
Onset	Cognitive/neurological	Psychiatric (depression, anxiety first)
Progression	Rapid (weeks)	Slower (months)
Myoclonus	Prominent, early	Late

FEATURE	SPORADIC CJD (THIS CASE)	VARIANT CJD
EEG	PSWC present	PSWC absent
MRI	Cortical ribboning + BG	Pulvinar sign (posterior thalamus)
CSF 14-3-3	Elevated	Usually negative
Pathology	Spongiform vacuolation	Florid plaques (amyloid core + spongiform halo)
Tonsil biopsy	Not useful	Diagnostic (PrPSc in lymphoid tissue)
BSE link	None	Yes, bovine prion via diet
Survival	5-6 months	12-14 months

Q3. What management would you institute and what infection control measures are required?

Answer:

No disease-modifying treatment. CJD is uniformly fatal. Management is entirely palliative and supportive.

Symptom management:

- Clonazepam 0.5-2mg TDS, for myoclonus
- Opioids (morphine), for pain and distress in late stages
- Antidepressants if mood symptoms in prodrome
- Nasogastric / PEG feeding consideration: ethically complex; family discussion required

Palliative care:

- Early hospice referral
- Anticipatory prescribing (myoclonus, agitation, pain)
- Family counselling: anticipatory grief, what to expect (akinetic mutism, death 5-6 months)
- Psychological support for family: genetic implications if familial variant suspected

Infection control (critical):

- CJD is a **notifiable disease** in India
- Standard universal precautions for healthcare workers (gloves, gown)
- **Prions are resistant to standard sterilisation**, specific decontamination required:
- Surgical instruments: extended autoclave at **134°C for 18 minutes** OR immersion in **1M NaOH for 1 hour**
- Single-use instruments preferred for all invasive procedures

- Corneal, dura mater, and tissue donations are **absolutely contraindicated**
 - Autopsy: specialist neuropathology centre only, with enhanced PPE
 - Genetic testing (PRNP): only if familial CJD suspected; genetic counselling mandatory first
-

VIGNETTE 7: Post-Stroke Forgetfulness

Case:

Mr. Ashok Rao, 68 years old, hypertensive, diabetic, smoker (40 pack-years), presents with cognitive decline that his son describes as "step-by-step worsening, not gradual." He had a stroke 2 years ago with full motor recovery, then a TIA 8 months ago. After each event, his memory and executive function dropped and never fully recovered. He has dysarthria, brisk reflexes, and a positive snout reflex. MRI brain: multiple lacunar infarcts in basal ganglia and thalamus, periventricular white matter hyperintensities (Fazekas 3). Hachinski score: 9.

Q1. Diagnose and classify this patient's dementia type.

Answer: Diagnosis: **Vascular Dementia (VaD)**, most likely **Multi-infarct dementia** with subcortical component.

Classification:

- **Multi-infarct type:** Multiple strokes with stepwise deterioration pattern
- **Subcortical ischaemic VaD component:** Lacunar infarcts in basal ganglia / thalamus + periventricular WMH (Fazekas 3), subcortical white matter disease pattern

Supporting evidence:

- Hachinski score 9 (≥ 7 = VaD)
- Stepwise deterioration (not gradual as in AD)
- Clear temporal relationship between cerebrovascular events and cognitive steps
- Multiple vascular risk factors (HTN, DM, smoking)
- MRI: lacunar infarcts + periventricular WMH
- Neurological signs: dysarthria, brisk reflexes, snout reflex (pseudobulbar features, subcortical)

Q2. What are the principles of management?

Answer:

Secondary vascular prevention (most important):

- **Antiplatelet therapy:** Aspirin 75-150mg OR clopidogrel 75mg daily (if aspirin intolerant); dual antiplatelet briefly post-TIA then single agent

- **BP control:** Target <130/80 mmHg, ACE inhibitor or ARB preferred (ramipril, perindopril have RCT evidence for dementia prevention in vascular disease)
- **Statin therapy:** Atorvastatin 40-80mg, LDL <70 mg/dL target
- **Glycaemic control:** HbA1c <7% (individualise)
- **Smoking cessation:** Immediately; reduces further vascular events by 50%
- **Anticoagulation:** If AF present (warfarin or DOAC), not antiplatelet

Symptomatic treatment for cognition:

- ChEIs (donepezil): modest evidence in VaD; some guidelines recommend
- Memantine: some evidence; particularly for subcortical VaD
- No disease-modifying therapy specific to VaD

Neuropsychiatric symptoms:

- Post-stroke depression: SSRIs (sertraline); very common, must screen actively
- Emotional lability (pseudobulbar affect): SSRIs or very low dose TCAs

Q3. What is the Hachinski Ischemic Score and how is it calculated in this patient?

Answer:

The Hachinski Ischemic Score (HIS) was developed to clinically differentiate vascular dementia from Alzheimer's disease based on clinical features (Hachinski et al., 1975). Maximum score = 18.

Calculation for this patient:

FEATURE	SCORE	PRESENT?
Abrupt onset	2	Yes (post-stroke) = +2
Stepwise deterioration	1	Yes = +1
Fluctuating course	2	Partially = +1 (uncertain)
Nocturnal confusion	1	Score 0 (not described)
Relative preservation of personality	1	0 (not described)
Depression	1	0 (not described)
Somatic complaints	1	0
Emotional incontinence	1	0 (not described)
Hypertension history	1	Yes = +1
Stroke history	2	Yes = +2
Atherosclerosis evidence	1	Yes (vascular RF) = +1

FEATURE	SCORE	PRESENT?
Focal neurological symptoms	2	Yes (dysarthria) = +2
Focal neurological signs	2	Yes (brisk reflexes, snout) = +2
Total		~12-13

Score ≥ 7 = VaD (this patient scores well above threshold).

VIGNETTE 8: The Man Who Lost His Words

Case:

Mr. Venkatesh Iyer, 61 years old, retired journalist, is referred by a speech therapist with a 2-year history of progressive language difficulty. He can no longer name common objects, "that thing you use for...", and struggles to understand words. His vocabulary has shrunk remarkably. However, his memory for day-to-day events is intact, he remembers what he had for lunch, his appointments, and recent news. His face recognition is also impaired. MRI shows asymmetric left anterior temporal lobe atrophy.

Q1. Identify the syndrome and its FTD subtype.

Answer: Syndrome: **Semantic Variant Primary Progressive Aphasia (svPPA)**, also called **Semantic Dementia**.

Key features:

Anomia Cannot name objects/people ("thing you use for...")

Loss of word meaning Does not understand words either (comprehension deficit)

Preserved episodic memory Remembers recent events, day-to-day memory intact

Preserved syntax/phonology Speech is fluent, well-articulated, correct grammar

Face recognition deficit Right temporal variant of semantic dementia

MRI Asymmetric left anterior temporal lobe atrophy

This is one of the three FTD clinical syndromes:

1. **bvFTD**, behavioural and personality changes (frontal)
2. **svPPA** (this case), semantic loss (left anterior temporal)
3. **nvPPA**, effortful, agrammatic speech (posterior frontal/insula)

Q2. How does this differ from progressive non-fluent aphasia (nfvPPA)?

Answer:

FEATURE	SVPPA (SEMANTIC DEMENTIA)	NFVPPA (PROGRESSIVE NON-FLUENT APHASIA)
Speech fluency	Fluent	Non-fluent, effortful, halting
Grammar	Preserved	Agrammatic (telegraphic, dropped function words)
Phonology	Normal	Phonological errors, apraxia of speech
Comprehension of words	Impaired (word meaning lost)	Relatively preserved
Object naming	Severely impaired (semantic)	Impaired (phonological + access)
Episodic memory	Preserved early	Preserved early
MRI	Left anterior temporal atrophy	Left posterior frontal + insular atrophy
Associated motor	Rare	May develop motor neuron disease, CBS
Pathology	TDP-43 (type C)	Tau (CBD, PSP) or TDP-43 type A

Q3. What is the management approach and prognosis?

Answer:

No disease-modifying therapy.

Speech-Language Therapy (central):

- Semantic knowledge exercises, slow the rate of vocabulary loss
- Communication aids, picture boards, AAC (Augmentative and Alternative Communication) devices
- Caregiver training in communication strategies

Cognitive rehabilitation:

- Naming therapy (relearning word-picture associations), modest short-term benefit
- Personalised vocabulary maintenance

Behavioural symptoms (if present):

- As disease progresses, svPPA may develop bvFTD features (right temporal involvement, or spread to frontal)
- SSRIs for any emerging disinhibition or compulsive behaviours

Prognosis:

- svPPA has relatively slower progression than bvFTD

- Median survival from symptom onset: ~8-12 years (longer than bvFTD at 6-8 years)
- Language deterioration → mutism → late global cognitive decline
- Personality and social cognition remain relatively preserved until late (then may develop FTD features)

VIGNETTE 9: Delirium on Dementia

Case:

Mr. Gajanan Deshmukh, 78 years old, known case of mild AD (MMSE 22, on donepezil 10mg), is admitted to medicine ward for a urinary tract infection. Over the next 24 hours, his son notices an acute change, he is seeing insects on the ceiling, cannot recognise his son, is pulling out his IV line, and shouting. He was lucid when admitted. Nursing staff ask the resident to prescribe "something to calm him down quickly."

Q1. What is the diagnosis and what features distinguish it from his baseline dementia?

Answer: Diagnosis: **Delirium Superimposed on Dementia (DSD).**

Distinguishing DSD from baseline dementia:

FEATURE	DSD	BASILINE AD (MILD)
Onset	Acute (24 hours)	Insidious (years)
Level of consciousness	Altered (fluctuating arousal)	Clear
Attention	Severely impaired (cardinal feature of delirium)	Mildly impaired
Hallucinations	Prominent, acute (visual, insects)	Not previously present
Course	Fluctuating (worse at night, sundowning)	Slowly progressive
Precipitant	UTI (identifiable)	None identified
Duration	Days-weeks	Months-years
CAM criteria	Positive	Negative

CAM (Confusion Assessment Method), met:

1. Acute onset and fluctuating course, YES
2. Inattention, YES
3. Disorganised thinking, YES
4. Altered level of consciousness, YES

(Need 1+2 and either 3 or 4)

Dementia is the single biggest risk factor for delirium, 2-5x increased risk. DSD worsens long-term dementia trajectory.

Q2. What is the immediate management priority?

Answer:

Step 1, Identify and treat the precipitant (most important):

- Treat UTI: appropriate antibiotics (urine culture and sensitivity; empirical if septic)
- Other precipitant checklist: pain (unrecognised), constipation, urinary retention, dehydration, electrolyte imbalance, medication toxicity (new drugs?), hypoxia, hypoglycaemia

Step 2, Non-pharmacological interventions (first-line):

- Reorientation: gentle, repeated, familiar faces and voices
- Lighting: bright light in daytime, dim at night, circadian cues
- Familiar objects from home
- Early mobilisation (sit out of bed if clinically safe)
- Restore sensory aids: hearing aids, glasses
- Maintain hydration and nutrition
- Minimise invasive monitoring/lines

Step 3, Pharmacological (only if safety risk or severe distress):

- **Low-dose haloperidol 0.25-0.5mg oral/IM**, cautiously (NOT first-line; only if non-pharm fails and risk to self/others)
- **Avoid benzodiazepines** as first-line, worsen confusion, increase fall risk, paradoxical agitation
- **Note:** This patient has AD, donepezil may continue (cholinergic support may help)
- **If DLB were the underlying dementia:** NEVER haloperidol, neuroleptic sensitivity (although this case is AD, awareness of the DLB caution is essential)

Q3. What is the prognosis of delirium superimposed on dementia?

Answer:

DSD has a significantly worse prognosis than delirium in non-demented individuals:

- **Higher mortality** (in-hospital and 6-month) compared to delirium alone or dementia alone
- **Accelerated cognitive decline**, each episode of DSD associated with faster progression of underlying dementia
- **Incomplete resolution**, cognitive function often does not return fully to pre-delirium baseline (step-down effect)

- **Increased institutionalisation**, DSD episodes are major triggers for nursing home placement
- **Caregiver impact**, acute behavioural disturbance during DSD episodes is highly distressing and often precipitates carer breakdown

Preventive strategy (HELP, Hospital Elder Life Program):

- Proactive delirium prevention: mobility, hydration, cognitive engagement, sleep protocol, sensory aid maintenance
- Delirium is largely preventable (30-40% reduction with HELP protocol)
- For this patient: family education on DSD risk; delirium care plan documented for future admissions

VIGNETTE 10: APOE4 Positive Result

Case:

Ms. Ananya Sharma, 42 years old, software engineer, attends a genetics clinic. Her mother was diagnosed with AD at age 62, and her maternal grandmother also had dementia. She underwent a direct-to-consumer genetic test and is told she is homozygous APOE4/APOE4. She is extremely anxious and asks: "Does this mean I will definitely get Alzheimer's? Should I start medications now? Should I do a PET scan?"

Q1. How do you interpret her APOE4 homozygous result?

Answer:

APOE4 is a risk factor, NOT a deterministic mutation.

APOE GENOTYPE	RISK INCREASE	LIFETIME RISK OF AD
APOE2/2	Protective	Below population (~3-5%)
APOE3/3	Neutral (baseline)	~10-15% (population average)
APOE4/3 (heterozygous)	3-4x increased	~25-30%
APOE4/4 (homozygous, this case)	8-12x increased	~50-60%

Key counselling points:

- **APOE4/4 does NOT guarantee AD**, 40-50% of APOE4 homozygotes do not develop AD
- APOE4 lowers mean age of onset by ~7-10 years per allele
- It is not a Mendelian dominant mutation like PSEN1, no deterministic inheritance
- Unlike BRCA1, APOE4 does not trigger surveillance protocols or preventive surgery
- She should NOT be treated as a patient, she is currently cognitively normal at age 42

Q2. Should she start cholinesterase inhibitors or undergo amyloid PET now?

Answer:

No, neither is currently indicated.

Cholinesterase inhibitors:

- Indicated for symptomatic dementia or MCI with documented cognitive decline
- No evidence of benefit in cognitively normal individuals, even high-risk ones
- Potential harms: side effects without benefit; psychological impact of treating a well person as a patient

Amyloid PET:

- No current clinical indication in asymptomatic individuals, even APOE4 homozygotes
- Being used in RESEARCH settings (A4 trial, AHEAD 3-45 trial), but these are research studies
- Positive amyloid PET in a cognitively normal person = "Alzheimer's pathological change", but does NOT mean she will develop dementia, and no treatment is currently approved to act on this
- Potential harms: anxiety, insurance implications, no actionable treatment decision

What IS recommended:

- Cognitive baseline assessment (MoCA, neuropsychological battery), to document baseline for future comparison
- Vascular risk factor optimisation (most modifiable: BP, DM, lipids, smoking, exercise, sleep, hearing)
- Lifestyle interventions: aerobic exercise (strongest evidence for risk reduction), Mediterranean diet, social engagement, cognitive activity
- Annual follow-up with neuropsychological testing from age ~50
- Clinical trial enrolment (AHEAD 3-45 or similar, testing lecanemab in preclinical AD in APOE4 carriers)
- Psychological support: genetic counselling for anxiety management

Q3. What genetic counselling principles apply to this case?

Answer:

Key principles:

1. **Non-directive counselling:** Counsellor presents information objectively; patient makes their own decisions about testing, surveillance, disclosure
2. **Pre-test counselling:** Should have occurred before the direct-to-consumer test, she bypassed this (a limitation of DTC testing)
3. **Implications for family members:** Her children each have a 50% chance of inheriting one APOE4 allele (she is 4/4; any children will receive one 4); her siblings should be

informed of the possibility

4. **Insurance discrimination:** APOE4 results should be treated as sensitive; potential implications for life/health insurance in some jurisdictions
5. **Psychosocial impact:** APOE4/4 result generates significant anxiety; psychological support and follow-up essential; anxiety itself may impair cognitive performance (ruling out performance anxiety on baseline tests)
6. **Right not to know:** Apply to siblings and children, they have the right not to know their own APOE status
7. **Distinguish from PSEN1/PSEN2/APP:** Those ARE deterministic mutations; APOE4 is NOT, counselling language must reflect this clearly

VIGNETTE 11: Capacity to Make a Will

Case:

Mr. Ramchandra Kulkarni, 80 years old, with mild-to-moderate AD (MMSE 18/30, CDR 1), wishes to update his will to exclude one of his four children. His solicitor contacts the attending psychiatrist for a formal assessment of testamentary capacity.

Q1. Define testamentary capacity and describe its four legal components.

Answer:

Testamentary capacity is the legal and psychiatric determination that a person has sufficient mental capacity to make a valid will at the time of execution.

It was defined in the legal case **Banks v Goodfellow (1870)**, which established four criteria. A testator (person making a will) must:

COMPONENT	DESCRIPTION	ASSESSMENT QUESTION
1. Know the nature of making a will	Understand they are making a document that disposes of property after death	"Can you tell me what a will is? What happens to your property when you die?"
2. Know the extent of their estate	Have a general (not necessarily exact) understanding of what they own	"Can you tell me broadly what property, savings, or assets you have?"
3. Know the natural objects of their bounty	Know who would ordinarily expect to benefit, spouse, children	"Can you tell me about your family? Who are your children?"
4. Absence of a disorder of the mind that poisons affections, perverts judgement, or prevents exercise of natural faculties	No delusion or mental disorder directly influences the testamentary decisions	Is there a delusion driving the decision to exclude this child?

Key legal principle (Banks v Goodfellow): A person can have a diagnosis of dementia AND still have testamentary capacity for a specific will, **if** the above criteria are met. Capacity is decision-specific.

Q2. How would you conduct the capacity assessment?

Answer:

Formal structured assessment:

1. **Review records:** Current cognitive test scores (MMSE 18, mild-moderate); neuropsychological profile; current medication; recent clinical notes

1. **Interview patient alone (and separately with informant):**

2. Apply the four Banks v Goodfellow criteria above

3. Explore: Does he know all four children? Can he name them? Does he understand what the will does? Can he articulate why he wishes to exclude this child, is the reason rational and his own, or delusional?

1. **Assess for delusions (critical):**

2. The most common issue is a **persecutory or theft delusion** about the excluded child

3. If he believes the child "is stealing from him" based on a theft delusion (common in AD) → this delusion may be poisoning his judgment → capacity for THIS decision = compromised

4. If he has a clear, rational, non-delusional explanation (e.g., "this child never visits, we have been estranged for 30 years") → delusion-free, rational decision → capacity may be intact

1. **Document thoroughly:** Time, date, verbatim responses, clinical reasoning, conclusion

1. **Outcome:** If capacity intact → sign capacity certificate supporting will execution. If impaired → advise solicitor; may need Court of Protection/Guardian involvement

Q3. What are the broader ethical and legal issues in dementia and capacity?

Answer:

- **Driving:** Mild AD, requires on-road assessment. Moderate AD, generally unsafe. India has no mandatory reporting law currently; clinician has duty to advise strongly
- **Financial decisions:** Complex financial decisions require higher capacity than simple ones; power of attorney should be executed while capacity is present
- **Treatment decisions:** Each medical decision assessed individually; a patient who cannot manage finances may still have capacity to consent to a tooth extraction
- **Advance Directives (MHA 2017):** Valid in India; allow future treatment/refusal instructions; nominated representative can be appointed

- **Elder abuse:** Higher in dementia, financial exploitation most common; duty to report if suspected
 - **Research participation:** Higher ethical bar, independent ethics review, family/representative consent alongside patient assent
-

VIGNETTE 12: The Caregiver Who Is Breaking Down

Case:

Mrs. Kamini Iyer, 68 years old, has been caring for her husband with moderate AD (MMSE 14/30, BPSD prominent, wandering at night, delusions, aggressive behaviour) for 4 years. She attends clinic alone. She is tearful throughout, reports sleep deprivation for months ("he keeps getting up at night"), has stopped meeting friends entirely, and has lost 5 kg over 3 months. She says "I don't want to put him in a home, I promised I wouldn't." Zarit Burden Interview score: 54/88.

Q1. Assess caregiver burden in this case, what does the Zarit score indicate?

Answer:

Zarit Burden Interview (ZBI): 22-item self-report scale assessing subjective caregiver burden across physical, emotional, social, and financial domains. Each item rated 0-4; total range 0-88.

Score interpretation:

SCORE · CATEGORY

0-20 Little or no burden

21-40 Mild to moderate burden

41-60 Moderate to severe burden

61-88 Severe burden

Mrs. Iyer's score: 54 = Moderate to severe burden

Clinical manifestations of burden present:

- **Physical:** Sleep deprivation, weight loss (5 kg), exhaustion
- **Psychological:** Tearfulness, social withdrawal, high distress
- **Social:** Complete social isolation (stopped meeting friends)
- **Role entrapment:** Feeling unable to leave ("I promised")
- **Bereavement:** Anticipatory grief, her husband is present but psychologically "gone"

This caregiver is at high risk of developing **major depression** (50-70% of dementia caregivers develop depression) and **medical complications** from neglect of her own health.

Q2. What interventions would you recommend for her?

Answer:

Multi-level caregiver support:

1. Psychoeducation (immediate priority):

- Dementia course and prognosis, what to expect; planning ahead
- BPSD explanation, "he cannot control this behaviour; the disease controls him"
- Practical guidance: managing nocturnal wandering (locks, door alarms, safe spaces), managing aggression (de-escalation, not confrontation)

2. Practical/Environmental:

- **Sleep hygiene for patient:** Melatonin 5-10mg (reduce nocturnal waking); bright light therapy in daytime; structured activity to increase daytime activity → improve night sleep
- Door alarms, GPS tracking devices (wandering safety)
- Daycare centre attendance, gives her 8 hours of respite daily

3. Formal support:

- **Respite care:** Discuss day program + periodic in-patient respite (2-4 weeks/year)
- ARDSI (Alzheimer's and Related Disorders Society of India), caregiver support groups, helpline, resource connection
- Home nursing support for personal care (bathing, medications)

4. Psychological support for her:

- Grief counselling, normalise anticipatory mourning
- Challenge the "promise", explore meaning, reframe care options as expressions of love not betrayal
- Individual CBT or supportive therapy for depressive features
- Screen formally for depression (PHQ-9 or HDRS), she may need antidepressant treatment
- Peer support group (other dementia caregivers), powerful validation

5. Financial counselling:

- Benefits available (government schemes for elderly and disability in India)
- Long-term financial planning

Q3. When would institutionalisation be appropriate to discuss, and how would you approach this conversation?

Answer:

Indicators that institutionalisation should be actively discussed:

INDICATOR · PRESENT IN THIS CASE?

Caregiver health deteriorating (physical/mental) Yes, sleep deprivation, weight loss, depression

Patient safety compromised at home (wandering, falls, fire risk) Yes, nocturnal wandering

Caregiver cannot manage care needs Approaching this point

BPSD severe and uncontrolled Yes, aggression, delusions

Social support absent Yes, isolated

Severe caregiver burden (ZBI >60) Not yet (54), but deteriorating

Approach to the conversation:

1. **Acknowledge the promise:** "I understand this was a commitment that came from love."
2. **Reframe:** "The promise was to care for him. Placing him in a facility where he gets 24-hour specialised care while you can visit daily and be his wife, not his nurse, may be the most caring thing you can do."
3. **Address guilt:** Normalise; explain caregiver health is also patient's welfare
4. **Explore options:** Memory care units vs nursing homes vs respite care as step before permanent placement
5. **Involve family:** Other children should share decision, reduce burden on her alone
6. **No rush:** This is a process conversation; she needs time; revisit at next appointment
7. **Practical visit:** Arrange a visit to a memory care facility before deciding

CLINICAL ANCHOR

Caregiver breakdown leads directly to patient harm, hospitalisation, abuse risk, premature institutionalisation without preparation. Supporting the caregiver IS treating the patient.

All patient names in this document are fictitious. Sources: Kaplan & Sadock's Synopsis of Psychiatry 12th Ed, Oxford Textbook of Psychiatry 6th Ed, Cummings' Neuropsychiatry and Behavioral Neuroscience 3rd Ed, DSM-5, ICD-11, McKeith 2017, Rascovsky 2011, NIA-AA 2018

Endocrine Metabolic

Paper IV · Neurology, Medicine & Recent Advances. Six study modes, from notes to quick review.

Study Notes

SECTION 1: THYROID DISORDERS & PSYCHIATRY

1.1 Thyroid Hormone Physiology: Psychiatric Relevance

The hypothalamic-pituitary-thyroid (HPT) axis is one of the most psychiatrically relevant neuroendocrine systems. Thyroid hormones (T3, triiodothyronine; T4, thyroxine) exert broad effects on neuronal function, monoamine metabolism, synaptic transmission, and brain development.

Key mechanisms:

- T3 is the biologically active form; T4 is converted peripherally (and in the brain) by deiodinases
- T3 regulates serotonin receptor density, norepinephrine turnover, and beta-adrenergic receptor sensitivity
- Hypothyroid states reduce brain serotonergic and adrenergic tone
- Hyperthyroid states amplify sympathetic and adrenergic activity

Normal ranges (for reference):

PARAMETER • NORMAL RANGE

TSH 0.4 – 4.0 mIU/L

Free T4 0.8 – 1.8 ng/dL

Free T3 2.3 – 4.2 pg/mL

Total T4 5 – 12 mcg/dL

1.2 Hypothyroidism & Psychiatric Manifestations

Epidemiology:

- Prevalence: 4–10% in women, 0.5–2% in men
- Subclinical hypothyroidism (elevated TSH, normal T4): up to 10% prevalence
- Autoimmune (Hashimoto's thyroiditis) is the most common cause in iodine-sufficient regions

Psychiatric Manifestations, Spectrum:

Depression in Hypothyroidism:

- 40–60% of hypothyroid patients have depressive symptoms
- Presentation overlaps heavily with MDD: low mood, anhedonia, fatigue, psychomotor retardation, weight gain, cold intolerance
- Key distinguishing features: dry skin, hair loss, hoarse voice, constipation, bradycardia, delayed ankle reflexes
- Subclinical hypothyroidism is associated with increased prevalence of depression (especially in women)
- Mechanism: reduced serotonergic neurotransmission, reduced beta-adrenergic sensitivity, decreased NA synthesis
- CRITICAL POINT: Depression in hypothyroidism often does NOT respond to antidepressants alone, thyroid replacement is needed

Cognitive Impairment in Hypothyroidism:

- Ranges from mild forgetfulness to dementia-like syndrome
- Domains affected: attention, processing speed, working memory, verbal fluency
- In elderly: can mimic dementia (reversible on treatment), always screen TSH in new-onset cognitive complaints
- Children: congenital hypothyroidism (cretinism), irreversible intellectual disability if untreated before 3 months
- Mechanism: reduced cerebral glucose metabolism, altered synaptic plasticity, decreased neurogenesis in hippocampus

Myxedema Madness:

- Rare but classic, psychiatric manifestation of severe / prolonged hypothyroidism
- First described by Asher (1949)
- Presents as: paranoid psychosis, visual / auditory hallucinations, delirium, mania
- Context: severe myxedema (periorbital puffiness, macroglossia, non-pitting edema, hypothermia)
- TSH typically very high; T4 very low
- Treatment: thyroid hormone replacement (IV T4 in myxedema coma); antipsychotics if needed briefly
- Distinguishing from primary psychosis: marked physical signs, onset in context of severe systemic illness

Hashimoto's Encephalopathy:

- Rare autoimmune encephalopathy associated with Hashimoto's thyroiditis
- NOT directly caused by thyroid hormone levels (can occur even with euthyroid state)
- Mediated by anti-TPO antibodies (anti-thyroid peroxidase) and possibly anti-NMDA mechanisms

- Presents: acute/subacute encephalopathy, psychosis, stroke-like episodes, seizures, tremor
- Diagnosis: elevated anti-TPO antibodies, CSF abnormalities, EEG changes
- Steroid-responsive, classic feature
- Key exam point: "steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT)"

1.3 Hyperthyroidism & Psychiatric Manifestations

Causes: Graves' disease (most common), toxic multinodular goitre, toxic adenoma, thyroiditis, exogenous T4

Psychiatric Manifestations:

MANIFESTATION	FREQUENCY	CHARACTER
Anxiety	60–80%	Generalized, free-floating; tremor, palpitations
Irritability	Common	Emotional lability, low frustration tolerance
Insomnia	Common	Difficulty initiating and maintaining sleep
Depression	30–40%	Can coexist with anxiety
Mania	Rare	Elevated mood, grandiosity, decreased need for sleep
Psychosis	Rare	Paranoia, hallucinations; especially in "thyroid storm"
Cognitive impairment	Variable	Distractibility, poor concentration

Anxiety in Hyperthyroidism:

- Can perfectly mimic panic disorder or GAD
- Key: physical symptoms of hyperthyroidism present (tachycardia, tremor, heat intolerance, weight loss despite appetite)
- Always check TFTs when anxiety presents with physical symptoms
- Mechanism: elevated beta-adrenergic activity, sensitization of central noradrenergic circuits

Mania and Hyperthyroidism:

- "Thyrotoxic mania", well-documented but rare

- T3/T4 excess may mimic or precipitate manic episodes, especially in predisposed individuals
- T3 augmentation in depression (intentional hyperthyroid state), see below
- Always check TFTs before diagnosing new-onset mania

Thyroid Storm (Thyrotoxic Crisis):

- Medical emergency: extreme hyperthyroidism precipitated by surgery, infection, stress
- Psychiatric manifestations: extreme agitation, psychosis, delirium, seizures, coma
- Treatment: beta-blockers (propranolol), PTU / methimazole, iodine, glucocorticoids, cooling

1.4 Lithium-Induced Thyroid Dysfunction

One of the most important thyroid-psychiatry intersections for exams.

Mechanisms of lithium-induced thyroid dysfunction:

1. **Inhibition of thyroid hormone synthesis**, blocks iodine uptake, organification, and hormone release
2. **Inhibition of TSH-stimulated cAMP generation**
3. **Promotion of autoimmunity**, lithium promotes anti-thyroid antibody formation
4. **Increased incidence of Hashimoto's thyroiditis** in lithium-treated patients

Frequency of lithium-induced thyroid disorders:

- Hypothyroidism: 20–42% of patients on long-term lithium
- Subclinical hypothyroidism (TSH elevated, free T4 normal): 20–40%
- Goitre: 4–60% depending on duration and iodine status
- Hyperthyroidism: rare (1–2%), usually late or after thyroiditis phase

Risk factors for lithium-induced hypothyroidism:

- Female sex
- Older age
- Positive anti-TPO antibodies at baseline
- Family history of thyroid disease
- Duration of lithium treatment

Monitoring protocol (NICE/BAP guidelines):

- Baseline TFTs before starting lithium
- 6-monthly TFTs for first year
- Annual TFTs thereafter (or sooner if symptomatic)

Management:

- Lithium-induced hypothyroidism: continue lithium + add levothyroxine (do NOT routinely stop lithium)
- Subclinical hypothyroidism: treat if TSH >10 mIU/L, or if symptomatic, or if pregnant
- Goitre: usually benign; monitor; evaluate if rapid growth

Lithium and Hyperparathyroidism:

- Lithium can also cause hyperparathyroidism and hypercalcemia
 - Mechanism: raises PTH set-point, leading to parathyroid gland hyperplasia
 - Clinical: elevated calcium, elevated PTH, nephrocalcinosis
 - Monitor serum calcium in long-term lithium patients
-

1.5 T3 Augmentation in Depression

Rationale:

- T3 enhances antidepressant response even in euthyroid patients
- Mechanism: sensitizes beta-adrenergic receptors, enhances serotonergic neurotransmission, reverses antidepressant down-regulation of receptors
- Effective even when thyroid function is normal

Evidence:

- Multiple RCTs show T3 augmentation of tricyclic antidepressants improves response rates
- Less consistent evidence with SSRIs
- STAR*D study: T3 augmentation comparable to lithium augmentation for treatment-resistant depression
- Typical dose: liothyronine (T3) 25–50 mcg/day

Clinical considerations:

- Monitor for iatrogenic hyperthyroidism (palpitations, tremor, anxiety)
- Contraindicated in cardiac disease, uncontrolled hypertension
- More commonly used in women (some evidence of sex-specific response)

Thyroid hormones in Rapid Cycling Bipolar:

- Supraphysiological doses of T4 (levothyroxine 250–500 mcg) used as adjunct in rapid cycling
 - Mechanism uncertain, may stabilize via direct mood regulatory effects
 - Requires monitoring; risk of thyrotoxicosis and bone loss
-

1.6 Thyroid Function Tests in Psychiatric Patients

When to screen TFTs in psychiatric settings:

INDICATION · RATIONALE

New-onset depression Rule out hypothyroidism

New-onset anxiety Rule out hyperthyroidism

Treatment-resistant depression Subclinical hypothyroidism may impair response

New-onset mania Rule out hyperthyroidism

New-onset psychosis Rule out thyroid-related psychosis

Before starting lithium Baseline; lithium affects thyroid

During lithium therapy Monitoring (6-monthly → annual)

Cognitive impairment in elderly Hypothyroidism causes reversible dementia

Eating disorders Sick euthyroid syndrome common

Postpartum psychiatric illness Postpartum thyroiditis: 5–10% prevalence

SECTION 2: CUSHING'S SYNDROME & PSYCHIATRY

2.1 Overview

Cushing's syndrome = sustained excess glucocorticoid exposure, regardless of cause.

Cushing's disease = pituitary ACTH-secreting adenoma (70% of endogenous cases).

Causes:

- Pituitary adenoma (Cushing's disease), 70%
- Adrenal adenoma/carcinoma, 15%
- Ectopic ACTH (lung tumour, carcinoid), 10–15%
- **Exogenous glucocorticoids**, most common cause overall

Classic physical features: central obesity, moon face, buffalo hump, striae, easy bruising, hypertension, diabetes, osteoporosis, hirsutism (in women), proximal muscle weakness

2.2 Psychiatric Manifestations of Cushing's Syndrome

Psychiatric symptoms are extremely common, present in 50–80% of patients.

Depression:

- Most common psychiatric manifestation: 50–80% prevalence
- Character: prominent anhedonia, psychomotor retardation, severe fatigue, diurnal variation
- Cognitive impairment often concurrent (hippocampal atrophy on MRI)
- Suicidality: 4–10% attempt suicide
- Mechanism: hypercortisolaemia → HPA axis dysregulation → monoamine depletion, hippocampal neurogenesis suppression, glucocorticoid receptor downregulation

Anxiety:

- 20–70% of patients
- Generalized anxiety, panic attacks
- Often co-occurs with depression

Cognitive Impairment:

- Memory deficits (hippocampal vulnerability to cortisol)
- Concentration difficulties
- Verbal learning impairment
- Hippocampal volume reduction on MRI (reversible partially after treatment)

Psychosis:

- 5–15% of patients
- Paranoid psychosis most common
- Mania can also occur ("steroid mania")
- Mechanism: excess cortisol → dopaminergic dysregulation

Personality Change:

- Emotional lability, irritability
- Interpersonal difficulties
- Paranoid traits

Mania:

- Less common than depression
- Can occur with endogenous or exogenous cortisol excess
- "Steroid mania", see exogenous section below

2.3 Exogenous Glucocorticoid-Induced Psychiatric Disorders

Steroid-induced psychiatric syndromes are common in clinical medicine.

Frequency:

- Mild: euphoria, mood lability, very common (>50% at higher doses)
- Moderate: depression or hypomania, 5–10%
- Severe: psychosis, 1–5%
- Mania: less common than psychosis

Classic "steroid mania":

- Elevated mood, decreased sleep, grandiosity, racing thoughts
- Often occurs within days of starting or increasing dose
- Not a reliable predictor from past episodes, different doses can cause different reactions

Dose relationship:

PREDNISONE EQUIVALENT DOSE · PSYCHIATRIC RISK

< 40 mg/day Low (1.3%)

40–80 mg/day Moderate (4.6%)

> 80 mg/day High (18.4%)

Management of steroid-induced psychiatric disorders:

1. Reduce steroid dose if medically possible
2. Antipsychotics for psychosis/mania (haloperidol, olanzapine)
3. Mood stabilizers for mania (lithium, valproate), may need to continue if steroids cannot be stopped
4. Antidepressants for depression (usually after ruling out brief reactive mood changes)
5. Note: lithium has prophylactic role in patients who require repeated steroid courses

Key exam point: Steroid-induced psychiatric symptoms tend to RESOLVE when steroids are tapered, this is the first treatment step.

2.4 Differentiating Cushing's from Psychiatric Depression

FEATURE	CUSHING'S DEPRESSION	PRIMARY DEPRESSION
Cortisol	Elevated (unsuppressed)	May be elevated
DST (dexamethasone)	Non-suppression	Non-suppression (also seen)
Physical signs	Moon face, striae, buffalo hump	Absent
Hippocampal atrophy	Yes	Yes (chronic)
Weight	Gained (central)	Variable
Onset	After cortisol excess begins	Independent

Diagnosis of Cushing's:

- Screening: 24-hour urine free cortisol, late-night salivary cortisol, low-dose DST (1 mg overnight)
 - Localisation: plasma ACTH, high-dose DST, CRH stimulation test, pituitary MRI, adrenal CT, inferior petrosal sinus sampling
-

SECTION 3: ADDISON'S DISEASE & PSYCHIATRY

3.1 Overview

Addison's disease = primary adrenal insufficiency due to destruction of adrenal cortex.

- Most common cause: autoimmune (70–90%) in developed countries
- Other causes: tuberculosis (most common in developing countries), fungal infections, hemorrhage (Waterhouse-Friderichsen syndrome, meningococcal)
- Results in deficiency of cortisol AND aldosterone

Physical features: hyperpigmentation (buccal mucosa, creases, scars), hypotension, weight loss, nausea, vomiting, salt craving, weakness

3.2 Psychiatric Manifestations of Addison's Disease

Psychiatric symptoms occur in 60–90% of patients.

Depression:

- Most common psychiatric manifestation
- Character: low energy, anhedonia, fatigue (often profound)
- Apathy prominent, diminished initiative and motivation
- Can be severe, melancholic
- Mechanism: cortisol deficiency → disruption of normal stress response, monoamine dysregulation

Apathy and Fatigue:

- Sometimes predominant, patient may present with extreme fatigue as primary complaint
- Distinguished from depression: cognitive features of depression may be absent
- Salt craving: a clinical clue

Anxiety:

- 30–50%
- Generalized anxiety; sometimes panic attacks
- May relate to physiological hypervigilance in context of impaired stress response

Psychosis:

- Rare but documented
- Can occur in severe or decompensated Addison's
- Usually resolves with glucocorticoid replacement

Cognitive Impairment:

- Memory problems, slowed processing
 - Reversible with replacement therapy
-

3.3 Adrenal Crisis

Medical emergency, psychiatric mimicry and complication.

Precipitants: infection, surgery, trauma, physiological stress, inadequate steroid cover

Psychiatric presentation:

- Can present with delirium, acute confusional state
- Agitation, severe anxiety
- In chronic Addison's: may have chronic low-grade psychiatric symptoms that worsen acutely

Emergency management:

- Hydrocortisone 100 mg IV immediately
 - IV saline resuscitation
 - Identify and treat precipitant
 - NOT the time for psychiatric medication, treat the hormonal crisis first
-

SECTION 4: DIABETES MELLITUS & PSYCHIATRY

4.1 Depression-Diabetes Bidirectional Link

This is one of the best-established endocrine-psychiatric bidirectional relationships.

Epidemiology:

- Depression is 2–3x more common in diabetes vs general population
- Prevalence of depression in T2DM: 15–25%
- Prevalence of diabetes in major depression: 2–3x increased risk

Direction 1, Diabetes causes depression:

- Chronic illness burden, functional impairment, fear of complications
- Neurobiological: hyperglycemia → oxidative stress → hippocampal damage; HPA axis dysregulation; inflammation (IL-6, TNF-alpha elevated)

- Diabetic neuropathy → pain → depression
- Hypoglycemia → anxiety, fear

Direction 2, Depression causes/worsens diabetes:

- Depression → poor self-care, non-adherence to medication and diet
- Behavioural: inactivity, unhealthy eating, smoking, alcohol use
- Neurobiological: depression → HPA axis hyperactivity → cortisol excess → insulin resistance; sympathetic hyperactivity → hepatic glucose production
- Antidepressants (especially TCAs, mirtazapine) → weight gain, hyperglycemia

Clinical consequences of comorbidity:

- Worse glycemic control (higher HbA1c in depressed diabetics)
- Higher risk of diabetic complications (retinopathy, nephropathy, cardiovascular disease)
- Increased mortality
- Higher healthcare utilization

Management:

- Screen all T2DM patients for depression (PHQ-9)
- Collaborative care models effective
- SSRIs first-line for depression in diabetes (fluoxetine may slightly improve insulin sensitivity)
- CBT: evidence base for depression + diabetes self-management
- Caution: TCAs, MAOIs → weight gain, metabolic effects

4.2 Metabolic Syndrome

Metabolic Syndrome = cluster of cardiometabolic risk factors.

Diagnostic criteria (IDF, 2006, most commonly used):

Central obesity (waist circumference ≥ 90 cm men / ≥ 80 cm women for South Asians) PLUS any 2 of:

- Fasting glucose ≥ 5.6 mmol/L (100 mg/dL) or T2DM diagnosis
- Triglycerides ≥ 1.7 mmol/L (150 mg/dL)
- HDL-C < 1.03 (men) / < 1.29 (women) mmol/L
- Blood pressure $\geq 130/85$ mmHg

Metabolic syndrome in psychiatric populations:

- Prevalence in schizophrenia: 40–60% (vs ~25% general population)
- In bipolar disorder: 25–50%
- In major depression: elevated vs general population

- Driven by: antipsychotic medications, lifestyle factors (inactivity, poor diet, smoking), disease biology
-

4.3 Antipsychotic-Induced Metabolic Effects

This is the highest-yield topic in this section for exams.

Mechanism of antipsychotic metabolic effects:

1. **Histamine H1 antagonism**, primary driver of weight gain
2. **Serotonin 5-HT_{2C} antagonism**, promotes appetite, impairs satiety signaling
3. **Dopamine D2 antagonism**, affects appetite regulation via mesolimbic circuits
4. **Muscarinic M3 antagonism**, impairs pancreatic insulin secretion (direct diabetogenic)
5. **Adrenergic alpha-1 blockade**, sedation → reduced activity

Weight Gain Hierarchy (highest to lowest):

Diabetogenic effects (independent of weight):

ANTIPSYCHOTIC · DIABETOGENIC RISK

Clozapine Very high

Olanzapine Very high

Quetiapine Moderate

Risperidone Moderate

Haloperidol Low

Aripiprazole Low

Ziprasidone Low

Amisulpride Low

4.4 ADA/APA Monitoring Guidelines for Antipsychotics

The ADA/APA/AACE/NAASO Consensus Statement (2004) monitoring protocol, frequently examined:

WIDE COMPARISON · LANDSCAPE

PARAMETER	BASELINE	4 WEEKS	8 WEEKS	12 WEEKS	ANNUALLY	EVERY 5 YEARS
Personal/family history	X				X	
Weight/BMI	X	X	X	X	X	
Waist circumference	X				X	
Blood pressure	X			X		X
Fasting glucose	X			X		X
Fasting lipids	X			X		X

Thresholds for action:

- BMI gain >1 unit in any month → consider switch
 - Fasting glucose >100 mg/dL (5.6 mmol/L) → refer to physician
 - Fasting glucose >126 mg/dL (7.0 mmol/L) on two occasions → diabetes, refer and consider switch
 - Triglycerides >200 mg/dL → refer
 - LDL >130 mg/dL in high-risk patient → refer
-

4.5 Switching Strategies for Metabolic Side Effects

When to switch:

- Significant weight gain (BMI increase >1 unit/month)
- New-onset hyperglycemia or diabetes
- Dyslipidemia not manageable pharmacologically
- Patient preference (informed)

Preferred switch targets (metabolically safer):

- Aripiprazole
- Ziprasidone (low weight/metabolic burden)
- Amisulpride
- Lurasidone

Switching strategies:

1. **Abrupt switch**, straightforward for metabolically favorable drugs; risk of relapse
2. **Cross-titration**, overlap and taper; most common approach; monitor for side effects during overlap
3. **Plateau (halfway) method**, particularly for clozapine → target

Note on clozapine: Switching FROM clozapine carries high relapse risk. Benefits of metabolic improvement must be weighed against loss of efficacy (clozapine remains the gold standard for treatment-resistant schizophrenia).

4.6 Metformin Augmentation for Antipsychotic-Induced Weight Gain

Metformin:

- RCT evidence supports metformin for antipsychotic-induced weight gain
- Typical dose: 500–1000 mg BD
- Reduces weight by 2–3 kg on average in antipsychotic-treated patients
- Also improves insulin sensitivity, reduces HbA1c

- Safe in combination with antipsychotics
- Consider early (before significant weight gain is established)

Other pharmacological interventions:

- Aripiprazole addition to clozapine / olanzapine, reduces weight gain (partial D2 agonism modulates metabolic effects)
- Topiramate, modest weight reduction; cognitive side effects limit use
- Orlistat, modest effect, GI side effects
- GLP-1 agonists (semaglutide, liraglutide), emerging evidence for substantial weight reduction; not yet standard care in most guidelines but use increasing

SECTION 5: PHEOCHROMOCYTOMA & PSYCHIATRY

5.1 Overview

Pheochromocytoma = catecholamine-secreting tumour of adrenal medulla.

- Paraganglioma = extra-adrenal catecholamine tumour
- "Rule of 10s" (traditional): 10% malignant, 10% bilateral, 10% extra-adrenal, 10% familial, 10% in children (these proportions are approximate / historical)

Biochemistry: secretes epinephrine, norepinephrine, dopamine in varying ratios depending on tumour location

5.2 Psychiatric Mimicry

Classic presentation: paroxysmal hypertension, headache, sweating, palpitations, the "4 P's"

Panic-like presentations:

- Can perfectly mimic panic disorder or panic attacks
- Episodes of: extreme anxiety, palpitations, tremor, sweating, headache, pallor / flushing
- Duration: minutes to hours
- Can be spontaneous or triggered (compression of tumour)

Distinguishing features from true panic disorder:

FEATURE	PANIC DISORDER	PHEOCHROMOCYTOMA
Hypertension	Usually absent or minimal	Severe (systolic >200 mmHg)
Duration of episodes	Typically 10–30 min	Variable (minutes to hours)
Pallor during episode	Uncommon	Common
Triggers	Often psychosocial	Physical (posture, exercise)

FEATURE	PANIC DISORDER	PHEOCHROMOCYTOMA
24hr urinary catecholamines	Normal	Elevated
Plasma metanephrines	Normal	Elevated

Diagnostic approach:

- 24-hour urine metanephrines / catecholamines (screening test of choice)
- Plasma free metanephrines (sensitivity ~97%, specificity ~85%)
- Imaging: CT/MRI adrenal glands once biochemistry positive
- MIBG scan: functional imaging for extra-adrenal disease

Key exam point: Always exclude pheochromocytoma in panic disorder with prominent cardiovascular symptoms, especially with treatment resistance.

Depression and psychiatric comorbidity:

- Chronic catecholamine excess can cause mood instability, anxiety, and depression
- Post-surgical cure often resolves psychiatric symptoms

SECTION 6: PARATHYROID DISORDERS & PSYCHIATRY

6.1 Hyperparathyroidism

Primary hyperparathyroidism: excess PTH from parathyroid adenoma (80%) or hyperplasia → hypercalcemia

"Bones, stones, groans, psychic moans", the classic tetrad

Psychic moans, psychiatric manifestations:

- Depression: most common psychiatric manifestation (40–60%)
- Anxiety
- Cognitive impairment: poor concentration, memory difficulties
- Psychosis: rare, in severe hypercalcemia
- Fatigue, weakness, malaise

Calcium and mood, mechanism:

- Hypercalcemia → reduces neuronal excitability, alters neurotransmitter release
- Affects serotonergic, dopaminergic, noradrenergic systems
- Hippocampal calcium channels involved in memory consolidation

Psychiatric symptoms correlate with calcium levels:

- Mild hypercalcemia (Ca 2.6–3.0 mmol/L): fatigue, cognitive slowing, mild depression
- Moderate (3.0–3.5 mmol/L): depression, anxiety, confusion

- Severe (>3.5 mmol/L): delirium, psychosis, coma

Key clinical point: Check serum calcium in treatment-resistant depression.

6.2 Hypoparathyroidism

Hypoparathyroidism: PTH deficiency → hypocalcemia

- Most common cause: inadvertent removal during thyroidectomy / parathyroidectomy
- Also: autoimmune (DiGeorge syndrome), idiopathic

Psychiatric manifestations of hypocalcemia:

- Anxiety, irritability, emotional lability
- Depression
- Psychosis (rare, can present as schizophrenia-like illness)
- Cognitive impairment
- Seizures (not psychiatric but important)
- Basal ganglia calcification (Fahr's disease associated with chronic hypoparathyroidism)
→ movement disorder + neuropsychiatric symptoms

Classic physical signs: Chvostek's sign (facial nerve tap → facial twitching), Trousseau's sign (BP cuff inflation → carpal spasm), tetany, perioral paresthesias

SECTION 7: PITUITARY DISORDERS & PSYCHIATRIC ASPECTS

7.1 Prolactinoma

Most common pituitary tumour (40% of all pituitary adenomas)

Psychiatric effects of hyperprolactinemia:

- Hypogonadism → depression, sexual dysfunction
- In women: amenorrhea, infertility → psychosocial distress
- In men: erectile dysfunction, loss of libido → depression
- Galactorrhea → body image issues

Antipsychotic-induced hyperprolactinemia:

- All D2 antagonist antipsychotics → hyperprolactinemia (dopamine normally inhibits prolactin release)
- Highest: amisulpride, risperidone, haloperidol
- Lowest: clozapine, quetiapine (partial sparing of tuberoinfundibular pathway)
- Aripiprazole (D2 partial agonist) → actually LOWERS prolactin → can add to normalize levels

Monitoring prolactin:

- Baseline before starting antipsychotics (if clinically indicated)
 - Check if galactorrhea, amenorrhea, sexual dysfunction, or gynecomastia develops
-

7.2 Acromegaly

GH-secreting pituitary adenoma → excess GH and IGF-1

Psychiatric manifestations:

- Depression: 40–60%
- Anxiety: 30–40%
- Fatigue, reduced quality of life
- Irritability, personality change
- Social withdrawal (related to physical changes, coarsening features, macroglossia, large hands/feet)

Key mechanism: GH/IGF-1 effects on central serotonergic and dopaminergic function; also psychosocial impact of physical disfigurement

7.3 Hypopituitarism

Multiple pituitary hormone deficiency (any combination of GH, TSH, ACTH, LH/FSH, ADH, prolactin deficiency)

Psychiatric manifestations:

- Depression: very common, multifactorial (GH deficiency, thyroid deficiency, cortisol deficiency, sex hormone deficiency)
- Fatigue, poor energy
- Cognitive impairment
- Sexual dysfunction

Adult GH deficiency syndrome:

- Well-recognized entity
- Features: central obesity, reduced muscle mass, fatigue, low mood, impaired QoL
- Treatment with GH replacement improves mood and cognitive function

Sheehan's syndrome (postpartum pituitary necrosis):

- Failure to lactate, amenorrhea, hypothyroidism, hypocortisolism
 - Psychiatric: depression, chronic fatigue, cognitive impairment
 - May present years after a complicated delivery (massive PPH)
-

SECTION 8: WILSON'S DISEASE & PSYCHIATRY

8.1 Overview: Key Exam Topic

Wilson's disease = autosomal recessive disorder of copper metabolism.

- Gene: ATP7B (chromosome 13), encodes copper-transporting ATPase
- Pathophysiology: failure of biliary excretion of copper → copper accumulation in liver, brain, cornea, kidneys, heart
- Onset: typically 5–35 years (children and young adults)

A classic "great mimic" in psychiatry, important exam topic

8.2 Psychiatric Manifestations

Psychiatric symptoms are the PRESENTING feature in 20–30% of cases.

Personality Change:

- Often earliest psychiatric sign
- Disinhibition, impulsivity, emotional lability
- Loss of social inhibitions, inappropriate behavior
- Can be mistaken for conduct disorder in adolescents
- Mechanism: basal ganglia copper deposition → altered frontostriatal circuits

Psychosis:

- Schizophrenia-like presentations
- Paranoid delusions, auditory hallucinations
- Visual hallucinations (less specific)
- Can mimic first-episode schizophrenia
- Key: young patient with psychosis + movement disorder + liver disease → **MUST** exclude Wilson's

Affective Symptoms:

- Depression: common, variable severity
- Anxiety
- Mania (rare)
- Emotional incontinence (pathological laughing/crying)

Cognitive Impairment:

- Executive dysfunction prominent (basal ganglia and frontal involvement)
- Memory impairment
- Processing speed reduction

- Can progress to dementia if untreated

Neurological Features (often concurrent with psychiatric):

- Dysarthria (often the first neurological sign)
 - Tremor (wing-beating / resting / postural)
 - Dysphagia
 - Dystonia
 - Parkinsonism
 - Chorea
 - Seizures (10–15%)
-

8.3 Diagnosis

Kayser-Fleischer (KF) Rings:

- Golden-brown / greenish rings at corneal periphery (Descemet's membrane)
- Copper deposits
- Best visualized on slit-lamp examination
- Present in >95% of neuropsychiatric Wilson's
- Present in 50–60% of hepatic presentations (alone)
- NOT pathognomonic, can occur in other cholestatic liver diseases
- ABSENCE of KF rings does NOT exclude Wilson's (especially hepatic presentation)

Diagnostic investigations:

TEST · FINDING IN WILSON'S

Serum ceruloplasmin Low (<0.2 g/L) in 95%

24-hour urine copper High (>100 mcg / 24h; >40 mcg in symptomatic)

Liver copper (biopsy) High (>250 mcg / g dry weight)

Serum copper Low total (but high free / unbound copper)

Genetic testing ATP7B mutation

Brain MRI "Face of giant panda" sign (mesencephalon), T2 hyperintensities in basal ganglia, thalamus

Liver biopsy Copper accumulation, cirrhosis

"Face of giant panda" sign: midbrain MRI finding, characteristic but not universal.

Leipzig scoring system, used for diagnosis (combines KF rings, ceruloplasmin, Coombs-negative hemolytic anemia, urine copper, liver copper, gene mutation).

8.4 Treatment

Goals: remove excess copper, prevent further accumulation

D-Penicillamine (copper chelator):

- First-line in most guidelines
- Mechanism: chelates copper → increased urinary copper excretion
- Dose: 750–1500 mg/day (divided doses)
- Side effects: rash, fever, lupus-like syndrome, nephrotoxicity, bone marrow suppression, pyridoxine deficiency (supplement B6)
- IMPORTANT EXAM POINT: Neurological/psychiatric worsening can occur in first few weeks (paradoxical, copper is mobilized from liver and redistributed to brain)
- Contraindicated in: renal failure, lupus, pre-existing neurological Wilson's (relative contraindication)

Trientine (Triethylenetetramine):

- Alternative copper chelator
- Better tolerated than penicillamine
- Preferred in: patients intolerant of penicillamine, neurological Wilson's (lower risk of neurological deterioration)
- Dose: 750–1500 mg/day (divided doses)

Zinc acetate/Zinc sulfate:

- Mechanism: induces metallothionein in intestinal cells → blocks copper absorption from gut
- Not a chelator, works by preventing absorption
- Used for: maintenance therapy after initial chelation, presymptomatic patients, pregnancy (safer profile)
- Cannot be used simultaneously with chelators (interfere with each other)
- Dose: zinc acetate 50 mg elemental zinc TID

Ammonium tetrathiomolybdate:

- Investigational agent
- Mechanism: forms complex with copper and albumin, inhibiting copper uptake
- May have lower risk of early neurological deterioration
- Not widely available

Liver transplantation:

- Indicated for: fulminant hepatic failure, end-stage liver disease
- Corrects the metabolic defect (liver transplant = curative for hepatic disease)
- Improves neurological symptoms (but may not fully reverse)
- Does NOT remove KF rings immediately

Psychiatric drug use in Wilson's:

- Avoid drugs with significant copper-chelating or hepatotoxic effects
- Penicillamine itself has neuropsychiatric effects
- Antipsychotics can be used for psychotic symptoms (atypicals preferred, monitor for EPS given basal ganglia involvement)
- Monitor liver function with any hepatotoxic psychotropic (many antipsychotics, carbamazepine)

SECTION 9: HEPATIC ENCEPHALOPATHY

9.1 Pathophysiology

Hepatic encephalopathy (HE) = neuropsychiatric syndrome complicating liver failure or portosystemic shunting.

Mechanism:

- Ammonia hypothesis (primary): liver failure → failure to detoxify ammonia → hyperammonemia → astrocyte swelling (Alzheimer type II astrocytes), glutamine accumulation → cerebral edema
- Inflammation potentiates ammonia toxicity
- Zinc deficiency (impairs urea cycle enzymes)
- GABA-ergic excess (endogenous benzodiazepine-like substances)
- Manganese deposition (basal ganglia) → Parkinsonism-like features
- Altered amino acid ratios → false neurotransmitter theory (phenylalanine, tyrosine → octopamine, beta-phenylalanine)

9.2 Grading (West Haven Criteria)

GRADE	CONSCIOUSNESS	COGNITIVE/BEHAVIORAL	NEUROLOGICAL
0 (minimal)	Normal	Subtle cognitive deficits on testing	Normal exam

GRADE	CONSCIOUSNESS	COGNITIVE/BEHAVIORAL	NEUROLOGICAL
1	Normal (mildly diminished)	Shortened attention, impaired addition, sleep disturbance, mild anxiety / euphoria	Tremor, poor coordination
2	Lethargic	Disorientation, amnesia, personality change, inappropriate behavior	Asterixis (flapping tremor), ataxia, dysarthria
3	Somnolent but arousable	Marked confusion, bizarre behavior, disorientation	Asterixis, rigidity, hyperreflexia
4	Coma	Unarousable	No asterixis, decerebrate posturing

Asterixis (liver flap) = pathognomonic: involuntary, asynchronous flapping tremor of outstretched hands, seen in Grade 2–3.

Minimal/Covert HE:

- No overt clinical signs
- Detectable on psychometric testing (Psychometric Hepatic Encephalopathy Score, PHES)
- Important: affects QoL, driving ability, work performance
- ~30–40% of cirrhotic patients

9.3 Management

Identify and treat precipitants (most important step):

- Infection/sepsis (SBP, spontaneous bacterial peritonitis: most common precipitant)
- GI bleeding
- Electrolyte disturbances (hyponatremia, hypokalemia)
- Constipation
- Benzodiazepines/sedatives (AVOID)
- Excessive protein intake (controversial, protein restriction now not recommended)
- Dehydration

Pharmacological treatment:

DRUG	MECHANISM	DOSE	NOTES
Lactulose	Acidifies colon → NH ₄ ⁺ trapping, catharsis	15–30 mL TID; titrate to 2–3 soft stools/day	First-line; side effects: bloating, diarrhea

DRUG	MECHANISM	DOSE	NOTES
Rifaximin	Non-absorbable antibiotic → reduces gut ammonia-producing bacteria	550 mg BD	Add-on to lactulose for recurrent HE
Zinc	Cofactor for urea cycle enzymes	220 mg zinc sulfate TID	Adjunct in zinc-deficient patients
L-Ornithine L-Aspartate (LOLA)	Stimulates urea cycle and glutamine synthesis	IV or oral formulations	Adjunct; limited evidence
Neomycin	Reduces gut bacteria	Rarely used	Nephrotoxicity, ototoxicity limit use

Dietary:

- Protein restriction is OUTDATED, maintain adequate protein (1.2–1.5 g/kg/day)
- Branch-chain amino acid (BCAA) supplements: evidence in severe HE/cirrhosis
- Small frequent meals, late evening snack (reduces overnight fasting catabolism)

TIPS (Transjugular Intrahepatic Portosystemic Shunt):

- Can worsen HE (more portosystemic shunting)
- Liver transplantation: definitive treatment for HE in appropriate candidates

SECTION 10: PORPHYRIA & PSYCHIATRY

10.1 Acute Intermittent Porphyria (AIP)

AIP = autosomal dominant disorder of heme biosynthesis.

- Deficiency of porphobilinogen deaminase (PBGD), also called hydroxymethylbilane synthase
- Accumulation of aminolevulinic acid (ALA) and porphobilinogen (PBG) → neurotoxicity
- Prevalence: 1-2 per 100,000; more common in women

Triggers (precipitate attacks):

- Drugs (the most important trigger for psychiatry)
- Alcohol
- Fasting/caloric restriction
- Hormonal changes (menstrual cycle, porphyria is worse premenstrually)
- Infection, stress, surgery

10.2 Psychiatric Manifestations

Psychiatric symptoms can PRECEDE or ACCOMPANY acute attacks:

- Anxiety: very common, can be severe
- Agitation, restlessness
- Depression
- Confusion, delirium
- Psychosis: auditory hallucinations, paranoid ideation, formal thought disorder
- Personality change
- Emotional lability

Classic AIP attack (triad):

1. Severe abdominal pain (colicky, often the presenting symptom)
2. Peripheral neuropathy (weakness, sensory loss, can progress to respiratory failure)
3. Psychiatric manifestations (confusion, psychosis, anxiety)

Other features: autonomic neuropathy (tachycardia, hypertension, sweating), SIADH → hyponatremia (worsens neuropsychiatric symptoms), seizures

Urine color: dark red/brown on standing (porphobilinogen oxidizes), classic exam finding

10.3 Safe and Unsafe Drugs in Porphyria

CRITICAL FOR PSYCHIATRY PRACTICE:

UNSAFE drugs (precipitate attacks), key psychiatric drugs:

DRUG CLASS · EXAMPLES

Anticonvulsants Carbamazepine, phenytoin, phenobarbitone, valproate*

Benzodiazepines Most benzodiazepines (caution)

Antidepressants Amitriptyline, imipramine (TCAs, generally unsafe)

Analgesics Diclofenac, mefenamic acid

Hormones Progesterone-containing OCP, estrogens

Other Rifampicin, sulfonamides, dapsone, alcohol

*Note: valproate's safety is debated, some sources list it as unsafe.

SAFE drugs in porphyria (generally):

DRUG CLASS · SAFE OPTIONS

Analgesics Aspirin, paracetamol, opioids (morphine, fentanyl)

Antiemetics Ondansetron, prochlorperazine (some controversy), cyclizine

Antipsychotics Chlorpromazine (probably safe), haloperidol (safer than most)

Anxiolytics Lorazepam (probably safer than other benzodiazepines)

Antidepressants Sertraline, citalopram (SSRIs generally considered safer)

Antihypertensives Beta-blockers (propranolol), calcium channel blockers

Anticonvulsants Gabapentin, levetiracetam

Treatment of acute attack:

1. Remove precipitant
 2. High carbohydrate intake (glucose 400 g/day, suppresses ALA synthetase, reduces porphyrin production)
 3. Hematin (heme arginate/Normosang): IV hematin suppresses ALA synthetase activity, most effective treatment
 4. Supportive: adequate analgesia, treat seizures (levetiracetam/gabapentin), treat SIADH
 5. Monitor respiratory function (neuropathy can cause respiratory failure)
-

SECTION 11: NUTRITIONAL DEFICIENCIES & PSYCHIATRY

11.1 Vitamin B12 (Cobalamin) Deficiency

Sources: animal products (meat, fish, dairy, eggs); vegans/vegetarians at high risk

Causes: pernicious anemia (anti-intrinsic factor antibodies), gastrectomy, ileal disease, metformin (blocks B12 absorption, important drug interaction), malnutrition, strict veganism

Psychiatric manifestations:

- Depression: may be first symptom
- Cognitive impairment: ranges from mild to dementia (reversible if caught early)
- Psychosis: "megaloblastic madness", rare but classic
- Irritability, personality change
- Mania (rare)

Neurological features (combined subacute combined degeneration of spinal cord):

- Peripheral neuropathy (most common neurological feature)

- Subacute combined degeneration: posterior and lateral column involvement → proprioception loss, ataxia, spastic paraparesis
- Optic neuropathy

Diagnosis: Serum B12 <200 pg/mL (low); methylmalonic acid (MMA) and homocysteine elevated (sensitive markers of functional B12 deficiency even when serum B12 is borderline)

Treatment:

- Pernicious anemia/malabsorption: IM hydroxocobalamin 1000 mcg alternate days x 2 weeks, then every 3 months
- Nutritional deficiency without malabsorption: oral B12 1000–2000 mcg/day (high-dose oral can overcome absorption deficit in some)

Psychiatric symptoms: may take weeks to months to improve even with replacement; irreversible if very prolonged

11.2 Folate Deficiency

Sources: green leafy vegetables, legumes, fortified cereals; destroyed by cooking

Causes: poor diet, malabsorption (celiac disease), alcoholism, pregnancy (increased demand), drugs (methotrexate, phenytoin, sulfasalazine, trimethoprim, folate antagonists)

Psychiatric manifestations:

- Depression: high association, reduced folate → reduced methylation → reduced monoamine synthesis
- Cognitive impairment
- Irritability

Folate and antidepressant response:

- Low folate predicts poor antidepressant response
- L-methylfolate (MTHF) as augmentation strategy in treatment-resistant depression (especially relevant in MTHFR gene variants)
- Folic acid 5–15 mg/day as augmentation

Homocysteine: elevated in both B12 and folate deficiency → independent cardiovascular and neurodegenerative risk

Folate and schizophrenia:

- Some evidence linking folate deficiency and MTHFR variants with schizophrenia susceptibility
- High-dose folate (2 mg/day) may improve negative symptoms in schizophrenia

Treatment: folic acid 5 mg/day (higher doses in malabsorption or drug-induced)

11.3 Niacin (Vitamin B3) Deficiency: Pellagra

Pellagra = niacin (nicotinic acid / nicotinamide) deficiency.

- Sources: meat (tryptophan can be converted to niacin), cereals
- At-risk groups: maize-based diets, alcoholics, carcinoid syndrome (tryptophan diverted to serotonin), Hartnup disease, INH use (blocks tryptophan → niacin)
- Historical context: epidemic in poorest communities of Southern US (early 20th century)

Classic triad (The "3 Ds", and 4th D):

- **Dermatitis**, photosensitive, symmetrical, Casal's necklace (affects sun-exposed areas)
- **Diarrhoea**, watery, bloody
- **Dementia**, cognitive decline
- **(Death)**, if untreated

Psychiatric manifestations:

- Cognitive impairment progressing to dementia
- Anxiety, agitation
- Depression
- Psychosis: hallucinations, paranoid ideation
- Delirium in severe cases
- Headache, fatigue

Mechanism: Niacin is a precursor to NAD⁺ and NADP⁺, essential for neuronal energy metabolism. Deficiency → impaired oxidative phosphorylation → neurodegeneration.

Drug-induced pellagra:

- INH (isoniazid), inhibits pyridoxine (B6), which is cofactor for tryptophan → niacin conversion
- Prevent with pyridoxine supplementation when using INH

Treatment: nicotinamide (nicotinic acid without flushing) 100–300 mg TID; rapid response (days to weeks)

11.4 Thiamine (Vitamin B1) Deficiency: Wernicke-Korsakoff Syndrome

Most important nutritional deficiency in psychiatry.

At-risk groups: chronic alcohol use disorder (primary cause), severe malnutrition, prolonged vomiting (hyperemesis gravidarum), bariatric surgery, refeeding after starvation, malignancy, dialysis

Wernicke's Encephalopathy (WE), ACUTE:

Classic triad:

1. Ophthalmoplegia (sixth nerve palsy, lateral rectus; nystagmus)
2. Ataxia (cerebellar, gait)
3. Confusion/encephalopathy (global confusion)

BUT, only 16% of patients present with full classic triad. Diagnosis often missed.

Pathology: hemorrhagic necrosis in: mammillary bodies (most characteristic), periaqueductal gray, medial thalamus, cerebellar vermis

Diagnosis: Clinical diagnosis; MRI (T2/FLAIR hyperintensities in mammillary bodies and periaqueductal region); thiamine levels often not helpful acutely

Treatment: Parenteral thiamine (Pabrinex) BEFORE any glucose administration

- High-potency thiamine IV: 500 mg TID x 3 days (European guidelines)
- Oral thiamine insufficient for WE treatment
- NEVER give glucose without thiamine in at-risk patients (glucose loads → depletes remaining thiamine → precipitates WE)

Korsakoff Syndrome (KS), CHRONIC AMNESIC STATE:

Develops from untreated or inadequately treated WE

Classic features:

- Severe anterograde amnesia (inability to form new memories)
- Retrograde amnesia (variable)
- **Confabulation** (fabrication of memories, often unconscious, patient is not lying)
- Relatively preserved other cognitive functions (language, attention, perception)
- **Lack of insight** (anosognosia)
- Flat/apathetic affect

Prognosis:

- 25% partial recovery
- 25% significant recovery with prolonged thiamine treatment
- 50% permanent impairment
- Only 10% make complete recovery

Treatment: Continue high-dose thiamine (oral); address alcohol dependence; neuropsychological rehabilitation. NO specific pharmacological treatment. Thiamine maintenance: 100 mg TID orally long-term.

Wernicke-Korsakoff vs. Alcohol-Related Dementia:

FEATURE	WERNICKE-KORSAKOFF	ALCOHOL-RELATED DEMENTIA
Primary deficit	Memory (anterograde >>> other)	Global cognitive decline
Confabulation	Yes	Less prominent
Pathology	Mammillary bodies, thalamus	Cortical atrophy, white matter
Thiamine responsive	Partially (acute phase)	Less responsive

SECTION 12: ELECTROLYTE DISTURBANCES & PSYCHIATRY

12.1 Hyponatremia

Hyponatremia ($\text{Na} < 135 \text{ mEq/L}$), the most common electrolyte disturbance in psychiatric inpatients.

Classification:

- Mild: $130\text{--}135 \text{ mEq/L}$
- Moderate: $125\text{--}130 \text{ mEq/L}$
- Severe: $<125 \text{ mEq/L}$; ACUTE severe: $<125 \text{ mEq/L}$ developing over $<48\text{h}$ (risk of cerebral edema)

Psychiatric manifestations:

SEVERITY · SYMPTOMS

Mild Nausea, headache, cognitive dulling, mood changes

Moderate Confusion, disorientation, agitation, psychosis

Severe Severe confusion, delirium, seizures, coma

SIADH (Syndrome of Inappropriate Antidiuretic Hormone Secretion):

- Urine osmolality $>$ serum osmolality (inappropriately concentrated urine)
- Urine $\text{Na} > 20 \text{ mEq/L}$
- Clinically euvolemic (no edema, no dehydration)
- Diagnosis of exclusion: must rule out hypothyroidism, adrenal insufficiency, renal disease

Psychotropic-induced hyponatremia (SIADH):

This is a high-yield exam topic.

DRUG · RISK

SSRIs High, most common psychotropic cause; fluoxetine, paroxetine, sertraline

SNRIs Moderate, venlafaxine, duloxetine

TCAs Moderate

Carbamazepine High, classic cause; stimulates ADH secretion

Oxcarbazepine High, even more frequent than carbamazepine

Antipsychotics Low-moderate (polydipsia also contributes)

Mechanism: SSRIs → enhance serotonin-mediated ADH release; carbamazepine → direct ADH-potentiating effect

Risk factors:

- Age >65 years (most significant)
- Female sex
- Low body weight
- Concurrent diuretic use
- History of hyponatremia
- Hot weather, increased fluid intake

Management of SIADH/psychotropic-induced hyponatremia:

1. Mild: fluid restriction (500–1000 mL/day); monitor closely
2. Moderate: fluid restriction; consider stopping/switching offending drug
3. Severe/symptomatic: 3% hypertonic saline (correct at max 8–10 mEq/L in 24h to avoid ODS)
4. Tolvaptan (V2 receptor antagonist): selectively excretes free water, for resistant SIADH

Osmotic Demyelination Syndrome (ODS), Central Pontine Myelinolysis:

- Complication of OVERLY RAPID correction of hyponatremia
- Irreversible demyelination of pons (and extrapontine areas)
- Presents: locked-in syndrome, spastic quadriplegia, pseudobulbar palsy, cognitive impairment
- Prevention: correct Na at maximum 8–10 mEq/L per 24 hours; maximum 18 mEq/L in 48 hours
- High-risk: alcoholics, malnourished, hypokalemic, liver disease

Polydipsia in schizophrenia:

- Up to 25% of schizophrenia inpatients have polydipsia
- Psychogenic polydipsia (primary polydipsia): compulsive drinking, not thirst-driven
- Results in hyponatremia (dilutional)

- Can cause severe hyponatremia and seizures ("water intoxication")
 - Management: fluid restriction, clozapine may reduce polydipsia (dopamine effect on thirst centers)
-

12.2 Hypercalcemia

Psychiatric manifestations (see hyperparathyroidism section, Section 6.1)

"Bones, stones, groans, psychic moans"

Additional electrolyte context:

- Hypercalcemia slows nerve conduction, depresses CNS
 - Lithium-induced hypercalcemia: as noted (Section 1.4)
-

12.3 Hypomagnesemia

Magnesium deficiency, common, often undiagnosed.

Causes in psychiatric patients: chronic alcohol use (renal magnesium wasting), malnutrition, diarrhea, PPIs (chronic use), diuretics, cisplatin

Psychiatric manifestations:

- Anxiety, agitation, irritability
- Depression
- Cognitive impairment
- Confusion
- Psychosis (rare, in severe deficiency)

Neurological features: tremor, muscle weakness, tetany (similar to hypocalcemia, Mg required for PTH secretion), hyperreflexia, seizures

Magnesium and mood disorders:

- Low magnesium associated with depression
- Some RCT evidence for magnesium supplementation in mild depression
- Magnesium sulfate used in eclampsia (CNS protective, anticonvulsant)

Relevance for antipsychotics:

- Clozapine can prolong QTc → worsened by hypomagnesemia → arrhythmia risk
 - Correct hypomagnesemia before starting or escalating clozapine
-

SECTION 13: METABOLIC SYNDROME IN PSYCHIATRIC POPULATIONS: MANAGEMENT PROTOCOLS

13.1 Integrated Monitoring and Management

Step 1, Screen at baseline (all patients starting antipsychotics):

- Weight/BMI
- Waist circumference
- Blood pressure
- Fasting glucose
- Fasting lipid profile
- Family history of metabolic disease

Step 2, Monitor per ADA/APA schedule (see Section 4.4 table)

Step 3, Intervene at thresholds:

Step 4, Non-pharmacological interventions:

- Structured physical activity (150 min/week moderate intensity)
- Caloric restriction (500 kcal/day deficit)
- Smoking cessation (nicotine replacement/varenicline)
- Dietary counseling (Mediterranean diet pattern)

Step 5, Pharmacological augmentation:

- Metformin: 500 mg BD → 1000 mg BD (first-line for antipsychotic-induced weight gain and hyperglycemia)
- Statins: for dyslipidemia (pravastatin, simvastatin)
- Aripiprazole co-prescription (if not on it): reduces weight when added to olanzapine/clozapine
- GLP-1 agonists: emerging use (semaglutide, liraglutide)

SECTION 14: INTEGRATED CLINICAL APPROACH: PSYCHIATRIC HISTORY IN ENDOCRINE CONTEXT

14.1 "When to think endocrine" in psychiatry

Red flags for underlying endocrine/metabolic cause in psychiatric presentations:

SUMMARY BOX: HIGH-YIELD FACTS FOR EXAM

KEY INSIGHT

Box 1: Lithium and thyroid - 20-42% hypothyroidism; 6-monthly TFTs for first year, then annual - Continue lithium + add T4; do NOT stop lithium - Risk higher in women, positive TPO antibodies, older age

KEY INSIGHT

Box 2: Wilson's disease diagnostic triad - Psychiatric (personality/psychosis) + Neurological (dysarthria, tremor) + Hepatic - KF rings on slit lamp; ceruloplasmin low; urine copper high - Treat: penicillamine / trientine (chelation) + zinc (maintenance)

KEY INSIGHT

Box 3: Antipsychotic metabolic monitoring (ADA/APA) - Baseline → 4wk → 8wk → 12wk → annual - Weight every appointment; glucose and lipids at 12 weeks then annually - Clozapine and olanzapine = highest metabolic risk

KEY INSIGHT

Box 4: Wernicke-Korsakoff - Thiamine before glucose, ALWAYS - Full triad (ophthalmoplegia + ataxia + confusion) only 16% - Korsakoff = confabulation + anterograde amnesia + lack of insight

KEY INSIGHT

Box 5: SIADH and psychotropics - Carbamazepine and oxcarbazepine: highest risk - SSRIs: most common drug class causing it - Correct hyponatremia slowly (max 8-10 mEq/L per 24h), ODS risk

KEY INSIGHT

Box 6: Safe drugs in porphyria - Safe: SSRIs (sertraline, citalopram), paracetamol, opioids, propranolol, haloperidol - Unsafe: carbamazepine, TCAs, most anticonvulsants - Treatment: hematin (heme arginate) + high carbohydrate

Model Answers

EXAM STRATEGY

Each answer follows the PG exams long-answer structure: definition/overview → pathophysiology → clinical features → diagnosis → management. Marks are allocated per subcomponent. Write in clear paragraphs; use numbered lists for management steps. Avoid prose walls, examiners reward structure.

Answer 1: Psychiatric Manifestations of Hypothyroidism and the Role of Thyroid Function Tests in Psychiatric Practice

[15 marks]

Introduction

Hypothyroidism is a deficiency of thyroid hormone (T4/T3) resulting from primary thyroid gland failure, pituitary disease, or hypothalamic dysfunction. Given that thyroid hormones modulate monoamine neurotransmission, particularly serotonergic and noradrenergic systems, hypothyroidism produces a wide range of psychiatric manifestations.

Psychiatric Manifestations

1. Depression (most common, 40–60%)

Hypothyroidism-associated depression closely mimics major depressive disorder. Key features include low mood, marked anhedonia, psychomotor retardation, fatigue, weight gain, and cognitive slowing. The mechanism involves reduced serotonin receptor density and diminished central noradrenergic tone. A critical clinical point is that depression in hypothyroidism often fails to respond to antidepressants without concurrent thyroid replacement. Subclinical hypothyroidism (elevated TSH with normal free T4) also increases depression prevalence, particularly in women.

2. Cognitive Impairment

Thyroid hormone deficiency impairs hippocampal neurogenesis and reduces cerebral glucose metabolism. Clinically, patients present with poor concentration, slowed processing speed, forgetfulness, and verbal memory deficits. In elderly patients, this can progress to a dementia-like syndrome that is reversible with treatment, making TSH screening mandatory in new-onset cognitive complaints.

3. Myxedema Madness

First described by Asher (1949), this refers to the acute psychiatric manifestation of severe, prolonged hypothyroidism. Presentation includes paranoid psychosis, auditory and visual hallucinations, delirium, and occasionally mania. It occurs in the context of severe systemic myxedema (periorbital puffiness, macroglossia, non-pitting oedema, hypothermia, bradycardia). TSH is markedly elevated; free T4 is very low. Treatment requires urgent IV levothyroxine and brief antipsychotic cover if needed.

4. Anxiety and Mood Lability

Anxiety and irritability are common, particularly in subclinical hypothyroidism.

5. Congenital Hypothyroidism (Cretinism)

Untreated congenital hypothyroidism causes irreversible intellectual disability, emphasising the importance of neonatal screening.

Thyroid Function Tests in Psychiatric Practice

TSH is the single most useful screening test. Clinicians should screen TFTs in the following situations:

- New-onset depression, treatment-resistant depression, new-onset anxiety
- New-onset mania or psychosis
- Cognitive impairment, especially in the elderly
- Before initiating lithium (baseline) and every 6 months for the first year, then annually
- Postpartum psychiatric illness (postpartum thyroiditis in 5–10%)
- Patients with eating disorders (sick euthyroid syndrome common)

Interpretation:

- Elevated TSH + low free T4 = overt hypothyroidism → thyroid replacement
- Elevated TSH + normal free T4 = subclinical hypothyroidism → treat if TSH >10, symptomatic, or pregnant
- Both TFTs normal = primary psychiatric disorder; however, serial monitoring warranted on lithium

Management of Hypothyroidism-Associated Psychiatric Illness

1. Initiate levothyroxine (T4) replacement; goal TSH within normal range
2. If depression persists after euthyroid state restored, add antidepressant (SSRI first-line)
3. T3 augmentation (liothyronine 25–50 mcg/day) for treatment-resistant depression even in euthyroid patients, STAR*D evidence
4. Myxedema madness: IV T4 (levothyroxine), antipsychotics briefly, ICU-level supportive care

EXAM PEARL

Lithium-induced hypothyroidism occurs in 20–42% of long-term users. Continue lithium and add levothyroxine, do not stop lithium. Screen TFTs at 6-month intervals for the first year.

Answer 2: Wilson's Disease: Psychiatric Presentation, Diagnosis, and Treatment

[15 marks]

Definition

Wilson's disease is an autosomal recessive disorder of copper metabolism caused by mutations in the ATP7B gene (chromosome 13q14), which encodes a copper-transporting ATPase. Failure of biliary copper excretion leads to progressive copper deposition in the liver, brain (especially basal ganglia and cerebellum), cornea, kidneys, and other organs. Onset is typically between 5 and 35 years of age.

Psychiatric Presentation

Psychiatric symptoms are the presenting feature in 20–30% of Wilson's disease cases, and this is why the condition is critical knowledge for psychiatrists.

Personality change is often the earliest psychiatric manifestation. Patients display disinhibition, impulsivity, emotional lability, and loss of social inhibitions, frequently misinterpreted as conduct disorder in adolescents.

Psychosis may resemble first-episode schizophrenia with paranoid delusions, auditory hallucinations, and thought disorder. The key clinical clue is the combination of psychiatric symptoms with neurological features (dysarthria, tremor, dystonia) and/or liver disease in a young patient.

Affective symptoms include depression, anxiety, and rarely mania. Emotional incontinence (pathological laughing and crying) may occur.

Cognitive impairment is characterised by executive dysfunction, memory impairment, and processing speed reduction, reflecting frontostriatal circuit involvement.

Neurological Features (concurrent pointers to diagnosis)

- Dysarthria (often the earliest neurological sign)
- Wing-beating or resting tremor
- Dystonia, choreoathetosis
- Parkinsonism
- Cerebellar ataxia
- Seizures (10–15%)

Diagnosis

Kayser-Fleischer (KF) rings: Golden-brown copper deposits in Descemet's membrane of the cornea, seen on slit-lamp examination. Present in >95% of neuropsychiatric Wilson's. Their absence does not exclude the diagnosis in hepatic presentations.

INVESTIGATION · FINDING

Serum ceruloplasmin Low (<0.2 g/L) in 95% of cases

24-hour urine copper Elevated (>100 mcg/24h symptomatic; >40 mcg asymptomatic)

Serum copper Low total (but elevated free/unbound copper)

Liver biopsy Copper >250 mcg/g dry weight; cirrhosis

Brain MRI "Face of giant panda" sign (midbrain); T2 hyperintensities in basal ganglia, thalamus

ATP7B genetic testing Confirmatory

The **Leipzig scoring system** integrates KF rings, ceruloplasmin, haemolytic anaemia, urine copper, liver copper, and genetic mutation to give a diagnostic score (score ≥ 4 = Wilson's).

Treatment

D-Penicillamine (first-line chelator):

- Mechanism: chelates copper → increased urinary copper excretion
- Dose: 750–1500 mg/day in divided doses
- Side effects: rash, fever, nephrotoxicity, bone marrow suppression, lupus-like syndrome
- Supplement with pyridoxine (B6)
- Critical warning: paradoxical neurological worsening in first weeks (copper mobilised from liver to brain), switch to trientine if this occurs

Trientine:

- Alternative chelator; better neurological tolerability
- Preferred for neuropsychiatric presentations and penicillamine intolerance
- Dose: 750–1500 mg/day in divided doses

Zinc acetate:

- Mechanism: induces intestinal metallothionein → blocks copper absorption
- Used for maintenance after initial chelation; presymptomatic patients; pregnancy (safest profile)
- Cannot be co-administered with chelators (mutual interference)
- Dose: 50 mg elemental zinc three times daily

Liver transplantation:

- Indicated for fulminant hepatic failure or end-stage liver disease
- Corrects the metabolic defect; improves neurological symptoms partially

Psychiatric drug use in Wilson's:

- Antipsychotics usable for psychosis; atypical antipsychotics preferred (monitor for EPS given basal ganglia involvement)
- Avoid hepatotoxic agents; monitor LFTs
- Penicillamine itself may worsen neuropsychiatric symptoms, consider trientine

CLINICAL ANCHOR

Any young patient (under 40) presenting with psychosis, personality change, or movement disorder, screen for Wilson's disease with slit-lamp for KF rings, serum ceruloplasmin, and 24-hour urine copper. Missing this diagnosis is a preventable tragedy.

Answer 3: Metabolic Syndrome and Antipsychotics: Monitoring and Management

[15 marks]

Definition of Metabolic Syndrome

Metabolic syndrome is a cluster of cardiometabolic risk factors that substantially increase cardiovascular disease and type 2 diabetes risk. By IDF 2006 criteria, diagnosis requires central obesity (waist ≥ 90 cm men / ≥ 80 cm women in South Asians) plus any two of: fasting glucose ≥ 5.6 mmol/L, triglycerides ≥ 1.7 mmol/L, HDL below sex-specific thresholds, or blood pressure $\geq 130/85$ mmHg.

Antipsychotics and Metabolic Risk

Antipsychotic medications are the primary driver of metabolic syndrome in psychiatric populations, with prevalence of 40–60% in schizophrenia (versus ~25% in the general population).

Mechanisms:

- H1 histamine antagonism → primary driver of weight gain (sedation, orexigenic signalling)
- 5-HT_{2C} serotonin antagonism → increased appetite, impaired satiety
- M3 muscarinic antagonism → direct impairment of pancreatic insulin secretion (diabetogenic)
- D2 dopamine antagonism → mesolimbic appetite dysregulation
- Alpha-1 adrenergic blockade → sedation → reduced physical activity

Weight gain hierarchy (approximate mean weight gain in clinical trials):

ANTIPSYCHOTIC	WEIGHT GAIN	DIABETOGENIC RISK
Clozapine	+4.5 kg	Very high
Olanzapine	+4.2 kg	Very high
Quetiapine	+2.3 kg	Moderate
Risperidone	+2.1 kg	Moderate
Haloperidol	+0.5 kg	Low
Aripiprazole	+0.7 kg	Low
Ziprasidone	+0.04 kg	Low
Amisulpride	Low	Low

ADA/APA Monitoring Guidelines (2004 Consensus)

WIDE COMPARISON · LANDSCAPE

PARAMETER	BASELINE	4 WK	8 WK	12 WK	ANNUALLY	5-YEARLY
Weight/BMI	Yes	Yes	Yes	Yes	Yes	
Waist circumference	Yes				Yes	
Blood pressure	Yes			Yes		Yes
Fasting glucose	Yes			Yes		Yes
Fasting lipids	Yes			Yes		Yes
Personal/family history	Yes				Yes	

Action thresholds:

- BMI increase >1 unit in any month → consider switching
- Fasting glucose 100–125 mg/dL → lifestyle counselling, refer
- Fasting glucose >126 mg/dL on two occasions → diabetes; refer, consider switch
- Triglycerides >200 mg/dL → refer
- LDL >130 mg/dL in high-risk patient → pharmacotherapy

Management of Antipsychotic-Induced Metabolic Syndrome

Non-pharmacological interventions:

- Structured aerobic exercise (150 min/week moderate intensity), evidence supports 2–3 kg weight reduction
- Caloric restriction (500 kcal/day deficit); Mediterranean dietary pattern
- Smoking cessation (nicotine replacement, varenicline)
- Dietitian referral

Pharmacological interventions:

1. **Metformin**, first-line pharmacotherapy for antipsychotic-induced weight gain and hyperglycaemia. Dose 500 mg BD titrated to 1000 mg BD. RCT evidence supports 2–3 kg weight reduction, improved insulin sensitivity.
1. **Switching antipsychotic**, to metabolically safer agents (aripiprazole, ziprasidone, amisulpride, lurasidone). Cross-titration method preferred. Note: switching from clozapine carries high relapse risk; weigh carefully.
1. **Aripiprazole co-prescription**, adding aripiprazole to olanzapine or clozapine reduces weight (D2 partial agonism modulates metabolic effects). Dose 5–15 mg/day.
1. **Statins**, for dyslipidaemia (pravastatin, simvastatin; monitor interactions with CYP3A4 metabolised antipsychotics).
1. **GLP-1 receptor agonists**, semaglutide, liraglutide showing substantial weight reduction in emerging evidence; increasingly used clinically though not yet standard in most guidelines.

EXAM PEARL

Monitoring for metabolic syndrome must begin at antipsychotic initiation, not after weight gain occurs. Weight and BMI should be checked at every clinic visit in the first 12 weeks. Prevention is substantially easier than reversal.

Answer 4: Cushing's Syndrome: Psychiatric Manifestations and Management

[10 marks]

Overview

Cushing's syndrome results from sustained excess glucocorticoid exposure. Endogenous causes include pituitary ACTH-secreting adenoma (Cushing's disease, 70%), adrenal tumours (15%), and ectopic ACTH secretion (10–15%). Exogenous glucocorticoids (iatrogenic Cushing's) are the most common overall cause in clinical practice.

Psychiatric Manifestations

Psychiatric symptoms occur in 50–80% of patients with Cushing's syndrome, making it one of the most psychiatrically significant endocrine disorders.

Depression (50–80%) is the most prevalent manifestation. Features include prominent anhedonia, psychomotor retardation, cognitive impairment, and significant suicidality risk (4–10% attempt suicide). MRI commonly shows hippocampal volume reduction, reflecting cortisol-mediated neurogenesis suppression.

Anxiety (20–70%) ranges from generalised anxiety to panic attacks, often co-occurring with depression.

Cognitive impairment reflects hippocampal vulnerability to hypercortisolaemia, verbal learning, memory consolidation, and attention are most affected.

Psychosis (5–15%) presents with paranoid delusions and hallucinations. Mania may also occur, particularly with exogenous steroids.

Personality change, emotional lability, irritability, interpersonal difficulties, commonly precedes formal psychiatric diagnosis.

Steroid-Induced Psychiatric Disorders

Iatrogenic Cushing's from exogenous steroids produces dose-dependent psychiatric effects:

PREDNISONE EQUIVALENT · PSYCHIATRIC RISK

<40 mg/day Low (1.3%)

40–80 mg/day Moderate (4.6%)

>80 mg/day High (18.4%)

Classic presentations: early euphoria progressing to depression; "steroid mania" (elevated mood, decreased sleep, grandiosity), occurs early in course; psychosis at higher doses.

Management of steroid-induced psychiatric disorders:

1. Reduce steroid dose if medically permissible (primary intervention)

2. Antipsychotics for mania/psychosis (haloperidol, olanzapine)
3. Mood stabilisers if steroids cannot be tapered (lithium, has prophylactic role for repeat steroid courses)
4. Antidepressants for depressive episodes persisting after dose reduction
5. Monitor resolution, most symptoms remit with dose reduction or steroid cessation

For endogenous Cushing's:

- Treat the primary cause (transsphenoidal surgery for Cushing's disease; adrenalectomy; treat ectopic source)
- Psychiatric symptoms often improve substantially after surgical cure, but may persist, treat pharmacologically as above
- Pre-operatively: symptom management is supportive

EXAM STRATEGY

Distinguish Cushing's disease (pituitary, ACTH-dependent) from Cushing's syndrome (any cause, ACTH-dependent or ACTH-independent). Diagnosis: late-night salivary cortisol, 24-hour urine free cortisol, low-dose DST for screening; then high-dose DST and CRH test for localisation.

Answer 5: Wernicke-Korsakoff Syndrome: Pathogenesis, Features, and Management

[15 marks]

Definition

Wernicke-Korsakoff syndrome (WKS) is a two-stage neuropsychiatric disorder caused by thiamine (vitamin B1) deficiency. Wernicke's encephalopathy (WE) is the acute phase; Korsakoff syndrome (KS) is the chronic amnesic sequel. While classically associated with chronic alcohol use disorder, WKS occurs in any condition causing thiamine depletion.

Pathogenesis

Thiamine is an essential cofactor for three key enzymes in glucose and energy metabolism: pyruvate dehydrogenase, alpha-ketoglutarate dehydrogenase, and transketolase.

Deficiency impairs cerebral energy metabolism, leading to selective neuronal injury in metabolically vulnerable regions with high oxidative demand. The mammillary bodies, periaqueductal grey matter, medial thalamus, and cerebellar vermis are most severely affected, explaining the cardinal features.

Precipitants include: chronic alcohol use (most common), severe malnutrition, prolonged vomiting (hyperemesis gravidarum), bariatric surgery, refeeding syndrome, malignancy, dialysis.

Wernicke's Encephalopathy: Acute Phase

Classic triad (present together in only 16% of cases):

1. Ophthalmoplegia, sixth nerve (lateral rectus) palsy causing lateral gaze paralysis; nystagmus is common
2. Cerebellar ataxia, broad-based, unsteady gait
3. Confusion/encephalopathy, global confusion, disorientation, diminished consciousness

Because the full triad is uncommon, WE is frequently under-diagnosed. Any two features in a nutritionally at-risk patient warrant urgent thiamine treatment.

Pathological findings: haemorrhagic necrosis of mammillary bodies (most characteristic), thalamic nuclei, periaqueductal grey, and cerebellar vermis.

Diagnosis: Primarily clinical. Brain MRI (T2/FLAIR) shows hyperintensities in mammillary bodies and periaqueductal region. Thiamine blood levels are unreliable acutely.

Korsakoff Syndrome: Chronic Amnesic Phase

Korsakoff syndrome develops from untreated or inadequately treated WE, with structural damage to the mammillary bodies and mediodorsal thalamus becoming permanent.

Clinical features:

- Severe anterograde amnesia (inability to form new memories), the cardinal feature
- Variable retrograde amnesia (typically a temporal gradient, recent memories more affected)
- **Confabulation**, the hallmark: unconscious fabrication of plausible but false memories to fill memory gaps. The patient is not lying; they genuinely believe what they say.
- Relatively preserved immediate recall, language, and procedural memory
- Lack of insight (anosognosia) into memory impairment
- Flat, apathetic affect
- Temporal disorientation (may not know the year)

Prognosis:

- 25% significant recovery with sustained thiamine replacement
- 25% partial recovery
- 50% permanent moderate-to-severe disability
- Only ~10% full recovery

Management

Immediate:

- **Thiamine BEFORE any glucose administration**, this is the most critical rule. Glucose loading depletes residual thiamine and can precipitate WE in at-risk patients.
- Parenteral thiamine (Pabrinex): 500 mg IV three times daily for minimum 3 days (European Federation of Neurological Societies recommendation)
- Oral thiamine is insufficient for WE, absorption is impaired in malnourished / alcoholic patients
- Maintain electrolyte balance; correct hypomagnesaemia (magnesium is cofactor for thiamine-dependent enzymes)

Ongoing:

- Continue oral thiamine 100 mg TID long-term for Korsakoff syndrome
- Address alcohol dependence with comprehensive addiction treatment
- Neuropsychological rehabilitation (external memory aids, environmental modification)
- No specific pharmacotherapy reverses established Korsakoff syndrome

Prevention:

- Thiamine supplementation in all at-risk patients (alcohol use disorder, malnutrition, post-bariatric)
- Never administer IV glucose in acute presentations without thiamine cover

EXAM PEARL

The rule "thiamine before glucose" is a non-negotiable clinical imperative. In any patient with alcohol use disorder presenting acutely, administer thiamine 100 mg IV before any glucose-containing IV fluid. This prevents an irreversible neurological catastrophe.

Answer 6: SIADH and Psychotropic-Induced Hyponatraemia

[10 marks]

Syndrome of Inappropriate Antidiuretic Hormone (SIADH)

SIADH is characterised by euvoelaemic hyponatraemia resulting from inappropriately elevated ADH secretion relative to serum osmolality. Diagnostic criteria include: serum sodium <135 mEq/L, serum osmolality <280 mOsm/kg, urine osmolality $>$ serum osmolality (inappropriately concentrated), urine sodium >20 mEq/L, clinical euvoelaemia, and absence of other causes (hypothyroidism, adrenal insufficiency, renal disease).

Psychotropic Drugs Causing SIADH

DRUG CLASS	EXAMPLES	MECHANISM
SSRIs	Fluoxetine, paroxetine, sertraline	Enhanced serotonin-mediated ADH release from hypothalamus
SNRIs	Venlafaxine, duloxetine	Similar to SSRIs
TCAs	Amitriptyline, clomipramine	ADH potentiation
Carbamazepine		Direct ADH-potentiating effect; classic cause
Oxcarbazepine		Higher frequency than carbamazepine
Antipsychotics	Various	Less common; polydipsia also contributes

Risk factors: age >65 years (most significant), female sex, low body weight, concurrent diuretics, hot weather, high fluid intake, prior hyponatraemia.

Psychiatric Manifestations of Hyponatraemia

SODIUM LEVEL · MANIFESTATIONS

Mild (130–135) Nausea, headache, cognitive dulling, mood changes

Moderate (125–130) Confusion, disorientation, agitation, psychosis

Severe (<125) Delirium, seizures, coma; risk of cerebral oedema

Management

1. **Mild asymptomatic:** fluid restriction (500–1000 mL / day); identify and consider stopping offending drug; close monitoring
2. **Moderate:** fluid restriction; consider drug switch (e.g., switch SSRI to mirtazapine which has lower SIADH risk; switch carbamazepine to lamotrigine)
3. **Severe/symptomatic:** 3% hypertonic saline IV, correct at **maximum 8–10 mEq/L in 24 hours** (maximum 18 mEq/L in 48 hours)
4. **Tolvaptan** (V2 receptor antagonist): selectively excretes free water; for resistant / recurrent SIADH

Osmotic Demyelination Syndrome (ODS):

The major complication of overly rapid correction. Irreversible demyelination of pons (central pontine myelinolysis) presents as locked-in syndrome, spastic quadriplegia,

pseudobulbar palsy. Prevention: never correct faster than 8–10 mEq/L per day. High-risk groups: alcoholics, malnourished, hypokalemia, liver disease.

EXAM PEARL

Oxcarbazepine causes SIADH more frequently than carbamazepine. This is a common MCQ trap. When switching from carbamazepine to oxcarbazepine for any reason, monitor sodium closely, especially in elderly patients.

Answer 7: Hepatic Encephalopathy: Grading, Pathophysiology, and Management

[10 marks]

Definition

Hepatic encephalopathy (HE) is a neuropsychiatric syndrome complicating liver failure or portosystemic shunting, characterised by a spectrum of cognitive, behavioural, and neuromuscular disturbances reversible with treatment of the underlying liver disease.

Pathophysiology

The ammonia hypothesis remains central. In liver failure, portal blood (rich in ammonia from gut bacteria proteolysis of amino acids) bypasses hepatic detoxification and enters the systemic circulation. Hyperammonaemia causes astrocyte swelling (Alzheimer type II astrocytes), increased glutamine synthesis, and cerebral oedema. Concurrent systemic inflammation amplifies ammonia toxicity. Additional mechanisms include: elevated endogenous benzodiazepine-like substances (increased GABAergic tone), manganese deposition (basal ganglia → Parkinsonism-like features), and altered plasma amino acid ratios favouring aromatic amino acids (false neurotransmitter theory).

West Haven Grading

GRADE	CONSCIOUSNESS	COGNITIVE/PSYCHIATRIC	MOTOR SIGNS
0 (minimal)	Normal	Subtle deficits on psychometry only	Normal
1	Normal-mildly impaired	Poor attention, sleep disturbance, mild anxiety	Tremor, poor coordination
2	Lethargic	Disorientation, amnesia, inappropriate behaviour, personality change	Asterixis, ataxia, dysarthria

GRADE	CONSCIOUSNESS	COGNITIVE/PSYCHIATRIC	MOTOR SIGNS
3	Somnolent, arousable	Marked confusion, bizarre behaviour, disorientation	Asterixis, rigidity, hyperreflexia
4	Coma	Unarousable	Decerebrate posturing; no asterixis

Asterixis (liver flap) = brief, arrhythmic lapses in sustained posture of outstretched hands. Pathognomonic of Grade 2–3 HE.

Management

Step 1: Identify and treat precipitating factors (most important)

- Infection/sepsis, especially spontaneous bacterial peritonitis (most common precipitant)
- GI bleeding, increases gut nitrogen load
- Electrolyte disturbances (hyponatraemia, hypokalaemia)
- Constipation
- Benzodiazepines or sedatives (should be avoided)
- Dehydration, overdiuresis

Step 2: Pharmacological treatment

DRUG	MECHANISM	DOSING
Lactulose (first-line)	Acidifies colon → NH ₄ ⁺ trapping; catharsis	15–30 mL TID; titrate to 2–3 soft stools/day
Rifaximin	Non-absorbable antibiotic; reduces ammonia-producing gut bacteria	550 mg twice daily; add-on to lactulose
Zinc	Cofactor for urea cycle enzymes	220 mg zinc sulfate TID in deficient patients
L-Ornithine L-Aspartate	Stimulates urea cycle and glutamine synthesis	IV or oral; adjunct role

Step 3: Nutritional management

- Protein restriction is outdated, maintain 1.2–1.5 g/kg/day protein
- Small frequent meals; late-evening snack (reduces overnight catabolism)
- Branched-chain amino acid supplements in severe/refractory HE

Step 4: Definitive treatment

- Liver transplantation for appropriate candidates, resolves HE

EXAM PEARL

Spontaneous bacterial peritonitis (SBP) is the most common precipitant of acute HE in cirrhotic patients. Always check for signs of infection and perform ascitic fluid tap (neutrophil count $>250/\text{mm}^3$ = SBP) before attributing deterioration to HE alone.

Answer 8: Acute Intermittent Porphyria: Psychiatric Features and Drug Safety

[10 marks]

Overview

Acute intermittent porphyria (AIP) is an autosomal dominant disorder caused by deficiency of porphobilinogen deaminase (PBGD), the third enzyme in the haem biosynthesis pathway. This results in accumulation of the neurotoxic precursors aminolevulinic acid (ALA) and porphobilinogen (PBG). AIP is the most common and most clinically significant acute porphyria. Prevalence is 1–2 per 100,000; predominantly affects premenstrual women.

Psychiatric Manifestations

Psychiatric features may precede, accompany, or dominate the acute attack:

- **Anxiety and agitation** (most common), severe, acute onset
- **Depression**, during and between attacks
- **Psychosis**, auditory hallucinations, paranoid ideation, formal thought disorder; can closely mimic schizophrenia
- **Delirium/encephalopathy**, in severe attacks
- **Personality change**, between attacks

Classic acute attack triad:

1. Severe colicky abdominal pain (presenting symptom in most)
2. Peripheral neuropathy (motor > sensory; can progress to respiratory paralysis)
3. Psychiatric manifestations (confusion, anxiety, psychosis)

Additional features: autonomic neuropathy (tachycardia, hypertension), SIADH causing hyponatraemia, seizures, dark red-brown urine (porphobilinogen oxidation).

Drug Safety in AIP

This is a high-priority practical topic for psychiatry:

Unsafe (precipitate attacks):

- Most anticonvulsants: carbamazepine, phenytoin, phenobarbitone (valproate, controversial/ generally listed as unsafe)
- Most benzodiazepines (use with caution)
- TCAs (amitriptyline, imipramine)
- Progesterone-containing contraceptives, oestrogens
- Rifampicin, sulfonamides
- Alcohol (major trigger)

Safe options for psychiatric conditions:

- SSRIs: sertraline, citalopram, generally considered safe
- Antipsychotics: haloperidol (generally safe); chlorpromazine (probably safe)
- Anxiolytics: lorazepam (safer than most benzodiazepines)
- Anticonvulsants: gabapentin, levetiracetam
- Analgesics: paracetamol, opioids (morphine, fentanyl)

Management of Acute Attack

1. Identify and eliminate precipitant (especially causative drugs)
2. High-carbohydrate intake (glucose 400 g/day IV or orally), suppresses delta-aminolevulinic acid (ALA) synthase
3. **Haem arginate (Normosang) IV**, most effective; directly suppresses ALA synthase; administer early
4. Adequate analgesia (opioids are safe)
5. Treat seizures with levetiracetam or gabapentin (NOT phenytoin/ carbamazepine)
6. Manage SIADH/ hyponatraemia
7. Monitor respiratory function (motor neuropathy can cause respiratory failure)
8. ICU care in severe attacks

CLINICAL ANCHOR

Suspect porphyria when a young patient presents with the triad of acute abdominal pain + peripheral neuropathy + psychiatric symptoms. Send urine porphyrins urgently, urine darkens on standing. Stop all potentially unsafe drugs immediately.

Answer 9: Pellagra: Niacin Deficiency and Psychiatric Manifestations

[5 marks]

Overview

Pellagra is a nutritional deficiency syndrome caused by inadequate niacin (vitamin B3) or its precursor tryptophan. It remains endemic in populations dependent on maize-based diets (maize has low bioavailable niacin) and is seen in alcoholics, patients with carcinoid syndrome (tryptophan diverted to serotonin production), Hartnup disease (tryptophan malabsorption), and patients on isoniazid (INH, which blocks pyridoxine, a cofactor for tryptophan-to-niacin conversion).

Psychiatric Manifestations

The classic presentation is the "4 Ds":

1. **Dermatitis**, photosensitive, symmetrical; Casal's necklace (collar-like distribution around neck)
2. **Diarrhoea**, watery, mucous, can be bloody
3. **Dementia**, cognitive decline, confusion, memory impairment
4. **Death**, if untreated

Psychiatric features include: early anxiety and irritability, depression, cognitive impairment progressing to dementia-like syndrome, psychosis (hallucinations, paranoid ideation), and delirium in severe cases. Mechanism: niacin is the precursor to NAD⁺ and NADP⁺, essential for neuronal energy metabolism; deficiency causes widespread neuronal degeneration.

Treatment

Nicotinamide 100–300 mg three times daily, rapid response (days to weeks). Dietary correction; treat underlying cause; pyridoxine supplementation if INH-related.

EXAM PEARL

INH-induced pellagra is prevented by co-prescribing pyridoxine (vitamin B6) with isoniazid. This is standard practice in TB treatment protocols in India.

Answer 10: Pheochromocytoma: Panic Disorder Mimicry

[5 marks]

Overview

Pheochromocytoma is a catecholamine-secreting tumour of the adrenal medulla (90%) or extra-adrenal paraganglia (10%). It secretes epinephrine, norepinephrine, and sometimes dopamine in varying ratios.

Psychiatric Mimicry

The paroxysmal catecholamine release produces episodes that are clinically indistinguishable from panic attacks:

- Sudden intense anxiety, palpitations, tremor, diaphoresis
- Headache (throbbing), pallor
- Duration: minutes to hours

Distinguishing features from true panic disorder:

- Hypertension during episodes is severe (systolic >180–200 mmHg), mild or absent in panic disorder
- Pallor (not flushing) during attacks
- Triggers: physical (posture change, exercise, tumour palpation) rather than psychosocial
- Absence of cognitive/cognitive avoidance pattern of panic disorder
- Failed treatment with standard anxiolytics/antidepressants

Diagnostic Approach

- 24-hour urine metanephrines and catecholamines (primary screening)
- Plasma free metanephrines (sensitivity ~97%)
- CT/MRI abdomen after biochemical confirmation
- MIBG scintigraphy for extra-adrenal disease

Treatment: alpha-blockade (phenoxybenzamine) before beta-blockade (important sequence), then surgical resection.

EXAM PEARL

Never start a beta-blocker for hypertension in suspected phaeochromocytoma without first establishing alpha-blockade, unopposed alpha stimulation from catecholamines can cause a hypertensive crisis.

Answer 11: Lithium-Induced Thyroid Dysfunction: Monitoring and Management

[10 marks]

Mechanisms

Lithium impairs thyroid function through multiple mechanisms:

1. Inhibits iodine uptake into thyroid follicular cells
2. Blocks organification of iodine and coupling of iodotyrosines
3. Inhibits TSH-stimulated cAMP generation (blocks thyroid hormone release)

4. Promotes anti-thyroid antibody formation (increased prevalence of Hashimoto's thyroiditis)

Clinical Manifestations

Hypothyroidism (most common): prevalence 20–42% in long-term lithium users. Clinical picture identical to primary hypothyroidism, depression, fatigue, weight gain, cognitive slowing, cold intolerance. Risk is higher in women, those with positive anti-TPO antibodies at baseline, older age, and longer duration of lithium treatment.

Subclinical hypothyroidism: elevated TSH with normal free T4; prevalence up to 40% in lithium-treated patients.

Goitre: diffuse or nodular; seen in 4–60% depending on iodine status and duration of treatment.

Hyperthyroidism: rare (1–2%); may represent a thyroiditis phase preceding permanent hypothyroidism.

Hyperparathyroidism/hypercalcaemia: lithium raises the set-point for PTH-calcium feedback → parathyroid gland hyperplasia → elevated PTH and calcium. Monitor serum calcium in long-term users.

Monitoring Protocol

- Baseline TFTs (TSH and free T4) before initiating lithium
- Every 6 months for the first year
- Annually thereafter (or sooner if symptomatic)
- Screen anti-TPO antibodies at baseline in high-risk patients

Management

- **Hypothyroidism on lithium:** continue lithium + add levothyroxine. Do NOT stop lithium (unless clinically indicated for other reasons). Treat-to-target TSH within normal range.
- **Subclinical hypothyroidism:** treat if TSH >10 mIU/L, or if TSH 5–10 with symptoms, or if pregnant
- **Goitre:** usually benign; monitor; investigate with ultrasound / fine needle aspiration if rapid growth or suspicious features
- **Hypercalcaemia:** refer to endocrinologist; may require parathyroidectomy in symptomatic primary hyperparathyroidism

EXAM PEARL

The correct management of lithium-induced hypothyroidism is NOT to stop lithium, it is to add levothyroxine while continuing lithium. Stopping lithium risks psychiatric relapse, which is almost always worse than manageable hypothyroidism.

Answer 12: Addison's Disease: Psychiatric Features

[5 marks]

Overview

Addison's disease (primary adrenal insufficiency) results from autoimmune destruction of the adrenal cortex in 70–90% of cases in developed countries (tuberculosis is the leading cause in developing countries). Both cortisol and aldosterone are deficient. Physical hallmark is hyperpigmentation (increased ACTH stimulates melanocortin receptors), particularly in buccal mucosa, skin creases, and scars.

Psychiatric Manifestations

Psychiatric symptoms occur in 60–90% of Addison's patients:

- **Depression** (most common): profound fatigue, anhedonia, apathy, low motivation. Mechanism: cortisol deficiency → disrupted stress response circuitry and monoamine dysregulation.
- **Apathy and fatigue**: sometimes the predominant presenting feature; may present to psychiatry before endocrine diagnosis established
- **Anxiety**: generalised anxiety, panic attacks
- **Psychosis**: rare; resolves with cortisol replacement
- **Cognitive impairment**: memory problems, slowed processing; reversible with treatment

Adrenal Crisis

Adrenal crisis is precipitated by physiological stress in an inadequately replaced patient. Psychiatric presentation: delirium, acute confusional state, severe agitation. Vitals reveal hypotension, hyponatraemia, hypoglycaemia. Emergency treatment: hydrocortisone 100 mg IV stat, IV saline, glucose; treat precipitant. Do not give psychotropics until the hormonal crisis is treated.

Answer 13: Vitamin B12 Deficiency: Neuropsychiatric Manifestations

[5 marks]

Overview

Vitamin B12 (cobalamin) is obtained exclusively from animal products. Deficiency results from pernicious anaemia (anti-intrinsic factor antibodies, most common cause), gastrectomy, ileal disease, metformin use (blocks ileal B12 absorption), malnutrition, or strict veganism.

Neuropsychiatric Features

- **Depression:** may be the presenting symptom; responds to B12 replacement
- **Cognitive impairment:** from mild memory complaints to dementia-like syndrome (reversible if treated early, irreversible if prolonged)
- **Megaloblastic madness:** classic psychosis from severe B12 deficiency, paranoia, auditory hallucinations
- **Irritability, personality change**

Neurological Features

Subacute combined degeneration of spinal cord (posterior + lateral columns): proprioception loss → sensory ataxia; spastic paraparesis; peripheral neuropathy (most common early feature).

Diagnosis and Treatment

Serum B12 <200 pg/mL; methylmalonic acid and homocysteine elevated (sensitive functional markers). Treatment: IM hydroxocobalamin 1000 mcg alternate days × 2 weeks, then 3-monthly. Psychiatric symptoms may take weeks to months to respond.

EXAM PEARL

Metformin commonly causes B12 deficiency, screen B12 annually in diabetic patients on long-term metformin, particularly those with psychiatric comorbidity or cognitive complaints.

Answer 14: Hyperparathyroidism: "Bones, Stones, Groans, Psychic Moans"

[5 marks]

Primary hyperparathyroidism (parathyroid adenoma in 80%) causes hypercalcaemia through excess PTH. The classic tetrad:

- **Bones:** osteitis fibrosa cystica, pathological fractures, subperiosteal resorption
- **Stones:** nephrolithiasis (calcium oxalate), nephrocalcinosis
- **Groans:** nausea, vomiting, constipation, peptic ulceration, pancreatitis
- **Psychic moans:** depression (40–60%; most common psychiatric manifestation), anxiety, cognitive impairment (memory, concentration), and psychosis in severe hypercalcaemia

Calcium and neuronal function: hypercalcaemia reduces neuronal excitability and alters monoamine neurotransmitter release. Severity of psychiatric symptoms correlates with calcium levels.

Management: surgical parathyroidectomy (definitive); hydration and bisphosphonates for acute hypercalcaemia. Psychiatric symptoms usually improve after calcium normalisation.

CLINICAL ANCHOR

Check serum calcium in any patient with treatment-resistant depression, particularly if accompanied by fatigue, constipation, or renal stones. Hyperparathyroidism is a correctable cause of depression.

Answer 15: Metabolic Effects of Antipsychotics: Mechanisms and Switching Strategies

[10 marks]

Mechanisms of Antipsychotic-Induced Metabolic Effects

Antipsychotic-induced metabolic syndrome arises through receptor-mediated mechanisms:

H1 histamine antagonism: the primary driver of weight gain. Blockade of hypothalamic H1 receptors impairs satiety signalling and promotes orexigenic NPY / AgRP neuronal activity. The degree of H1 affinity strongly predicts weight gain potential, clozapine and olanzapine have the highest H1 affinity.

5-HT_{2C} serotonin antagonism: promotes appetite and impairs the serotonin-mediated satiety signal from the ventromedial hypothalamus. Compounds with combined H1 + 5-HT_{2C} blockade (clozapine, olanzapine) cause the most weight gain.

M3 muscarinic antagonism: directly impairs pancreatic beta-cell insulin secretion and reduces peripheral glucose uptake, producing hyperglycaemia independent of weight gain. This explains why clozapine can cause new-onset diabetes even before significant weight gain.

D2 dopamine antagonism: mesolimbic D2 blockade may dysregulate the dopaminergic reward circuit's role in appetite regulation.

Alpha-1 adrenergic blockade: sedation and fatigue → reduced physical activity → secondary metabolic consequences.

Weight Gain Hierarchy

Highest risk: clozapine, olanzapine → moderate: quetiapine, risperidone → low: haloperidol, aripiprazole, ziprasidone, amisulpride.

Switching Strategies

Indications for switching: significant weight gain (BMI increase >1 unit/month), new-onset hyperglycaemia or T2DM, dyslipidaemia, patient preference.

Switch targets: aripiprazole, ziprasidone, amisulpride, lurasidone (low metabolic burden).

Methods:

1. **Abrupt switch:** straightforward for lower-risk medications; higher relapse risk
2. **Cross-titration:** overlap and taper (most common); reduces withdrawal effects while introducing new drug
3. **Plateau method:** used particularly for clozapine, taper clozapine to a plateau dose while building up the new agent, then continue tapering clozapine

Special case, clozapine: switching away from clozapine carries a high risk of relapse (clozapine is used for treatment-resistant schizophrenia, alternatives are less effective).

Metabolic benefits of switching must be carefully weighed against efficacy loss. Preferred approach: add aripiprazole (5–15 mg) to clozapine rather than switching, reduces weight by ~1.5–2 kg while maintaining clozapine's efficacy.

Pharmacological augmentation without switching:

- Metformin 500–1000 mg BD (first-line)
 - Aripiprazole co-prescription to olanzapine / clozapine
 - GLP-1 agonists (emerging evidence; increasingly used)
 - Statins for dyslipidaemia
 - Structured exercise programme (150 min/week)
-

Mnemonics & Memory Tricks

EXAM STRATEGY

These mnemonics are grouped by topic. Each has a device (the thing you memorise), an expansion (what it means), and a clinical hook (why it matters in the exam). The box format means you can scan these in 10 minutes before a paper.

THYROID DISORDERS

MNEMONIC

LOW TSH = HYPER, HIGH TSH = HYPO

Direction check: TSH moves opposite to thyroid hormone levels. TSH is high when thyroid is lazy; TSH is low when thyroid is overactive (pituitary gets suppressed).

MNEMONIC

WISE HAT, Wilson's, Infections, Steroids, Endocrine, Hashimoto's, Autoimmune, Tumour

Secondary causes of dementia/cognitive impairment that are reversible. Every new cognitive presentation deserves this screen. Hypothyroidism is the E in Endocrine, the most common reversible endocrine cause.

MNEMONIC

LITHO DAMAGES THYROID, Lithium Inhibits Thyroid Hormone Output; Deduce And Monitor; Augment Getting Extra Synthesis = add levothyroxine

Simplified: Lithium → thyroid damage → monitor 6-monthly → add levothyroxine if hypothyroid. Do NOT stop lithium.

MNEMONIC

T3 STARS, T3 Speeds Treatment-resistant And Resistant-to-SSRIs

T3 augmentation (liothyronine 25–50 mcg) is used in treatment-resistant depression. Evidence from STAR*D trial. Works even in euthyroid patients.

MNEMONIC

ASHER'S MAD MYX, Myxedema Madness: Asher described it, presents as Acute-onset Delirium, Hallucinations, Elevated (paranoid) ideation, Reversed with thyroid Substitution, Myxedema = MAD

Myxedema madness = severe hypothyroidism + acute psychosis. Name-drop: Asher, 1949.

CUSHING'S & ADRENAL

MNEMONIC

CUSHING DEPRESSES, Cognitive decline, Ugly striae, Suicide risk, Hypertension, Insomnia, Neuropsychiatric change, Glucose (diabetes), Depression, Euphoria (early), Psychosis, Round face, Episodes of mania, Swelling (central obesity), Steroid-induced

All psychiatric and systemic features of Cushing's in one device. Depression = 50–80%; earliest psychiatric signs often euphoria/irritability.

MNEMONIC

DOSE DRIVES DANGER (3 thresholds), Below 40: Docile; 40–80: Dangerous (4.6%); Above 80: Dread (18.4%)

Prednisone dose thresholds for psychiatric risk. Numbers are approximate but the relationship is reliable.

MNEMONIC

ADDISON APATHY, Addison's gives Apathy, Depression, Darkening (hyperpigmentation), Insomnia, Salt-craving, Orthostatic hypotension, Nausea, **ADDISON**

Psychiatric and physical features of Addison's disease linked to the eponym. Apathy and fatigue are often the entry point into psychiatric services.

WILSON'S DISEASE

MNEMONIC

WILSON'S COPPER PSYCH, W=Wilson's; Chromosome 13; O=Autosomal recessive; Per=Personality change FIRST; Psychosis second; Slit-lamp for KF rings; Young (under 40); Chelate (D-penicillamine); Heavy metals (copper); = **Psychiatric + Neurological + Hepatic**

The three-system rule: any young patient with psychiatric + neurological + liver disease = Wilson's until proved otherwise.

MNEMONIC

PTZKA, Penicillamine Then Zinc Keeps Adequate (copper control)

Treatment sequence: penicillamine (or trientine) for initial chelation → zinc for maintenance. Never give both simultaneously (they compete). PTZKA: P (penicillamine) → T (trientine if intolerant) → Z (zinc for maintenance) → K (keep monitoring) → A (avoid hepatotoxins).

MNEMONIC

KF RINGS ARE IN THE EYE, NOT THE BRAIN, Kayser-Fleischer in cornea (Descemet's membrane), slit-lamp exam, present in >95% neuropsychiatric Wilson's but only 50–60% pure hepatic Wilson's

Common exam error: assuming KF rings are a brain finding. They are corneal copper deposits. Slit-lamp is mandatory.

WERNICKE-KORSAKOFF

MNEMONIC

WACO, Wernicke: Ataxia, Confusion, Ophthalmoplegia

The classic triad of Wernicke's encephalopathy. Only 16% have all three. But WACO is how you remember to look for it.

MNEMONIC

THIAMINE BEFORE GLUCOSE, TBG

The single most important rule in WKS management. TBG: Thiamine Before Glucose. Any at-risk patient + IV glucose without thiamine cover = potential Wernicke's trigger.

MNEMONIC

KORSAKOFF CONFABULATES, Korsakoff = Anterograde Amnesia + Confabulation + no insight (Anosognosia)

The three cardinal features. Confabulation = unconscious, not deliberate lying. Anterograde > retrograde amnesia.

METABOLIC SYNDROME & ANTIPSYCHOTICS

MNEMONIC

CLOZA-OLAN METABOLIC TWINS, Clozapine and Olanzapine: highest H1 + 5-HT_{2C} blockade = maximum weight gain + maximum diabetes risk

These two are always paired in the metabolic hierarchy. Weight gain ~4–4.5 kg. Diabetogenic effect independent of weight (M3 muscarinic blockade).

MNEMONIC

ADA/APA MONITORING, Base 4–8–12–Annual

Baseline → 4 weeks → 8 weeks → 12 weeks → annually. Weight checked at every visit in first 12 weeks. Glucose and lipids at 12 weeks then annually. Memory hook: "Base camp, then 4 checkpoints" (B-4-8-12-A).

MNEMONIC

METFORMIN FIRST, Metabolic side effects = give Metformin First, then consider Reallocation (switch) if insufficient

For antipsychotic-induced weight gain: metformin 500 mg BD is first-line pharmacotherapy. Switch only if metformin + lifestyle insufficient or metabolic harm is severe.

HYPONATRAEMIA & SIADH

MNEMONIC

CARBA-OXA SODIUMS FALL, Carbamazepine and Oxcarbazepine cause SIADH; Oxcarbazepine MORE than carbamazepine; Sodiums Fall = hyponatraemia

Highest-risk AED / mood stabiliser for SIADH. Oxcarbazepine > carbamazepine is the exam trap. Check sodium in every patient on these drugs, especially elderly.

MNEMONIC

CORRECT SLOW OR CENTRAL PONTINE, Max 8-10 mEq/L per day. Faster = ODS

ODS = osmotic demyelination syndrome = central pontine myelinolysis. Irreversible. Locked-in. "Correct slow or central pontine" = the consequence of correcting too fast.

PORPHYRIA

MNEMONIC

AIP PAIN PSYCH NERVE, Acute (attacks); Intermittent; Porphyrin; Abdominal Pain (colicky); Psychiatric (psychosis/anxiety); Peripheral Nerve (motor neuropathy); dark urine

The triad of AIP: abdominal pain + psychiatric symptoms + peripheral neuropathy. Dark urine is the diagnostic clue. Urine porphyrins confirm.

MNEMONIC

HAEM FIXES PORPHYRIA, Haem arginate (Normosang) is the definitive treatment, suppresses ALA synthase. HAEM = Haem arginate + Avoid trigger + Eat carbs (400g/day) + Monitor respiratory function

Treatment sequence for acute AIP attack. Carbs suppress ALA synthase; haem arginate is definitive.

MNEMONIC

SAFE PSYCHIATRY IN PORPHYRIA = SSH-G, SSRIs (sertraline, citalopram), Haloperidol, Gabapentin/Levetiracetam

The safe psychiatric drugs. Mnemonic: SSH-G = Safe, Serotonin-reuptake inhibitors, Haloperidol, Gabapentin.

NUTRITIONAL DEFICIENCIES

MNEMONIC

B12 DEFICIENCY = SACD + MAD, Subacute Combined Degeneration (SACD) of the spinal cord; Megaloblastic Anaemia and Dementia (MAD)

Two classic B12 deficiency syndromes. SACD = posterior + lateral column degeneration. MAD = megaloblastic madness (psychosis). Together they cover all exam angles.

MNEMONIC

PELLAGRA 4Ds, Dermatitis, Diarrhoea, Dementia, Death

In order of appearance (roughly). Death is the outcome if untreated. INH use → B6 deficiency → tryptophan conversion blocked → niacin deficiency → pellagra. Prevent with pyridoxine.

MNEMONIC

FOLATE METHYLATES, Folate provides methyl groups for monoamine synthesis; low folate = low antidepressant response; augment with L-methylfolate (MTHF)

Folate's mechanism in mood. L-methylfolate is the active form; MTHFR gene variants reduce conversion → supplementation rationale.

PARATHYROID DISORDERS

MNEMONIC

BONES STONES GROANS PSYCHIC MOANS, Hyperparathyroidism tetrad

Psychiatric manifestations = the "psychic moans." Depression (40–60%) is the most common; psychosis in severe hypercalcaemia. Always check calcium in treatment-resistant depression.

HEPATIC ENCEPHALOPATHY

MNEMONIC

GRADE HE BY ASTERIXIS ONSET, Grade 1: no asterixis, Grade 2: asterixis appears, Grade 3: asterixis + somnolent, Grade 4: coma no asterixis

Asterixis (liver flap) is the motor landmark of Grade 2–3. Grade 4 = coma; asterixis disappears because volitional muscle tone is lost.

MNEMONIC

LACTULOSE FIRST, RIFAXIMIN SECOND, LFRS

HE treatment sequence. Lactulose is first-line; rifaximin is add-on for recurrent/refractory HE. Protein restriction is outdated, maintain 1.2–1.5 g/kg/day.

LITHIUM MONITORING

MNEMONIC

LITHIUM BIG THREE MONITORING, TFTs, RFTs, Calcium (parathyroid)

Three organ systems lithium affects: thyroid (hypothyroidism), kidney (diabetes insipidus, CKD), parathyroid (hypercalcaemia). Monitor all three long-term: TFTs 6-monthly → annual; RFTs 6-monthly; calcium annually.

PHEOCHROMOCYTOMA

MNEMONIC

4Ps = Phaeochromocytoma, **P**aroxysmal hypertension, **P**alpitations, **P**erspiration (diaphoresis), **P**allor/**P**ain (headache)

The classic paroxysmal presentation. Differentiates from panic disorder by severe hypertension and pallor (not flushing), and physical rather than psychosocial triggers.

Quick Cross-Reference Table

TOPIC	MNEMONIC DEVICE	KEY FACT
Hypothyroidism	LOW TSH = HYPER, HIGH TSH = HYPO	Direction logic
Myxedema madness	ASHER'S MAD MYX	Asher 1949; severe hypothyroid + psychosis
Cushing's psych	CUSHING DEPRESSES	Depression 50–80%; suicide risk
Addison's	ADDISON APATHY	Apathy / fatigue = psychiatric entry point
Wilson's	PTZKA	Penicillamine → Trientine → Zinc for maintenance
Wilson's diagnosis	KF RINGS IN THE EYE	Slit-lamp, corneal copper, ≥95% neuropsychiatric
Wernicke's	WACO	Ataxia + Confusion + Ophthalmoplegia
WKS rule	TBG	Thiamine Before Glucose, always
Korsakoff	CONFABULATES	Anterograde amnesia + confabulation + no insight
Metabolic antipsychotics	CLOZA-OLAN TWINS	Highest H1 + 5HT2C = max weight/diabetes
ADA/APA monitoring	B-4-8-12-A	Baseline, then 4/8/12 weeks, then annual
SIADH risk	CARBA-OXA SODIUMS FALL	Oxcarbazepine > carbamazepine
ODS prevention	CORRECT SLOW	Max 8–10 mEq/L/day
Porphyria safe drugs	SSH-G	SSRIs, Haloperidol, Gabapentin

TOPIC	MNEMONIC DEVICE	KEY FACT
AIP triad	AIP PAIN PSYCH NERVE	Pain + Psychiatry + Neuropathy
Pellagra	4Ds	Dermatitis, Diarrhoea, Dementia, Death
B12	SACD + MAD	Spinal cord + Megaloblastic madness
Hypercalcaemia psych	BONES STONES GROANS PSYCHIC MOANS	Depression most common psychiatric feature
HE grading	ASTERIXIS ONSET	Grade 2 = asterixis appears
HE treatment	LFRS	Lactulose First, Rifaximin Second
Phaeochromocytoma	4Ps	Paroxysmal HP + Palpitations + Perspiration + Pallor
Lithium monitoring	BIG THREE	TFTs + RFTs + Calcium

High-Yield Comparisons

EXAM STRATEGY

Comparison tables are the fastest way to score marks in structured answers. When a question asks you to "compare," "differentiate," or "enumerate differences," reproduce these tables verbatim. Each table is designed to fit on a single exam page.

Table 1: Hypothyroidism vs Hyperthyroidism: Psychiatric Features

FEATURE	HYPOTHYROIDISM	HYPERTHYROIDISM
Primary psychiatric presentation	Depression (40–60%)	Anxiety (60–80%)
Mood	Low, flat, anhedonic	Elevated, labile, irritable
Energy	Severely reduced; fatigue dominant	Increased; restlessness
Cognition	Slowed; memory impairment; verbal fluency reduced	Distractible; poor concentration
Sleep	Hypersomnia; excessive sleep	Insomnia; difficulty initiating and maintaining sleep
Psychosis	Myxedema madness (severe hypothyroid)	Rare; thyroid storm
Mania	Rare	Thyrotoxic mania (rare but documented)
Anxiety	Mild; secondary	Prominent; free-floating; panic attacks
Appetite/weight	Increased weight despite normal/low appetite	Weight loss despite increased appetite
Physical clues	Dry skin, hair loss, constipation, bradycardia, delayed reflexes	Sweating, tremor, tachycardia, heat intolerance, goitre
Mechanism	Reduced serotonergic + noradrenergic tone	Amplified beta-adrenergic + noradrenergic activity
TSH	Elevated	Suppressed
Treatment focus	Levothyroxine; antidepressants if needed	Beta-blockers; antithyroid drugs; treat underlying cause

EXAM PEARL

Both hypothyroidism and hyperthyroidism can cause anxiety, but hypothyroid anxiety is mild and secondary, while hyperthyroid anxiety is prominent and physically driven (palpitations, tremor, diaphoresis). TSH differentiates them immediately.

Table 2: Wilson's Disease vs First-Episode Schizophrenia

FEATURE	WILSON'S DISEASE	FIRST-EPIISODE SCHIZOPHRENIA
Age of onset	5–35 years	18–35 years (typical)
Psychiatric presentation	Personality change, psychosis, affective symptoms	Psychosis, negative symptoms, cognitive decline
Personality change	Prominent; often first sign	Present but less prominent early
Motor features	Dysarthria, tremor, dystonia, ataxia	Minimal (unless antipsychotic-induced EPS)
Liver involvement	Hepatitis, cirrhosis, hepatic failure	Absent
Corneal signs	Kayser-Fleischer rings (slit-lamp)	Absent
Serum ceruloplasmin	Low (<0.2 g/L)	Normal
Urine copper	Elevated (>100 mcg/24h)	Normal
Brain MRI	Basal ganglia T2 hyperintensities; "face of giant panda" sign	May show non-specific changes; cortical thinning in chronic
Family history	Autosomal recessive (consanguinity increases risk)	Polygenic; first-degree relative risk 10%
Response to antipsychotics	Partial; neurological features persist	Good response to first-line antipsychotics
Treatment	Copper chelation (penicillamine/trientine) + zinc	Antipsychotics; psychosocial interventions
Prognosis with treatment	Stabilisation/improvement possible if treated early	Variable; ~20% achieve remission

CLINICAL ANCHOR

Young patient with psychosis + ANY of: movement disorder, liver disease, personality change as the FIRST symptom, or family history of liver disease in a sibling, investigate for Wilson's before committing to schizophrenia diagnosis.

Table 3: Wernicke's Encephalopathy vs Korsakoff Syndrome

FEATURE	WERNICKE'S ENCEPHALOPATHY	KORSAKOFF SYNDROME
Phase	Acute	Chronic amnesic
Cause	Active thiamine deficiency	Permanent structural damage from untreated WE
Pathology	Haemorrhagic necrosis in mammillary bodies, periaqueductal grey, thalamus	Mammillary body + mediodorsal thalamic atrophy
Consciousness	Confused, drowsy, may be delirious	Alert (usually)
Memory	Global confusion; not a pure memory syndrome	Severe anterograde > retrograde amnesia
Confabulation	Not a feature	Hallmark feature
Ophthalmoplegia	Present (6th nerve palsy, nystagmus)	Absent (may resolve partially)
Ataxia	Present	May persist partially
Insight	Variable	Markedly impaired (anosognosia)
Reversibility	Fully reversible if treated promptly	Partially reversible at best; 50% permanent
Treatment	IV thiamine (Pabrinex 500 mg TID × 3 days) STAT	Oral thiamine long-term; rehabilitation
Key rule	Thiamine before glucose, ALWAYS	No specific reversal agent

EXAM PEARL

Only 16% of Wernicke's present with the full classic triad (WACO). In any nutritionally at-risk patient with ANY of ataxia, confusion, or eye signs, give IV thiamine immediately. Do not wait for the full triad.

Table 4: Panic Disorder vs Pheochromocytoma

FEATURE	PANIC DISORDER	PHAEOCHROMOCYTOMA
Mechanism	Dysregulated fear circuitry; HPA/autonomic sensitisation	Paroxysmal catecholamine (adrenaline/noradrenaline) secretion
Onset of episodes	Sudden, often unpredictable	Paroxysmal; may be triggered

FEATURE	PANIC DISORDER	PHAEOCHROMOCYTOMA
Triggers	Psychosocial, conditioned; sometimes spontaneous	Physical: posture change, exercise, abdominal pressure, surgery
Duration	Typically 10–30 minutes	Minutes to hours
Hypertension during episode	Absent or mild	Severe (systolic often >200 mmHg)
Colour during episode	Flushing	Pallor (noradrenaline-dominant tumours)
Headache	Variable; tension-type	Prominent, throbbing
Weight	Normal or variable	Weight loss (hypermetabolic state)
Cardiac	Palpitations, mild tachycardia	Severe tachycardia; may cause cardiomyopathy
Between episodes	Normal or anticipatory anxiety	May have sustained or labile hypertension
24h urine metanephrines	Normal	Elevated
Plasma free metanephrines	Normal	Elevated (sensitivity ~97%)
Response to anxiolytics/SSRIs	Good	Poor
Treatment	CBT; SSRIs; benzodiazepines (acute)	Alpha-blockade first, then beta-blockade; surgical resection

Table 5: Cushing's Syndrome Depression vs Primary MDD

FEATURE	CUSHING'S SYNDROME DEPRESSION	PRIMARY MAJOR DEPRESSION
Cortisol	Markedly elevated; unsuppressed on DST	May be elevated; non-suppression in ~50%
DST	Non-suppression (of limited discriminant value here)	Non-suppression in ~50% of melancholic MDD
Physical signs	Moon face, buffalo hump, central obesity, striae, proximal weakness	Absent
Weight pattern	Gained centrally; muscle wasting peripherally	Variable (loss or gain)
Blood glucose	Elevated (steroid diabetes)	Normal unless metabolic syndrome
Onset	Follows cortisol excess	Independent

FEATURE	CUSHING'S SYNDROME DEPRESSION	PRIMARY MAJOR DEPRESSION
Hippocampal volume	Reduced (cortisol-mediated)	Reduced (chronic)
Suicide risk	High (4–10% attempt)	High
Antidepressant response	Partial at best without treating underlying Cushing's	Good response expected
Treatment priority	Treat Cushing's first; antidepressant adjunct	Antidepressant + psychotherapy
Diagnosis	Late-night salivary cortisol; 24h UFC; LDDST	Clinical; no biomarker

EXAM PEARL

Non-suppression of cortisol on DST occurs in both Cushing's syndrome AND severe/melancholic MDD, this test cannot differentiate the two. Clinical features (physical signs of Cushing's, onset in context of weight gain/striae/hypertension) are the differentiators.

Table 6: Antipsychotic Metabolic Risk Comparison

ANTIPSYCHOTIC	WEIGHT GAIN	DIABETES RISK	DYSLIPIDAEMIA	PROLACTIN ELEVATION	QTC PROLONGATION
Clozapine	Very high (+4.5 kg)	Very high	High	Low	Moderate
Olanzapine	Very high (+4.2 kg)	Very high	High	Moderate	Low
Quetiapine	Moderate (+2.3 kg)	Moderate	Moderate	Low	Moderate
Risperidone	Moderate (+2.1 kg)	Moderate	Moderate	Very high	Low
Amisulpride	Low	Low	Low	Very high	Moderate
Haloperidol	Low (+0.5 kg)	Low	Low	High	Low-moderate
Aripiprazole	Low (+0.7 kg)	Low	Low	Lowers prolactin	Low
Ziprasidone	Minimal (+0.04 kg)	Low	Low	Low	High
Lurasidone	Low	Low	Low	Low	Low

ANTIPSYCHOTIC	WEIGHT GAIN	DIABETES RISK	DYSLIPIDAEMIA	PROLACTIN ELEVATION	QTC PROLONGATION
Asenapine	Low-moderate	Low	Low	Moderate	Low

EXAM PEARL

Amisulpride and risperidone cause the highest prolactin elevation among commonly used antipsychotics. Aripiprazole (partial D2 agonist) actually lowers prolactin, it can be added to normalise prolactin in patients on high-prolactin-causing agents.

Table 7: Safe vs Unsafe Drugs in Acute Intermittent Porphyria

DRUG CATEGORY	UNSAFE (PRECIPITATE ATTACKS)	SAFE (GENERALLY)
Anticonvulsants	Carbamazepine, phenytoin, phenobarbitone, valproate (debated)	Gabapentin, levetiracetam
Antidepressants	TCAs (amitriptyline, clomipramine)	SSRIs (sertraline, citalopram, escitalopram)
Benzodiazepines	Most, use with caution	Lorazepam (generally safer)
Antipsychotics	Most phenothiazines (caution)	Haloperidol, chlorpromazine (probably safe)
Analgesics	Diclofenac, mefenamic acid, pentazocine	Paracetamol, aspirin, opioids (morphine, fentanyl)
Antibiotics	Sulfonamides, rifampicin, chloramphenicol	Penicillins, cephalosporins
Hormones	Progesterone-containing OCP, oestrogens	
Miscellaneous	Alcohol, dapsone, griseofulvin	Beta-blockers, calcium channel blockers

CLINICAL ANCHOR

Before prescribing any new drug to a patient with known porphyria, check the European Porphyria Network (EPNET) drug database. This is the gold standard reference. In exams: always name 3 safe + 3 unsafe drugs in each class.

Table 8: Hyponatraemia: SIADH vs Psychogenic Polydipsia

FEATURE	SIADH	PSYCHOGENIC POLYDIPSIA
Mechanism	Excess ADH → water retention → dilutional hyponatraemia	Compulsive water intake → overwhelms renal excretion capacity
Primary diagnosis association	Any cause of SIADH; psy- chotropic drugs	Schizophrenia (up to 25% of inpatients)
Serum osmolality	Low (<280 mOsm/kg)	Low (<280 mOsm/kg)
Urine osmolality	High (>serum osmolality), in- appropriately concentrated	Low (maximally dilute, urine osmolality <100 mOsm/kg)
Urine sodium	High (>20 mEq/L)	Low (<20 mEq/L)
Volume status	Euvolaemic	Euvolaemic to mildly expanded
Thirst	Normal or reduced	Compulsively increased (not physiological)
Responsible drugs	SSRIs, carbamazepine, oxcar- bazepine, TCAs	Antipsychotics (via D2 in thirst centres); polydipsia is behavioural
Management	Fluid restriction; tolvaptan; switch offending drug	Fluid restriction; clozapine may reduce polydipsia; behavioural intervention
Correction rule	Max 8–10 mEq/L per 24h	Max 8–10 mEq/L per 24h (same rule)

Table 9: Nutritional Deficiency Neuropsychiatric Syndromes

NUTRIENT	DEFICIENCY SYNDROME	CORE PSYCHIATRIC FEATURES	KEY PHYSICAL SIGN	TREATMENT
Vitamin B1 (Thiamine)	Wernicke-Korsakoff	Confusion, an- terograde amne- sia, confabulation	Ophthalmoplegia , ataxia	IV thiamine be- fore glucose
Vitamin B3 (Niacin)	Pellagra	Anxiety, depres- sion, dementia, psychosis	Dermatitis (Casal's necklace), diarrhoea	Nicotinamide 100–300 mg TID
Vitamin B9 (Folate)	Folate deficiency	Depression, poor antidepressant response, irritability	Megaloblastic anaemia	Folic acid 5 mg/day; L- methylfolate for augmentation

NUTRIENT	DEFICIENCY SYNDROME	CORE PSYCHIATRIC FEATURES	KEY PHYSICAL SIGN	TREATMENT
Vitamin B12 (Cobalamin)	Subacute combined degeneration; Megaloblastic madness	Depression, cognitive impairment, psychosis	Posterior column signs, peripheral neuropathy	IM hydroxocobalamin
Magnesium	Hypomagnesaemia	Anxiety, agitation, depression, confusion	Tremor, tetany, hyperreflexia	IV/oral magnesium; correct before QTc-prolonging antipsychotics
Zinc	Zinc deficiency	Irritability, depression, cognitive impairment	Dermatitis, impaired taste/smell, poor wound healing	Zinc supplementation; also used therapeutically in Wilson's

Table 10: Hepatic Encephalopathy: West Haven Grades at a Glance

GRADE	ALERTNESS	PSYCHIATRIC/COGNITIVE	MOTOR	ASTERIXIS
0 (Minimal/Covert)	Normal	Subtle deficits only on psychometry (PHES)	Normal	Absent
1	Normal to mildly impaired	Shortened attention; sleep-wake reversal; mild anxiety or euphoria; impaired serial subtraction	Tremor; poor coordination	Absent
2	Lethargic	Disorientation; personality change; amnesia; inappropriate behaviour	Asterixis; dysarthria; ataxia	Present
3	Somnolent but rousable	Marked confusion; bizarre behaviour; gross disorientation; semipurposive response to stimuli	Asterixis; rigidity; hyperreflexia; Babinski	Present

GRADE	ALERTNESS	PSYCHIATRIC/COGNITIVE	MOTOR	ASTERIXIS
4	Coma; not rousable	No purposive response	Decerebrate or decorticate posturing; no asterixis	Absent

EXAM PEARL

Asterixis appears at Grade 2 and disappears at Grade 4 because it requires voluntary muscle tone to be present. Its appearance is the clinical signal to escalate treatment urgency. Minimal HE (Grade 0) is important for quality of life, it impairs driving and work performance even when clinically invisible.

PYQ Frequency Analysis

EXAM STRATEGY

This analysis is based on patterns across PG exams, and TN MGR MD Psychiatry papers over the past 15+ years. Topics are ranked by appearance frequency. High-frequency topics deserve the most revision time. The final section maps each topic to the answer structure it demands.

Section 1: Frequency Heat Map

Section 2: Topic-by-Topic PYQ Profile

Wilson's Disease ★★★★★ HIGH PRIORITY

How it appears:

- Long answer (15 marks): "Describe the psychiatric manifestations, diagnosis, and management of Wilson's disease."
- Short answer (5–10 marks): "Kayser-Fleischer rings, significance in psychiatry," "Treatment of Wilson's disease," "Psychiatric presentation of Wilson's disease"
- MCQ: ceruloplasmin levels, ATP7B gene locus, safe antipsychotic use, penicillamine side effects

Exact phrasings seen:

- "A 22-year-old presents with personality change, slurred speech, and a first episode of psychosis. Discuss your approach."
- "Enumerate the psychiatric manifestations of Wilson's disease and outline its management."
- "What is the role of zinc in Wilson's disease?"

What examiners want:

1. Pathophysiology (ATP7B, copper accumulation)
2. Three-system triad: psychiatric + neurological + hepatic
3. KF rings on slit-lamp, must name slit-lamp specifically
4. Investigations table (ceruloplasmin, 24h urine copper, liver biopsy values)
5. Treatment: penicillamine → trientine → zinc (maintenance), all three drugs with mechanisms

6. Neurological worsening warning with penicillamine

EXAM STRATEGY

Wilson's disease is the single most asked topic in this chapter. If you have time to master only one topic, this is it. Learn the Leipzig score concept, even briefly, examiners reward it.

Antipsychotic-Induced Metabolic Effects ★★★★★ HIGH PRIORITY

How it appears:

- Long answer: "Metabolic syndrome and antipsychotics, discuss with reference to monitoring guidelines."
- Short answer: "ADA / APA monitoring guidelines for antipsychotic-induced metabolic syndrome," "Weight gain with antipsychotics, mechanism and management"
- MCQ: which antipsychotic causes most weight gain; monitoring interval for fasting glucose; mechanism of olanzapine-induced diabetes

Exact phrasings seen:

- "Discuss the metabolic complications of second-generation antipsychotics and their monitoring."
- "A patient on clozapine develops weight gain and hyperglycaemia. How will you manage?"
- "Enumerate receptor mechanisms by which antipsychotics cause metabolic syndrome."

What examiners want:

1. Receptor mechanisms (H1, 5-HT_{2C}, M3, D2, all four)
2. Weight gain hierarchy table (clozapine and olanzapine at the top)
3. ADA / APA monitoring table (baseline → 4 → 8 → 12 weeks → annual)
4. Management: metformin, switching strategy, aripiprazole augmentation
5. Special note: clozapine switching dilemma (efficacy vs metabolic risk)

Wernicke-Korsakoff Syndrome ★★★★★ HIGH PRIORITY

How it appears:

- Long answer: "Describe the clinical features, pathology, and management of Wernicke-Korsakoff syndrome."
- Short answer: "Korsakoff syndrome," "Thiamine deficiency and psychiatry," "Confabulation, clinical significance"
- MCQ: pathological site affected; treatment dose; rule about glucose administration

Exact phrasings seen:

- "A 48-year-old man with alcohol dependence is brought in confused, with lateral gaze palsy and unsteady gait. Discuss."
- "What is the rule of thiamine and glucose administration? Why is it important?"
- "Enumerate the features of Korsakoff psychosis."

What examiners want:

1. Pathogenesis: thiamine → pyruvate dehydrogenase → energy failure → mammillary bodies
 2. WACO triad, with the caveat that only 16% have all three
 3. Pathological sites: mammillary bodies (most characteristic), periaqueductal grey, thalamus
 4. Thiamine before glucose rule, stated explicitly
 5. IV Pabrinex dose: 500 mg TID × 3 days minimum
 6. Korsakoff: anterograde amnesia + confabulation + anosognosia
 7. Prognosis: 25/25/50 rule
-

Thyroid Disorders & Psychiatry ★★★★★

How it appears:

- Long answer: "Thyroid disorders and their psychiatric manifestations, a comprehensive account."
- Short answer: "Myxedema madness," "T3 augmentation in depression," "Hashimoto's encephalopathy"
- MCQ: TFT values, lithium monitoring intervals, T3 mechanism in depression

Exact phrasings seen:

- "Discuss the role of thyroid hormones in psychiatry with special reference to treatment of depression."
- "What is myxedema madness? How is it different from primary psychosis?"
- "Enumerate the indications for TFT screening in psychiatric practice."

What examiners want:

1. Spectrum of hypothyroid psychiatric manifestations (depression → myxedema madness)
 2. Hyperthyroid anxiety/mania, brief
 3. T3 augmentation: mechanism, dose, STAR*D evidence
 4. Lithium-thyroid interactions: monitoring protocol, management of hypothyroidism
 5. When to screen TFTs, comprehensive list
-

Lithium-Induced Thyroid Dysfunction ★★★★★

How it appears:

- Short answer (most common): "Lithium and thyroid, what does the clinician need to know?"
- Part of longer answer on lithium monitoring
- MCQ: monitoring interval, management, risk factors for hypothyroidism

What examiners want:

1. Four mechanisms of lithium-thyroid interaction
 2. Prevalence: 20–42% hypothyroidism
 3. Risk factors (female, anti-TPO positive, older, longer duration)
 4. Monitoring: 6-monthly for year 1, then annual
 5. Management: continue lithium + add levothyroxine
-

Metabolic Syndrome Monitoring ★★★★★

How it appears:

- Short/medium answer: "ADA / APA monitoring guidelines for antipsychotic-induced metabolic syndrome"
- Part of larger antipsychotic question

What examiners want:

- The full monitoring table reproduced accurately
 - Action thresholds for each parameter
 - Metformin as first-line pharmacological intervention
-

Hepatic Encephalopathy ★★★★★

How it appears:

- Long/medium answer: "Hepatic encephalopathy, grading, pathophysiology, management."
- Short answer: "West Haven grading of hepatic encephalopathy," "Role of lactulose in HE"
- MCQ: precipitants, grade of asterixis, first-line treatment

Exact phrasings seen:

- "Describe the West Haven grading of hepatic encephalopathy with clinical features."
- "Enumerate the precipitants of hepatic encephalopathy and outline its management."

What examiners want:

1. Ammonia hypothesis, brief pathophysiology
 2. West Haven grades 0–4 table (full features)
 3. Asterixis: grade 2 onset, grade 4 disappears
 4. Precipitants: SBP most common
 5. Lactulose first-line; rifaximin add-on; protein restriction is outdated
-

Cushing's Syndrome ★★★

How it appears:

- Long answer: "Psychiatric manifestations of Cushing's syndrome and steroid-induced psychiatric disorders."
- Short answer: "Steroid-induced mania," "Dose-response relationship of glucocorticoids and psychiatric side effects"
- MCQ: most common psychiatric manifestation; dose threshold; management

Exact phrasings seen:

- "A patient on high-dose prednisolone for SLE develops manic symptoms. Discuss."
- "Enumerate the psychiatric manifestations of Cushing's syndrome."

What examiners want:

1. Psychiatric manifestations: depression (50–80%) > anxiety > psychosis > mania
 2. Dose-response table (the three thresholds)
 3. Steroid mania, early, dose-related
 4. Management: reduce dose → antipsychotics → mood stabilisers
 5. Lithium prophylaxis for repeated steroid courses
-

SIADH and Psychotropic-Induced Hyponatraemia ★★★

How it appears:

- Medium answer: "Psychotropic-induced hyponatraemia, causes, features, management."
- Short answer: "SIADH and SSRIs," "Osmotic demyelination syndrome"
- MCQ: which drug causes most SIADH; correction rate; ODS risk factors

Exact phrasings seen:

- "Enumerate psychotropic drugs that cause SIADH and outline management of hyponatraemia."
- "What is osmotic demyelination syndrome? How is it prevented?"

What examiners want:

1. Drug list with mechanism (SSRIs, carbamazepine, oxcarbazepine, oxcarbazepine > carbamazepine)
 2. Diagnostic criteria for SIADH
 3. Correction rate: max 8–10 mEq/L per 24h
 4. ODS, definition, features, prevention
-

Acute Intermittent Porphyria ★★ ★

How it appears:

- Medium answer: "Acute intermittent porphyria, psychiatric features and drug safety."
- Short answer: "Safe drugs in porphyria," "Treatment of acute porphyria attack"
- MCQ: unsafe anticonvulsant; safe analgesic; treatment

Exact phrasings seen:

- "A patient with recurrent abdominal pain, peripheral neuropathy, and psychosis is suspected to have porphyria. Discuss."
- "Enumerate safe and unsafe psychiatric drugs in acute intermittent porphyria."

What examiners want:

1. Triad: abdominal pain + neuropathy + psychiatric features
 2. Dark urine (PBG oxidation)
 3. Drug safety table, at least 3 unsafe + 3 safe in each class
 4. Treatment: haem arginate + high carbohydrate + levetiracetam for seizures
-

Nutritional Deficiencies ★★ ★

How it appears:

- Medium answer: "Neuropsychiatric features of nutritional deficiencies."
- Short answer: "Pellagra," "B12 deficiency and psychiatry," "Wernicke's encephalopathy" (crossover with WKS section)
- MCQ: deficiency → specific syndrome; treatment drug

What examiners want:

The B-vitamin table: B1 (Wernicke-Korsakoff), B3 (Pellagra, 4Ds), B9 (Folate, depression/ antidepressant augmentation), B12 (SACD + megaloblastic madness)

Phaeochromocytoma ★★

How it appears:

- Short answer or MCQ only

- "Panic disorder vs phaeochromocytoma, how to differentiate?"
- MCQ: diagnostic test, distinguishing feature

What examiners want:

- 4Ps (paroxysmal hypertension, palpitations, perspiration, pallor/pain)
- Distinguishing features from panic disorder (severe BP, pallor, physical triggers)
- Diagnostic test: 24h urine metanephrines / plasma free metanephrines
- Management sequence: alpha-blockade before beta-blockade

Section 3: Mark Allocation Patterns

MARKS	TOPIC TYPE	EXPECTED STRUCTURE
15 marks	Wilson's disease; Wernicke-Korsakoff; Antipsychotic metabolic effects	Full long answer: definition → pathophysiology → clinical features → diagnosis → management + table
10 marks	Cushing's; SIADH; Lithium-thyroid; HE grading	Shorter long answer: key mechanisms + clinical features + management
5 marks	Pellagra; Phaeochromocytoma; Addison's; Hyperparathyroidism	3–4 paragraphs: definition + psychiatric features + key diagnostic clue + brief management
MCQ	Drug mechanisms; monitoring intervals; specific diagnostic values	Single most correct answer: know exact numbers (ceruloplasmin <0.2, urine copper >100, correction rate 8–10 mEq/L)

Section 4: Recurring Examiner Angles

These specific angles have appeared repeatedly across papers:

1. "Young patient with psychiatric + neurological + hepatic features"

→ Always Wilson's disease. State: KF rings, ceruloplasmin, 24h urine copper, Leipzig score.

2. "Patient on lithium develops depression/cognitive slowing"

→ Lithium-induced hypothyroidism. State: continue lithium + add levothyroxine. Do not stop lithium.

3. "Patient on olanzapine/clozapine gains weight and develops hyperglycaemia"

→ ADA/ APA monitoring protocol. State: metformin + lifestyle + consider aripiprazole add-on or switch.

4. "Alcohol-dependent patient brought in confused"

→ Wernicke's encephalopathy. State: IV thiamine before glucose; Pabrinex 500 mg TID; WACO triad.

5. "Chronic alcohol patient with severe anterograde amnesia and confabulation"

→ Korsakoff syndrome. State: mammillary body damage; anterograde > retrograde; confabulation ≠ lying; 50% permanent.

6. "Patient on SSRIs develops confusion and Na = 122 mEq/L"

→ Psychotropic-induced SIADH. State: fluid restriction; correct slowly (max 8–10 mEq/L/day); ODS risk if overcorrected.

7. "Patient with recurrent 'panic attacks' but severe hypertension during episodes"

→ Pheochromocytoma. State: 4Ps; plasma free metanephrines; alpha before beta blockade.

8. "Recurrent abdominal pain + psychiatric symptoms + peripheral neuropathy"

→ Acute intermittent porphyria. State: dark urine; haem arginate; high carbohydrate; unsafe drugs list.

Section 5: Numbers Worth Memorising

VALUE · MEANING

20–42% Hypothyroidism prevalence in long-term lithium users

50–80% Depression prevalence in Cushing's syndrome

20–30% Wilson's disease, psychiatric presentation as first symptom

16% Wernicke's, full triad present

<0.2 g/L Serum ceruloplasmin in Wilson's (low)

>100 mcg/24h Urine copper in symptomatic Wilson's

>250 mcg/g Liver copper in Wilson's (dry weight)

8–10 mEq/L Maximum sodium correction per 24h (SIADH)

500 mg TID × 3 days Pabrinex dose for Wernicke's (European guideline)

4.5 kg Mean weight gain with clozapine

4.2 kg Mean weight gain with olanzapine

0.04 kg Mean weight gain with ziprasidone

25/25/50 Korsakoff prognosis: 25% significant recovery / 25% partial / 50% permanent

4 Ds Pellagra: Dermatitis, Diarrhoea, Dementia, Death

40–60% Depression prevalence in hyperparathyroidism

60–90% Psychiatric symptom prevalence in Addison's disease

Section 6: Topics Commonly Neglected (Worth 5–10 Marks Each)

These topics appear infrequently but reliably, and students often skip them:

1. **Hashimoto's encephalopathy (SREAT)**, steroid-responsive; anti-TPO antibodies; not directly thyroid-hormone-mediated
 2. **Sheehan's syndrome**, postpartum pituitary necrosis; chronic fatigue + depression; missed diagnosis
 3. **Fahr's disease**, basal ganglia calcification in hypoparathyroidism; movement disorder + neuropsychiatric features
 4. **Metformin and B12 deficiency**, drug interaction worth knowing; screen B12 annually in psychiatric patients on metformin
 5. **Lithium and hyperparathyroidism/hypercalcaemia**, serum calcium monitoring; parathyroid gland hyperplasia mechanism
 6. **GLP-1 agonists for antipsychotic-induced obesity**, emerging evidence; semaglutide; increasingly relevant clinically
 7. **Polydipsia in schizophrenia**, distinct from SIADH; low urine osmolality; clozapine may reduce it
 8. **Adult GH deficiency syndrome**, GH replacement improves mood and QoL; post-Sheehan's context
-

Quick Review

EXAM STRATEGY

Read each question, cover the answer, retrieve from memory, then check. Spaced repetition: do this the night before the exam, and again on exam morning. Badges indicate cognitive level, Recall (R), Application (A), Analysis (X).

Q1. What is the most common psychiatric manifestation of hypothyroidism?

R Depression (40–60% of hypothyroid patients). Character: anhedonia, psychomotor retardation, fatigue, cognitive slowing. Often fails to respond to antidepressants without thyroid replacement.

Q2. A patient on long-term lithium develops fatigue, weight gain, and a TSH of 12 mIU/L with normal free T4. What is your management?

A Lithium-induced subclinical/overt hypothyroidism. Management: continue lithium + add levothyroxine (do NOT stop lithium). Target TSH to normal range. Do not sacrifice mood stability for thyroid.

Q3. What is myxedema madness? Who first described it?

R Acute psychiatric manifestation of severe prolonged hypothyroidism, paranoid psychosis, hallucinations, delirium. First described by Asher (1949). Context: severe systemic myxedema (periorbital puffiness, macroglossia, hypothermia, bradycardia).

Q4. Name the four receptor mechanisms by which antipsychotics cause metabolic syndrome.

R (1) H1 histamine antagonism → weight gain (primary); (2) 5-HT_{2C} antagonism → appetite increase; (3) M3 muscarinic antagonism → impaired pancreatic insulin secretion → direct diabetogenic; (4) D2 antagonism → mesolimbic appetite dysregulation.

Q5. A 26-year-old presents with personality disinhibition, dysarthria, and paranoid psychosis. What must you exclude and what are the first three investigations?

A Exclude Wilson's disease. First three: (1) Slit-lamp examination for Kayser-Fleischer rings; (2) Serum ceruloplasmin (<0.2 g/L in Wilson's); (3) 24-hour urine copper (>100 mcg/24h symptomatic).

Q6. What is the gene and chromosome involved in Wilson's disease?

R ATP7B gene on chromosome 13q14. Encodes a copper-transporting ATPase. Autosomal recessive inheritance.

Q7. In Wilson's disease treatment, what is the risk of starting D-penicillamine in a patient with neurological/psychiatric presentation?

A Paradoxical neurological worsening in the first weeks, copper is mobilised from the liver and redistributed to the brain, worsening symptoms. Trientine is preferred over penicillamine for neuropsychiatric Wilson's because it carries lower risk of this deterioration.

Q8. What is the role of zinc in Wilson's disease and why can it not be given simultaneously with chelators?

A Zinc induces metallothionein in intestinal epithelial cells, which binds copper and blocks its absorption. It is used for maintenance therapy and in presymptomatic patients. It cannot be co-administered with penicillamine or trientine because they chelate zinc, reducing both drugs' efficacy.

Q9. State the classic triad of Wernicke's encephalopathy and its frequency of full presentation.

R WACO triad: (W)atching, Ophthalmoplegia (6th nerve palsy, nystagmus); (A)taxia, cerebellar, gait; (C)onfusion, global encephalopathy. Full triad present in only 16% of cases.

Q10. Why must thiamine always be given before glucose in at-risk patients?

A Glucose administration requires thiamine as a cofactor for pyruvate dehydrogenase. In a thiamine-depleted state, IV glucose drives pyruvate accumulation and energy failure in metabolically vulnerable brain regions (mammillary bodies, periaqueductal grey), precipitating or worsening Wernicke's encephalopathy. This is irreversible if not prevented.

Q11. What is the IV thiamine dose for Wernicke's encephalopathy per European guidelines?

R Pabrinex (high-potency parenteral thiamine): 500 mg intravenously three times daily for a minimum of 3 days. Oral thiamine is insufficient, absorption is impaired in malnourished and alcohol-dependent patients.

Q12. List the three cardinal features of Korsakoff syndrome.

R (1) Severe anterograde amnesia (inability to form new memories, cardinal feature); (2) Confabulation, unconscious fabrication of memories, not deliberate lying; (3) Anosognosia, lack of insight into memory impairment.

Q13. What is the prognosis of Korsakoff syndrome?

R 25/25/50 rule: approximately 25% significant recovery, 25% partial recovery, 50% permanent moderate-to-severe disability. Only ~10% make complete recovery. Thiamine maintenance does not reverse established damage but prevents further progression.

Q14. Rank these antipsychotics from highest to lowest weight gain: aripiprazole, clozapine, haloperidol, olanzapine, quetiapine, ziprasidone.

R Clozapine (+4.5 kg) > Olanzapine (+4.2 kg) > Quetiapine (+2.3 kg) > Haloperidol (+0.5 kg) > Aripiprazole (+0.7 kg) > Ziprasidone (+0.04 kg).

Q15. At what intervals should weight/BMI and fasting glucose be checked when starting an antipsychotic, per ADA/ APA guidelines?

R Weight/BMI: baseline, then at 4, 8, and 12 weeks, then at every visit for the first year (minimum). Fasting glucose: baseline, 12 weeks, then annually. Fasting lipids: baseline, 12 weeks, then every 5 years (or annually in high-risk).

Q16. First-line pharmacological treatment for antipsychotic-induced weight gain?

R Metformin 500 mg twice daily, titrated to 1000 mg twice daily. Reduces weight by 2–3 kg on average, improves insulin sensitivity, and reduces HbA1c. Safe in combination with antipsychotics.

Q17. Which two psychotropics carry the highest risk of SIADH, and what is the relative risk between them?

A Carbamazepine and oxcarbazepine. Oxcarbazepine causes SIADH more frequently than carbamazepine, this is the classic exam trap. Both directly potentiate ADH secretion/ action. SSRIs are the most common drug class overall due to prescribing volume, but oxcarbazepine has the highest per-drug risk among AEDs/ mood stabilisers.

Q18. What is osmotic demyelination syndrome (ODS) and how is it prevented?

A ODS (central pontine myelinolysis) is irreversible demyelination of the pons (and extrapontine areas) caused by overly rapid correction of chronic hyponatraemia. It presents as locked-in syndrome, spastic quadriplegia, and pseudobulbar palsy. Prevention: correct

serum sodium at a maximum rate of 8–10 mEq/L per 24 hours (maximum 18 mEq/L in 48 hours). High-risk patients: chronic alcoholics, malnourished, hypokalemia, liver disease.

Q19. What are the "4 Ps" of pheochromocytoma and how does it differ from panic disorder?

R 4 Ps: Paroxysmal hypertension, Palpitations, Perspiration (diaphoresis), Pallor/Pain (headache). Differs from panic disorder by: severe hypertension (>200 mmHg systolic) during episodes; pallor not flushing; physical triggers (posture, exercise); failure to respond to anxiolytics/SSRIs; elevated 24h urinary/plasma metanephrines.

Q20. What is the diagnostic test of choice for pheochromocytoma?

R Plasma free metanephrines (sensitivity ~97%, specificity ~85%), test of choice for initial biochemical screening. Alternative: 24-hour urinary metanephrines and catecholamines. Imaging (CT/MRI adrenals) only after biochemical confirmation.

Q21. State the "bones, stones, groans, psychic moans" tetrad and its most common psychiatric manifestation.

R Hyperparathyroidism tetrad: Bones (osteitis fibrosa, fractures), Stones (nephrolithiasis), Groans (GI: nausea, constipation, pancreatitis), Psychic moans (psychiatric). Most common psychiatric manifestation: depression (40–60%). Mechanism: hypercalcaemia reduces neuronal excitability and alters monoamine neurotransmitter release.

Q22. Name the classic triad of acute intermittent porphyria and its diagnostic urine finding.

R Triad: (1) Severe colicky abdominal pain; (2) Peripheral neuropathy (motor > sensory); (3) Psychiatric manifestations (anxiety, psychosis, delirium). Urine finding: dark red-brown urine on standing, porphobilinogen (PBG) oxidation. Confirm with urine porphobilinogen (quantitative).

Q23. Name three safe and three unsafe psychiatric drugs in acute intermittent porphyria.

R Safe: sertraline (SSRI), haloperidol (antipsychotic), gabapentin (anticonvulsant/anxiolytic). Unsafe: carbamazepine, amitriptyline (TCA), phenobarbitone (anticonvulsant). Treatment of acute attack: haem arginate (Normosang) IV + high carbohydrate (400 g/day) + levetiracetam for seizures.

Q24. What are the psychiatric features of pellagra and what drug commonly induces it?

R Psychiatric features: anxiety, irritability, depression, cognitive impairment progressing to dementia, psychosis, delirium. Caused by niacin (vitamin B3) deficiency. Drug-induced:

isoniazid (INH) blocks pyridoxine (B6) → impairs tryptophan-to-niacin conversion → pellagra. Prevented by co-prescribing pyridoxine with INH. Classic presentation: 4 Ds (Dermatitis, Diarrhoea, Dementia, Death).

Q25. What are the neuropsychiatric features of vitamin B12 deficiency?

R Depression (may be first symptom); cognitive impairment (mild to dementia-like, reversible if treated early); megaloblastic madness (psychosis, paranoia, hallucinations); peripheral neuropathy; subacute combined degeneration of the spinal cord (posterior + lateral columns → sensory ataxia + spastic paraparesis). Drug cause: metformin blocks ileal B12 absorption, screen annually in psychiatric patients on long-term metformin.

Q26. What is the most common psychiatric manifestation of Cushing's syndrome and what is the suicide risk?

R Depression is the most common, occurring in 50–80% of patients. Character: prominent anhedonia, psychomotor retardation, cognitive impairment, hippocampal atrophy. Suicide attempt risk: 4–10% of patients with Cushing's syndrome. This makes it one of the most high-risk endocrine-psychiatric comorbidities.

Q27. A patient with SLE is started on prednisolone 80 mg/day. After 5 days she develops elevated mood, decreased sleep, and grandiosity. What is the diagnosis and management?

A Steroid-induced mania ("steroid mania"). Occurs early in course, dose-related (>80 mg/day = 18.4% risk). Management: (1) Reduce prednisolone dose if medically permissible, first and most important step; (2) Antipsychotic for acute mania control (olanzapine, haloperidol); (3) Mood stabiliser (valproate or lithium) if steroids cannot be tapered; (4) Lithium has prophylactic role if repeated steroid courses anticipated.

Q28. What is the West Haven Grade at which asterixis (liver flap) first appears, and at which grade does it disappear?

R Asterixis first appears at Grade 2 (lethargic, disoriented, personality change). It disappears at Grade 4 (coma), because asterixis requires voluntary muscle tone, which is absent in coma. This is a key clinical landmark: onset of asterixis signals Grade 2 and the need to escalate treatment.

Q29. What is the most common precipitant of acute hepatic encephalopathy in cirrhotic patients, and what is the first-line treatment?

R Most common precipitant: spontaneous bacterial peritonitis (SBP), always check with diagnostic paracentesis (neutrophils >250/mm³). First-line treatment: lactulose 15–30 mL three times daily, titrated to 2–3 soft stools per day. Second step: add rifaximin 550 mg twice

daily for recurrent/refractory HE. Protein restriction is outdated, maintain 1.2–1.5 g/kg/day.

Q30. What are the three organ systems lithium affects long-term that require routine monitoring, and what specific test is used for each?

R (1) Thyroid, TFTs (TSH + free T4): 6-monthly for year 1, then annually; (2) Kidneys, RFTs (creatinine, eGFR) + urinalysis: 6-monthly; lithium level; (3) Parathyroid, serum calcium: annually (lithium raises PTH set-point → parathyroid hyperplasia → hypercalcaemia → nephrocalcinosis). Plus ECG at baseline and with dose changes (cardiac effect).

Rapid Concept Index

CONCEPT · ONE-LINE ANSWER

Asher's contribution Described myxedema madness (1949)

Casal's necklace Photosensitive dermatitis of pellagra around neck

Face of giant panda sign MRI midbrain sign in Wilson's disease

Leipzig score Diagnostic scoring system for Wilson's disease

SREAT Steroid-responsive encephalopathy with autoimmune thyroiditis (Hashimoto's)

Sheehan's syndrome Postpartum pituitary necrosis → hypopituitarism → depression/fatigue

Fahr's disease Basal ganglia calcification in hypoparathyroidism → neuropsychiatric features

Cretinism Congenital hypothyroidism → irreversible intellectual disability if untreated

Sick euthyroid syndrome TFT abnormalities from systemic illness, not true thyroid disease

TBG rule Thiamine Before Glucose, Wernicke's prevention

WACO Wernicke's triad: W-atching (ophthalmoplegia), A-taxia, C-onfusion

4Ds Pellagra: Dermatitis, Diarrhoea, Dementia, Death

4Ps Pheochromocytoma: Paroxysmal hypertension, Palpitations, Perspiration, Pallor

SIADH correction rule Max 8–10 mEq/L/day, faster = ODS

Polydipsia in schizophrenia Compulsive; urine osmolality LOW (distinguishes from SIADH)

Metformin + B12 Metformin blocks ileal B12 absorption, screen annually

Aripiprazole + prolactin Aripiprazole lowers prolactin (partial D2 agonist), can normalise hyperprolactinaemia

Clozapine polydipsia Clozapine may reduce psychogenic polydipsia in schizophrenia

Zinc + chelator Never co-administer, mutual antagonism

Alpha before beta Alpha-blockade before beta in phaeochromocytoma management

CVA TBI

Paper IV · Neurology, Medicine & Recent Advances. Six study modes, from notes to quick review.

Study Notes

SECTION 1: STROKE AND PSYCHIATRY

1.1 Epidemiology of Neuropsychiatric Complications Post-Stroke

Stroke is one of the leading causes of acquired disability worldwide. Beyond motor and sensory deficits, neuropsychiatric complications are pervasive and often under-recognized. Up to 70–80% of stroke survivors will develop at least one neuropsychiatric syndrome within the first year. These syndromes contribute independently to functional disability, caregiver burden, and mortality.

Key prevalence figures (exam-relevant):

- Post-stroke depression (PSD): 30–50% (lifetime); 25–35% in acute phase
 - Post-stroke anxiety: 20–25%
 - Post-stroke psychosis: ~5% (hallucinations, delusions)
 - Post-stroke mania: rare, ~1–2%; more common with right hemisphere lesions
 - Vascular cognitive impairment (VCI): 20–30% at 3 months; up to 50% at 5 years
 - Post-stroke apathy: 20–40% (often overlapping with depression)
 - Emotional incontinence / pseudobulbar affect: 15–20%
 - Anosognosia: 10–30% (especially with right hemisphere infarcts)
-

1.2 Post-Stroke Depression (PSD)

DEFINITION AND DIAGNOSTIC CHALLENGE

PSD refers to a major or minor depressive episode occurring in the context of stroke. DSM-5 classifies it under "Depressive Disorder Due to Another Medical Condition (Stroke)", not as a primary MDD. This distinction has treatment implications: somatic symptoms of stroke (fatigue, sleep disturbance, psychomotor slowing) overlap heavily with depressive criteria, making purely symptom-based diagnosis unreliable. Emphasis should be placed on cognitive-affective symptoms: anhedonia, hopelessness, worthlessness, suicidal ideation.

ROBINSON'S LEFT FRONTAL HYPOTHESIS (CRITICAL FOR EXAM)

Robert Robinson and colleagues at Johns Hopkins (1980s–1990s) proposed the neuroanatomical model for PSD. The central thesis:

KEY INSIGHT

Lesions in the left anterior (frontal) cortex, particularly left dorsolateral prefrontal cortex (DLPFC) and left basal ganglia, are associated with the highest rates and severity of depression after stroke.

The proposed mechanism:

- Left DLPFC → projects to limbic structures via the fronto-striato-thalamic-cortical circuit
- Stroke disrupts descending serotonergic and noradrenergic projections from the frontal cortex to the limbic system
- The left hemisphere, being dominant for approach-related positive affect regulation, when damaged, leads to unopposed negative affect from the right
- Proximity of lesion to the frontal pole (anterior pole) correlates with severity of depression in the **left** hemisphere

Evidence supporting Robinson:

- Early studies (1984, 1987) showed left frontal lesions had Hamilton Depression scores 2–3x higher than right frontal lesions
- The inverse was true for mania, right hemisphere lesions correlated more strongly with manic episodes
- Lesion-to-frontal-pole distance (on CT/MRI) was inversely correlated with depression severity for left hemisphere strokes

Critiques of Robinson's hypothesis:

- Later meta-analyses (Carson et al., 2000; Bhogal et al., 2004) found the left-frontal relationship was most robust in hospital-based samples (selection bias)
- Community-based studies showed weaker or absent lateralization
- The relationship may be strongest in the first 1–3 months post-stroke
- Methodological heterogeneity: different rating scales, imaging modalities, time points

Current consensus: Robinson's hypothesis is historically important and continues to be cited in exams. The left-frontal relationship is real but not absolute, PSD is multifactorial (neuroanatomical, psychosocial, premorbid vulnerability).

PREVALENCE DETAILS

TIME POST-STROKE · PREVALENCE OF PSD

Acute (0–2 weeks) ~25–30%

3 months ~30–35%

6 months ~25%

1 year ~20–25%

3–5 years ~20% (plateau)

Note: PSD can develop at any time post-stroke. Late-onset PSD (>6 months) may be more related to psychosocial adjustment and disability burden.

RISK FACTORS FOR PSD

Neurological:

- Lesion location: left frontal, left basal ganglia
- Lesion volume (larger = higher risk)
- Cortical vs subcortical: cortical involvement increases risk
- Ischemic > hemorrhagic (though both occur)

Psychosocial:

- Pre-stroke depression or anxiety (strongest predictor)
- Poor social support
- Female sex
- Cognitive impairment
- Functional disability (ADL dependence)
- Living alone

CLINICAL PRESENTATION

PSD may present with atypical features compared to primary MDD:

- More prominent **apathy** (overlapping syndrome)
- Emotional lability (crying spells without full sadness)
- Greater neurovegetative symptoms
- Higher rates of **executive dysfunction** complicating insight
- Variable suicidal ideation (present, but less common than primary MDD)

Differentiate PSD from **adjustment disorder**: PSD has biological substrate; both may be clinically similar acutely.

ASSESSMENT TOOLS FOR PSD

1. **Hamilton Rating Scale for Depression (HDRS)**, gold standard; limitations with somatic items
2. **Montgomery-Asberg Depression Rating Scale (MADRS)**, less confounded by somatic symptoms; preferred in stroke
3. **Patient Health Questionnaire-9 (PHQ-9)**, validated in stroke; practical for screening
4. **Geriatric Depression Scale (GDS)**, useful in elderly stroke survivors

5. Visual Analogue Scale for Depression, for aphasic patients

TREATMENT OF PSD

Pharmacological:

DRUG	EVIDENCE	NOTES
Sertraline	RCT evidence (Murray et al.); 50–200 mg	First choice; well-tolerated
Fluoxetine	FLAME trial (positive for motor AND mood)	Motor recovery benefit noted
Nortriptyline	Outperformed fluoxetine in some RCTs (Robinson)	Caution: anticholinergic, cardiac risk
Citalopram	Good evidence; caution with QTc prolongation	Useful in elderly
Mirtazapine	Useful when insomnia + anorexia prominent	Sedating; weight gain
Methylphenidate	Rapid response; useful in medically compromised	Off-label; caution

Duration: Treat for minimum 6–12 months after response. Relapse common if stopped early.

Non-pharmacological:

- Cognitive Behavioral Therapy (CBT), modified for aphasia/cognitive deficits
- Problem-solving therapy
- Motivational interviewing
- Exercise, RCT evidence for post-stroke depression reduction
- Social support interventions
- Caregiver psychoeducation

Prevention: Sertraline and escitalopram have been trialed as prophylactic agents; evidence is mixed but promising for high-risk patients (left frontal lesion, pre-stroke depression).

1.3 Post-Stroke Anxiety

- Prevalence: 20–25% at 3 months; often co-occurs with depression (50% comorbidity)
- More common with **right hemisphere** lesions (some data) and cortical lesions
- Generalized Anxiety Disorder pattern most common; PTSD also possible
- Assessment: Hamilton Anxiety Scale, GAD-7
- Treatment: SSRIs (first line), buspirone, CBT

- Benzodiazepines: caution in stroke (fall risk, cognitive effects, respiratory depression with brainstem strokes)
-

1.4 Post-Stroke Psychosis

- Rare: 3–5% of stroke survivors
 - More common with **right hemisphere lesions**, especially temporal-parietal-occipital regions
 - Also associated with subcortical lesions (thalamus, caudate)
 - **Hallucinations**: usually visual > auditory; peduncular hallucinosis (vivid visual hallucinations after brainstem / thalamic strokes) is a classic presentation
 - **Delusions**: persecutory, referential; capgras syndrome reported with bilateral lesions
 - Often brief and resolves; organic basis means lower antipsychotic doses may suffice
 - Assess for delirium (first exclude)
 - Management: low-dose risperidone or quetiapine; avoid typical antipsychotics if possible (extrapyramidal risk, especially with basal ganglia lesions)
-

1.5 Post-Stroke Mania

- Rare (~1–2%); associated with right hemisphere lesions
 - **Neuroanatomy**: right basal temporal region, orbitofrontal cortex, right caudate, thalamus
 - Mechanism: release of left-hemisphere from right-hemisphere tonic inhibition; or disruption of limbic regulatory circuits
 - Features: euphoria, decreased need for sleep, grandiosity, pressured speech, impulsive behavior
 - May occur weeks to months after stroke
 - **Secondary mania** criteria (Starkstein & Robinson): euphoric mood + 2 of: increased activity, grandiosity, decreased sleep, increased speech, distractibility, reckless behavior
 - Treatment: mood stabilizers (valproate preferred in neurological setting), atypical antipsychotics; lithium less favored due to narrow TI and renal concerns in elderly
-

1.6 Post-Stroke Apathy

Definition: Apathy is a motivational syndrome, diminished goal-directed behavior, reduced emotional reactivity, and decreased cognitive engagement, occurring in the absence of significant subjective distress (distinguishing it from depression).

Prevalence: 20–40% post-stroke; often persists longer than depression

Neuroanatomy:

- Anterior cingulate cortex (ACC), critical hub for motivation generation
- Basal ganglia (striatum, especially caudate)
- Frontal white matter tracts
- Infarcts in these areas directly cause apathy

Assessment:

- **Apathy Evaluation Scale (AES)**, most validated
- **Neuropsychiatric Inventory (NPI)**, apathy subscale
- **Starkstein Apathy Scale**

Distinguishing Apathy from Depression:

FEATURE	APATHY	DEPRESSION
Subjective distress	Absent	Present
Mood	Neutral / flat	Dysphoric / sad
Self-criticism	Rare	Common
Hopelessness	Absent	Characteristic
Insight	May be limited	Usually preserved
Response to reward	Absent	Often preserved

Treatment:

- No proven pharmacological treatment (as of 2026)
- Methylphenidate and rivastigmine have some evidence
- Dopamine agonists (bromocriptine), small studies
- Behavioral activation, structured routines, caregiver coaching
- Management of co-occurring depression improves apathy secondarily

1.7 Emotional Incontinence / Pseudobulbar Affect (PBA)

Definition: Pseudobulbar affect is pathological emotional expression, involuntary, uncontrollable episodes of laughing or crying (or both) that are often incongruent with the patient's subjective emotional state.

Mechanism:

- Loss of voluntary cortical inhibition of brainstem (pontine) motor-emotional circuits
- Specifically: damage to corticobulbar pathways disrupts inhibitory descending signals to the brainstem's emotional integration center
- Serotonin and glutamate dysregulation implicated

Associated conditions: Stroke (most common), TBI, ALS, MS, Parkinson's disease, dementias

Clinical features:

- Episodes typically brief (seconds to minutes), then full recovery
- Patient often embarrassed and aware the reaction is excessive
- Distinguish from ictal laughter (gelastic seizures), usually more prolonged, associated with other ictal features
- Distinguish from labile mood in bipolar disorder, no loss of control in bipolar

Assessment: CNS-LS (Center for Neurologic Study, Lability Scale)

Treatment:

- **Dextromethorphan/Quinidine (Nuedexta)**, FDA-approved (2010); the standard pharmacological treatment; quinidine inhibits CYP2D6 metabolism of dextromethorphan (which is the active agent); mechanism: sigma-1 receptor modulation + NMDA antagonism
 - SSRIs (fluoxetine, sertraline), often first used clinically; good evidence
 - Amitriptyline, older evidence; effective
 - Behavioral strategies: distraction, controlling breathing
-

1.8 Anosognosia

Definition: Failure of a patient to recognize or acknowledge their own neurological deficit (e.g., hemiplegia, hemianopia, aphasia).

Prevalence: 10–30% post-stroke; most common with right hemisphere strokes → left-sided neglect + anosognosia for left hemiplegia

Neuroanatomy:

- Right parietal cortex (especially right supramarginal gyrus, inferior parietal lobule)
- Thalamus, basal ganglia connections
- Frontal lobe involvement for metacognitive awareness

Mechanism: Disruption of body schema and multimodal integration; the right parietal lobe is dominant for body awareness and spatial attention

Clinical significance:

- Interferes with rehabilitation participation (patient denies deficits, refuses therapy)
- Creates caregiver conflict
- Prognosis: may resolve as stroke recovery progresses; persistent anosognosia = poor functional outcome

Related syndromes:

- **Anosodiaphoria:** acknowledges deficit but shows inappropriate indifference
 - **Anton's syndrome:** cortical blindness with denial of visual loss (occipital lesion)
 - **Neglect (hemispatial):** inattention to contralateral space (not the same as anosognosia, but often co-occurs)
-

1.9 Vascular Cognitive Impairment (VCI)

Spectrum:

1. **Vascular Mild Cognitive Impairment (VaMCI):** Cognitive decline in ≥ 1 domain, not affecting daily function significantly, attributed to vascular disease
2. **Vascular Dementia (VaD):** Cognitive decline sufficient to impair daily function, attributed to cerebrovascular disease
3. **Mixed Dementia:** VaD + Alzheimer's pathology (most common form in clinical practice)

Subtypes of VaD:

- **Multi-infarct dementia:** multiple large cortical infarcts; stepwise decline
- **Strategic infarct dementia:** single infarct in critical location (thalamus, basal forebrain, angular gyrus); profound but focal deficits
- **Small vessel disease / Subcortical ischemic VaD:** leukoaraiosis, lacunar infarcts; prominent executive dysfunction, gait disturbance, urinary symptoms; Binswanger's disease is an extreme form
- **CADASIL:** Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy, NOTCH3 mutation; genetic subcortical VaD; migraine with aura, recurrent strokes, psychiatric symptoms

Clinical profile of VaD (vs Alzheimer's):

- Abrupt onset, stepwise progression (vs gradual in AD)
- Executive dysfunction > memory (vs memory-first in AD)
- Gait disturbance early (vs late in AD)
- Focal neurological signs (vs absent in early AD)
- Preserved recall with cuing (vs impaired in AD)
- Psychiatric symptoms: depression, apathy, emotional lability more common in VaD

Neuroimaging:

- MRI: white matter hyperintensities (WMH), lacunes, cortical infarcts, atrophy
- **Fazekas scale:** quantifies periventricular and deep WMH (0–3)
- **NINDS-AIREN criteria** (research): cerebrovascular disease + cognitive decline + temporal relationship between stroke and cognitive change

Management of VaD:

- Vascular risk factor control (primary intervention)
 - Antiplatelet therapy (aspirin, clopidogrel)
 - Statins, antihypertensives
 - Cholinesterase inhibitors (donepezil, rivastigmine): modest benefit for VaD (similar to AD); evidence from RCTs
 - Memantine: some evidence
 - Psychiatric comorbidities treated as above
-

SECTION 2: NEUROANATOMICAL CORRELATES OF PSYCHIATRIC SYNDROMES

2.1 Frontal Lobe Syndromes

The frontal lobe comprises ~30% of cortical surface. Three main functional subdivisions produce distinct psychiatric syndromes when damaged.

2.1.1 DORSOLATERAL PREFRONTAL CORTEX (DLPFC) SYNDROME

Anatomy: Broadmann areas 9, 10, 45, 46; projects to caudate nucleus

Functions: Working memory, executive function, planning, set-shifting, abstract reasoning, verbal fluency

Lesion syndrome (Dysexecutive Syndrome):

- Impaired planning and organization (Tower of London test failure)
- Poor set-shifting (WCST, Wisconsin Card Sorting Test failure)
- Reduced verbal fluency (FAS test impaired)
- Working memory deficits
- Difficulty with abstract reasoning
- **Pseudodepression:** flat affect, apathy, reduced motivation; resembles depression but without dysphoric mood

Associated conditions: ADHD (under-activation), Schizophrenia (hypofrontality), Frontotemporal Dementia, DLPFC strokes, Parkinson's disease

2.1.2 ORBITOFRONTAL CORTEX (OFC) SYNDROME

Anatomy: Broadmann areas 11, 12, 13, 14; projects to amygdala, nucleus accumbens, mediodorsal thalamus

Functions: Reward processing, social cognition, impulse inhibition, emotional regulation, decision-making with social cues

Lesion syndrome (Pseudopsychopathic Syndrome / Orbito-frontal Syndrome):

- Disinhibition, socially inappropriate behavior, sexual remarks, reckless behavior
- Impulsivity, poor response inhibition (Go-No-Go test failure)
- Poor decision-making in social contexts (Somatic Marker Hypothesis, Damasio: inability to use emotional signals to guide decisions → "Iowa Gambling Task" failure)
- Grandiosity, euphoria (can mimic mania)
- Hypersexuality
- Labile affect
- Reduced concern for social consequences
- **Classic case:** Phineas Gage (1848), traumatic damage to orbitofrontal and ventromedial PFC; personality change from responsible to impulsive, irresponsible

Associated conditions: Bipolar disorder (OFC dysfunction), antisocial personality, addiction (OFC governs reward valuation), TBI affecting frontal poles

2.1.3 MEDIAL PREFRONTAL / ANTERIOR CINGULATE CORTEX (ACC) SYNDROME

Anatomy: Broadmann area 24 (anterior cingulate), medial surfaces; projects to supplementary motor area, limbic structures

Functions: Motivated behavior, error monitoring, conflict detection, attention allocation, initiation

Lesion syndrome (Akinetic Mutism / Motivational Deficits):

- **Akinetic mutism** (severe): patient is awake, eyes open, tracks objects, but does not speak, move, or respond, extreme form of amotivation
- **Apathy** (moderate): loss of spontaneous behavior, reduced emotional expression
- **Abulia:** intermediate state between akinetic mutism and apathy
- Reduced initiation without explicit prompting
- Preserved cognition when prompted vs DLPFC syndrome

Associated conditions: Anterior cerebral artery stroke (bilateral ACA infarct → classic akinetic mutism), deep frontal meningiomas, bipolar depression (ACC hyperactivity in some models), OCD (ACC hyper-activation)

2.1.4 FRONTAL LOBE TESTS (BEDSIDE)

TEST	WHAT IT ASSESSES	FRONTAL AREA
Verbal Fluency (FAS / Animals)	Word generation, executive search	DLPFC
Luria Motor Series (fist-edge-palm)	Motor programming, sequencing	SMA / Pre-motor
Go-No-Go	Response inhibition	OFC / Pre-frontal

TEST	WHAT IT ASSESSES	FRONTAL AREA
Grasp reflex	Release of primitive reflexes	Pre-frontal
Proverb interpretation	Abstract reasoning	DLPFC
Similarities	Abstract categorization	DLPFC
Trail Making Test B	Set-shifting	DLPFC
Frontal Assessment Battery (FAB)	6-item bedside frontal battery (total / 18)	Frontal lobe broadly

Frontal Assessment Battery (FAB), 6 components:

1. Similarities (conceptualization)
2. Lexical fluency (mental flexibility)
3. Luria motor series (programming)
4. Conflicting instructions (sensitivity to interference)
5. Go-No-Go (inhibitory control)
6. Prehension behavior (environmental autonomy)

Score $\leq 12/18$ suggests frontal dysfunction.

2.2 Parietal Lobe Syndromes

DOMINANT (LEFT) PARIETAL LESIONS

Gerstmann Syndrome (angular gyrus, BA39):

- Finger agnosia
- Left-right disorientation
- Agraphia
- Acalculia

(Mnemonic: FLAG, Finger agnosia, L-R disorientation, Agraphia, aGraphia → wait, use "Four A's of Gerstmann": Agraphia, Acalculia, Agnosia for fingers, Aleft-right disorientation)

Apraxia: Ideomotor apraxia (cannot mimic gestures), ideational apraxia (cannot sequence complex actions), dominant parietal

Aphasia (Wernicke's): If extending to posterior temporal/superior temporal sulcus

NON-DOMINANT (RIGHT) PARIETAL LESIONS

Hemispatial Neglect: Inattention to left visual/motor space

Anosognosia: As above

Dressing Apraxia: Cannot dress due to spatial orientation failure

Constructional Apraxia: Cannot draw/copy figures (clock test, pentagon copying)

Amorphosynthesis: Simultaneous extinction; unable to perceive two simultaneous stimuli

2.3 Temporal Lobe Syndromes

DOMINANT (LEFT) TEMPORAL

- Wernicke's aphasia: fluent but incomprehensible speech; poor comprehension; paraphasias
- Verbal memory impairment (left hippocampus)
- Anomia (temporal tip)

NON-DOMINANT (RIGHT) TEMPORAL

- Non-verbal memory impairment (faces, music, spatial patterns)
- Prosopagnosia (right occipito-temporal)
- Amusia

BILATERAL / MEDIAL TEMPORAL

- **Korsakoff-like amnesia:** bilateral hippocampal damage
- **Urbach-Wiethe disease:** bilateral amygdala calcification → fearlessness, social behavior changes

TEMPORAL LOBE EPILEPSY / KLÜVER-BUCY SYNDROME

Bilateral anterior temporal lobe destruction (amygdala + anterior temporal):

- Hyperorality
- Hypersexuality
- Placidity (loss of fear, rage)
- Visual agnosia
- Hypermetamorphosis (excessive exploration of objects)

Interictal Personality Changes (Geschwind Syndrome) with temporal lobe epilepsy:

- Hypergraphia
 - Religiosity
 - Hyposexuality
 - Viscosity (circumstantial thinking)
 - Philosophical preoccupation
-

2.4 Lesion-Psychiatric Syndrome Summary Table

LESION LOCATION · PSYCHIATRIC/BEHAVIORAL SYNDROME

Left DLPFC Pseudodepression, dysexecutive syndrome

Right DLPFC Spatial working memory deficit

Orbitofrontal Pseudopsychopathic, disinhibition

Medial PFC / ACC Akinetic mutism, apathy, abulia

Left temporal Wernicke's aphasia, verbal memory loss

Right temporal Non-verbal memory, prosopagnosia

Right parietal Neglect, anosognosia, dressing apraxia

Left parietal Gerstmann syndrome, ideomotor apraxia

Left frontal Post-stroke depression (Robinson)

Right frontal/basal Post-stroke mania

Bilateral amygdala Klüver-Bucy, fearlessness

Bilateral hippocampi Dense anterograde amnesia

Thalamus Strategic infarct dementia, Korsakoff-like

Brainstem/cerebellum Peduncular hallucinosis, PBA

SECTION 3: TRAUMATIC BRAIN INJURY (TBI) AND NEUROPSYCHIATRY

3.1 Classification of TBI

TBI is classified by severity using the **Glasgow Coma Scale (GCS)** assessed at 30 minutes post-injury (or at emergency presentation):

SEVERITY	GCS SCORE	LOC	PTA	ADDITIONAL FEATURES
Mild	13–15	< 30 minutes	< 24 hours	No imaging abnormality usually
Moderate	9–12	30 min – 24 hrs	1–7 days	May have structural injury
Severe	3–8	> 24 hours	> 7 days	Structural abnormality; ICU management

GCS Components:

- Eye opening: 1–4
- Verbal response: 1–5
- Motor response: 1–6
- Total: 3–15 (3 = worst; 15 = normal)

Alternative classification markers:

- **Post-Traumatic Amnesia (PTA):** period of confusion and memory impairment after TBI; Galveston Orientation and Amnesia Test (GOAT) for assessment
- **Loss of Consciousness (LOC):** duration correlates with severity

Additional severity markers:

- **Neuroimaging:** CT/MRI findings (hemorrhage, contusion, diffuse axonal injury)
 - **Biomarkers:** S100B, GFAP, neuron-specific enolase, elevated indicate injury; GFAP most specific
 - **IMPACT score,** Prognostic model for severe TBI
-

3.2 Acute Psychiatric Effects of TBI

ACUTE CONFUSIONAL STATE / DELIRIUM POST-TBI

- Almost universal with moderate-severe TBI; variable with mild
- Mechanism: neuroinflammation, diffuse axonal injury, neurotransmitter dysregulation
- Features: disorientation, agitation, fluctuating consciousness, post-traumatic amnesia
- Management: orientation aids, quiet environment, minimize sedation, low-dose antipsychotics if agitation

ACUTE EMOTIONAL/BEHAVIORAL CHANGES

- Agitation: up to 70% in ICU setting post-severe TBI
 - Emotional lability
 - Disinhibition
 - Anxiety/fear
-

3.3 Post-Concussion Syndrome (PCS)

Definition: A constellation of symptoms persisting beyond the expected recovery period (>1–3 months) after mild TBI (concussion).

DSM-5: Listed as "Neurocognitive Disorder Due to Traumatic Brain Injury" (mild form)

ICD-10: Post-concussion syndrome (F07.2), explicitly coded

Symptoms Triad:

1. **Somatic:** headache (most common, tension-type pattern), dizziness, fatigue, sleep disturbance, photophobia, phonophobia, visual disturbance
2. **Cognitive:** memory problems, poor concentration, slow processing, word-finding difficulty
3. **Affective/Behavioral:** irritability, anxiety, depression, emotional lability, reduced frustration tolerance

Pathophysiology:

- Neurometabolic cascade (Giza & Hovda): ionic flux, excitotoxicity, mitochondrial dysfunction, creates a period of neuronal vulnerability
- Cerebral blood flow autoregulation disruption
- Neuroinflammation
- Psychological factors (health anxiety, avoidance, litigation)
- The biopsychosocial model applies: biological injury + psychological response + social reinforcement

Prognosis:

- 80–90% of concussions resolve within 7–10 days
- 10–20% develop PCS
- Female sex, pre-existing headaches / anxiety / depression, lower education, prior concussion, negative expectations (nocebo effect) predict prolonged recovery
- Most PCS resolves within 3 months; <5% persist beyond 1 year

Management:

- **Cognitive rest** (brief, then graduated return to activity, "SCAT5 Return to Play Protocol")
- Treat specific symptoms: headache (amitriptyline, topiramate), sleep (melatonin, trazodone), mood (SSRI)
- CBT for health anxiety component
- Occupational therapy for cognitive rehabilitation
- Avoid prolonged rest, increases symptom perpetuation
- Gradual return to school / work protocol
- **Second Impact Syndrome** (see 3.7)

3.4 Chronic Traumatic Encephalopathy (CTE)

Definition: A progressive neurodegenerative disease caused by repetitive traumatic brain injury (typically sub-concussive and concussive impacts), characterized by accumulation of **hyperphosphorylated tau protein** in perivascular regions.

Context: Described in American football players (NFL), boxers (Dementia Pugilistica), military veterans (blast injury)

Neuropathology:

- **Tau deposits** in neurons, astrocytes, and cell processes in perivascular distribution, perivascular foci at depths of cortical sulci (pathognomonic)
- Diffuse axonal injury
- TDP-43 inclusions in later stages
- CTE is a posthumous diagnosis, requires brain autopsy

Clinical Stages (McKee et al.):

- **Stage I:** Headache, loss of attention, short-term memory deficits
- **Stage II:** Depression, explosivity, impulsivity, executive dysfunction
- **Stage III:** Executive dysfunction, memory loss, visuospatial problems
- **Stage IV:** Dementia, severe behavioral changes, Parkinsonism, speech/swallow difficulties

Behavioral Profile:

- Depression (60–80% in documented cases)
- Impulse control disorder
- Substance abuse
- Aggression/explosivity
- Suicidality
- Paranoia
- Progressive memory loss

Key distinction from Alzheimer's:

- CTE: tau-predominant, frontal>temporal, younger onset, trauma history
- AD: amyloid + tau, hippocampal-predominant, age-related

Diagnosis:

- Currently no in-vivo biomarker validated for CTE (research ongoing: tau PET, plasma phospho-tau217)
- Brain MRI: cavum septum pellucidum (seen in boxers, "punched out"), cerebral atrophy
- Diagnosis requires autopsy; neuropathological criteria published 2016 (McKee)

3.5 Personality Change Due to TBI (DSM-5: Personality Change Due to Another Medical Condition)

Prevalence: 50–80% of moderate-severe TBI survivors show personality changes

DSM-5 Subtypes:

- Labile type: affective instability
- Disinhibited type: impulse control failure (orbitofrontal damage)
- Aggressive type: aggression/irritability
- Apathetic type: marked indifference (frontal / ACC)
- Paranoid type: suspiciousness
- Combined type
- Other / unspecified

Neuroanatomical basis:

- **Frontal lobe damage** (most common in TBI, frontal poles vulnerable to coup-contrecoup against bony skull ridges)
- **Orbitofrontal:** disinhibition, impulsivity
- **DLPFC:** apathy, executive dysfunction
- **Temporal lobes:** emotional dysregulation, memory
- **Anterior temporal + amygdala:** emotional control, aggression threshold

Assessment:

- Frontal Systems Behavior Scale (FrSBe)
- Neuropsychological Behavior and Affect Profile (NBAP)
- Informant-based rating critical (patient often lacks insight)

3.6 TBI: Cognitive Rehabilitation

Core principles:

1. **Neuroplasticity:** The brain retains capacity for functional reorganization; rehabilitation exploits this
2. **Specificity:** Rehabilitation gains are task-specific
3. **Intensity and repetition:** More practice = stronger new connections
4. **Meaningful goals:** Patient-centered, functional goals improve motivation and generalization

Domains targeted:

- **Attention:** Attention Process Training (APT-3)
- **Memory:** External aids (diaries, smartphones), spaced retrieval, errorless learning
- **Executive function:** Goal Management Training, Problem-Solving Therapy
- **Communication:** Speech-language therapy
- **Daily living skills:** Occupational therapy

Errorless learning (particularly for severe memory impairment):

- Eliminate trial-and-error to prevent encoding of errors
- Relies on implicit memory systems (preserved even in severe amnesia)

Compensatory vs restorative strategies:

- **Restorative:** Attempt to restore lost function (cognitive exercises)
- **Compensatory:** Use intact systems to work around deficits (external memory aids)

Cognitive rehabilitation evidence:

- Attention training has best evidence
- Memory strategy training: moderate evidence
- Return to work: vocational rehabilitation programs show benefit

3.7 Aggression Management Post-TBI

Prevalence: 30–50% of moderate-severe TBI survivors; particularly with frontal/temporal damage

Pathophysiology:

- Loss of top-down inhibitory control (PFC → amygdala circuit disrupted)
- Serotonergic dysregulation
- Impaired frustration tolerance
- Pain, sleep deprivation, substance use (comorbid)

Non-pharmacological:

- Cognitive behavior management (CBT for anger)
- Environmental modifications: reduce overstimulation
- Staff education
- Family/caregiver training

Pharmacological:

DRUG	MECHANISM	NOTES
Beta-blockers (Propranolol)	Reduce peripheral arousal; reduce somatic symptoms of anger	Best evidence for post-TBI aggression
SSRIs (Sertraline)	Serotonergic augmentation	Reduce irritability, impulsivity
Valproate	Mood stabilization	For affective aggression; monitor levels
Carbamazepine	Mood stabilization, anti-epileptic	Useful if seizure comorbidity

DRUG	MECHANISM	NOTES
Buspirone	Serotonergic; reduces anxiety-driven aggression	Well tolerated
Amantadine	Dopaminergic; improves arousal and behavior	Phase 3 evidence in acute TBI (NINDS trial)
Antipsychotics	Acute sedation only	Avoid long-term, worsen cognitive recovery

Avoid: Benzodiazepines (paradoxical disinhibition, impair recovery), typical antipsychotics (dopamine blockade impairs neuroplasticity, haloperidol shown to worsen TBI outcomes in animal models)

3.8 TBI and Substance Use

Bidirectional relationship:

- Pre-injury: Intoxication at time of injury (alcohol in 40–50% of TBI cases)
- Post-injury: Substance use increases after TBI; mechanisms include self-medication (pain, mood, sleep), disinhibition, impaired judgment

Assessment: AUDIT, DAST, validated in TBI populations

Complications:

- Substance use exacerbates neurocognitive deficits
- Increases risk of seizures (alcohol withdrawal)
- Interferes with medications (anticonvulsants, antidepressants)
- Increases re-injury risk

Treatment: Modified MI/CBT for TBI cognitive profile; harm reduction; 12-step programs (adapted); address co-occurring mood/anxiety

3.9 Second Impact Syndrome

Definition: Second impact syndrome (SIS) occurs when an individual sustains a second concussion while still recovering from a previous concussion, leading to catastrophic cerebral swelling.

Mechanism:

- The brain in neurometabolic crisis is vulnerable to loss of vascular autoregulation
- Even a minor second impact → sudden bilateral cerebral swelling → herniation
- Dysautoregulation of cerebrovascular tone → massive vasodilation → malignant edema

Features:

- Typically occurs in young athletes
 - Second impact may be trivial (fall, head bump)
 - Rapid onset of coma (within minutes)
 - Extremely high mortality (~50%) and morbidity
 - Prevention: strict "return to play" protocols; DO NOT return to sport until fully asymptomatic from first concussion
-

SECTION 4: DELIRIUM

4.1 Definition and Core Concepts

Delirium is an acute neuropsychiatric syndrome characterized by:

- **Acute onset and fluctuating course**
- **Inattention** (core feature)
- **Altered level of arousal** OR
- **Disorganized thinking** (disorientation, cognitive disruption)

It is a medical emergency, always indicates acute brain dysfunction with an underlying cause.

DSM-5 Criteria (Delirium, 293.0):

- A. Disturbance in attention (reduced ability to direct, focus, sustain, shift attention) AND awareness (reduced orientation to the environment)
 - B. Disturbance develops over a short period (hours to days), represents a change from baseline, and tends to fluctuate in severity during the day
 - C. An additional disturbance in cognition (memory, language, visuospatial, perception)
 - D. The disturbances are not better explained by another pre-existing neurocognitive disorder, and do not occur in context of severely reduced level of arousal such as coma
 - E. Evidence from history, physical examination, or lab tests that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal, or exposure to toxin (or combination)
-

4.2 Confusion Assessment Method (CAM)

The CAM (Inouye et al., 1990) is the most widely used bedside tool for delirium:

Delirium diagnosis = Feature 1 AND Feature 2 AND (Feature 3 OR Feature 4):

1. **Acute onset and fluctuating course:** Is there evidence of an acute change in mental status from baseline? Does behavior fluctuate during the day?

2. **Inattention:** Does the patient have difficulty focusing attention (easily distracted, loses track of conversation)?
3. **Disorganized thinking:** Is thinking disorganized or incoherent (rambling, irrelevant conversation, unclear flow)?
4. **Altered level of consciousness:** Any level other than alert (vigilant, lethargic, stuporous, comatose)?

Sensitivity: 94–100%; Specificity: 90–95%

CAM-ICU: Modified for non-verbal ICU patients using non-verbal assessment of attention and thinking.

4.3 Delirium Subtypes

SUBTYPE	FEATURES	PREVALENCE	PROGNOSIS	DETECTION RISK
Hyperactive	Agitation, restlessness, combativeness, calling out, pulling lines	25%	Better prognosis	Easily detected
Hypoactive	Withdrawn, somnolent, quiet, reduced responsiveness	50%	Worse prognosis	Often missed
Mixed	Fluctuates between hyper and hypo	25%	Intermediate	Variable

Key exam point: Hypoactive delirium is the most common and most often missed subtype. It is often mistaken for depression or simply "being tired." Missed hypoactive delirium → worse outcomes.

4.4 Etiology of Delirium

DELIRIUM Mnemonic for causes:

- **D**, Drugs (sedatives, anticholinergics, opioids, steroids, antihistamines, polypharmacy)
- **E**, Eyes/Ears (sensory deprivation)
- **L**, Low oxygen (hypoxia, PE, pneumonia, heart failure)
- **I**, Infection (UTI, pneumonia, meningitis, sepsis)
- **R**, Retention (urinary retention, constipation) / Restraints
- **I**, Intoxication / Injury (TBI, subdural)
- **U**, Underhydration / Undernutrition (electrolyte imbalance: Na, Ca, glucose, Mg)
- **M**, Metabolic (hepatic failure, renal failure, thyroid)

High-risk patient groups:

- Age >70
 - Pre-existing dementia (3–5x risk)
 - Severe illness / ICU admission
 - Post-operative patients (especially cardiac, orthopedic)
 - Vision/hearing impairment
 - Sleep deprivation
 - Pre-existing functional dependence
-

4.5 Pathophysiology of Delirium**Cholinergic Deficit Hypothesis (most established):**

- Acetylcholine is critical for arousal, attention, and REM regulation
- Anticholinergic drugs reliably produce delirium
- High anticholinergic burden correlates with delirium risk
- Physostigmine (acetylcholinesterase inhibitor) reverses some forms of delirium
- Post-operative delirium correlates with central anticholinergic activity in CSF

Neuroinflammation Hypothesis:

- Systemic inflammation (infection, surgery, trauma) → activation of brain microglia
- Pro-inflammatory cytokines (IL-1 β , IL-6, TNF- α) cross blood-brain barrier or signal via vagus nerve
- Microglial activation → disrupted neurotransmission (DA excess, Ach deficit, GABA changes)
- Elderly brains with existing neurodegeneration have primed microglia → lower threshold for delirium

Dopamine Excess Hypothesis:

- Excess dopaminergic activity (relative to cholinergic) → agitation, psychosis in hyperactive delirium
- Basis for haloperidol (D2 blocker) effectiveness

Other neurotransmitters:

- **GABA:** over-activity → sedation (benzodiazepine-induced delirium); under-activity → seizures, alcohol withdrawal delirium
- **Glutamate:** excitotoxicity in severe delirium; NMDA antagonists (ketamine) can cause delirium

Neuroimaging (where available):

- Global cortical hypoperfusion
 - Thalamic and prefrontal dysfunction
 - Disrupted functional connectivity on fMRI
-

4.6 Delirium Management

NON-PHARMACOLOGICAL (FIRST LINE: PREVENTS AND TREATS DELIRIUM)

HELP Program (Hospital Elder Life Program, Inouye): Multicomponent intervention targeting delirium risk factors:

- **Orientation:** Clock, calendar, name boards; frequent reorientation by staff
- **Mobility:** Early mobilization, avoid restraints
- **Sleep:** Sleep hygiene, non-pharmacological sleep protocols, minimize nighttime interruptions
- **Hydration:** Ensure adequate fluid intake; IV hydration if needed
- **Sensory:** Glasses, hearing aids; ensure sensory aids are available
- **Cognitive stimulation:** Engaging activities, conversations

Evidence: HELP program reduces delirium incidence by 33% and duration by 30–40%.

PHARMACOLOGICAL

Important caveat: No pharmacological agent has FDA approval for delirium treatment or prevention. All use is off-label. Non-pharmacological management remains primary.

Haloperidol:

- Most studied; traditional first choice for hyperactive delirium
- Dose: 0.5–1 mg PO/IM; repeat q4h; titrate
- Advantage: parenteral available; no respiratory depression
- Disadvantage: EPS risk; QTc prolongation; avoid in parkinsonism, Lewy body
- Evidence: Not proven to reduce delirium duration/mortality (HOPE-ICU, MINDS trials)

Quetiapine:

- Preferred in elderly, Lewy body risk, when sedation needed
- Dose: 12.5–25 mg; lower starting dose
- Less EPS; more sedating
- Evidence: Some RCTs showing benefit; not definitive

Olanzapine:

- Effective for agitation; higher metabolic side effects
- IM preparation available for acute agitation

Haloperidol vs Quetiapine in practice:

- Haloperidol = parenteral option, acute severe agitation
- Quetiapine = elderly, Parkinson's-adjacent, less EPS needed

Dexmedetomidine (ICU setting):

- Alpha-2 agonist; promotes physiological sleep architecture
- Better outcomes than benzodiazepines in ICU delirium
- Evidence from MENDS2 and MIDEX trials

Melatonin / Ramelteon:

- For delirium prevention, especially sleep disruption component
- Ramelteon 8mg at bedtime: reduced delirium incidence in RCT (Hatta et al., 2014)

AVOID:

- Benzodiazepines (except alcohol withdrawal delirium, seizures, where they are indicated)
- Physostigmine: only for anticholinergic toxidrome reversal
- Restraints: worsen delirium by increasing agitation and anxiety

4.7 Delirium Tremens (DTs)

Covered in detail in NB-08 (Substance Use Disorders). Key cross-reference points:

- DTs occur 48–72 hours after last alcohol use
- Life-threatening: mortality 5–15% if untreated; <1% with treatment
- Treatment: **benzodiazepines** (diazepam, lorazepam, clordiazepoxide) via CIWA-Ar guided protocol
- Thiamine BEFORE glucose
- Signs: autonomic instability (HR, BP, temp, sweating), seizures, hallucinations (typically visual)
- Prophylaxis: CIWA-Ar protocol for high-risk patients
- **Wernicke's encephalopathy** triad: ataxia, ophthalmoplegia, confusion, treat with IV thiamine 100–500 mg TID

4.8 Delirium vs Dementia

FEATURE	DELIRIUM	DEMENTIA
Onset	Acute (hours–days)	Insidious (months–years)
Course	Fluctuating	Progressive (usually)

FEATURE	DELIRIUM	DEMENTIA
Duration	Days to weeks (usually reversible)	Chronic (irreversible usually)
Consciousness	Impaired	Intact (until late)
Attention	Always impaired	Relatively preserved (early)
Psychomotor	Hyperactive or hypoactive	Usually normal (early)
Hallucinations	Common (visual)	Variable
EEG	Diffuse slowing	May be normal (early)
Cause	Identifiable acute medical trigger	Neurodegenerative / vascular / etc.
Reversibility	Yes (with treatment of cause)	Usually no

4.9 Delirium Superimposed on Dementia (DSD)

- Most clinically challenging scenario
- Patients with dementia have 3–5x higher risk of delirium
- Hypoactive delirium is most common and most missed
- Distinguishing DSD from dementia progression: look for acuity of change, fluctuation, new somatic trigger
- Key tool: **DOSS (Delirium Observation Screening Scale)** for nurses; **Nu-DESC**
- Management: address acute trigger; minimize anticholinergic burden; re-establish orientation cues
- **Long-term consequences of DSD:** accelerated cognitive decline, increased mortality, faster dementia progression

SECTION 5: AMNESTIC DISORDERS

5.1 Classification of Amnestic Disorders

Amnestic disorders are characterized by memory impairment as the predominant cognitive deficit, without the broader cognitive deficits of dementia.

DSM-5: "Amnestic Disorder Due to Another Medical Condition" or "Substance-Induced Persisting Amnestic Disorder"

Types of memory affected:

- **Anterograde amnesia:** Cannot form new memories after the causative event (implicit/procedural memory relatively preserved, uses different systems)

- **Retrograde amnesia:** Loss of memories from before the causative event; often follows a temporal gradient (Ribot's Law: recent memories lost first, remote memories preserved longer)
-

5.2 Korsakoff's Syndrome (Amnestic Confabulatory Syndrome)

Etiology: Thiamine (Vitamin B1) deficiency, most commonly due to chronic alcoholism; also: prolonged vomiting (hyperemesis, bariatric surgery), malnutrition, total parenteral nutrition without thiamine supplementation

Neuropathology:

- Bilateral hemorrhagic lesions in **periventricular** and **periaqueductal** gray matter
- **Mammillary bodies**, atrophied (characteristic on MRI; pathognomonic)
- Medial dorsal thalamus (most important for amnesia)
- Anterior thalamic nuclei
- Fornix white matter

Clinical Features:

- **Dense anterograde amnesia** (cannot form new memories)
- **Retrograde amnesia** (variable; follows Ribot's Law)
- **Confabulation:** Fabrication of information to fill memory gaps; patient has no insight that confabulations are false, **provoked confabulation** (answering questions with fabricated responses) vs **spontaneous confabulation** (unprompted false memories)
- **Relative preservation of:** Procedural memory, working memory, social/emotional memory
- **Apathy, flatness of affect**
- Perseveration
- Disorientation (especially temporal, cannot track date/time)

Relationship to Wernicke's Encephalopathy:

- Wernicke's encephalopathy (WE) = **acute** thiamine deficiency crisis
- Classic triad: **Confusion + Ataxia + Ophthalmoplegia** (nystagmus, lateral rectus palsy, conjugate gaze palsy)
- Only ~16% present with full triad
- WE → Korsakoff's if thiamine not replaced promptly (20–80% of untreated WE → Korsakoff's)
- "Wernicke-Korsakoff Syndrome" = continuum

Treatment:

- Thiamine replacement: IV 200–500 mg TID (Pabrinex) for acute WE

- ALWAYS give thiamine BEFORE glucose (glucose administration without thiamine can precipitate WE in thiamine-deficient patients)
 - Korsakoff's: many do not fully recover; some improvement with abstinence and thiamine
 - Long-term: supported accommodation, external memory aids, supervised living
-

5.3 Transient Global Amnesia (TGA)

Definition: A syndrome of sudden-onset, transient anterograde amnesia lasting up to 24 hours, with preserved personal identity and consciousness.

Epidemiology: Middle-aged to elderly (50–70 years); annual incidence 5–10/100,000

Clinical Features:

- Abrupt onset
- Dense anterograde amnesia, cannot form new memories
- **Repetitive stereotyped questioning** ("Where are we? What are we doing here?"), pathognomonic
- Preserved personal identity (unlike dissociative amnesia)
- No focal neurological deficits
- Normal level of consciousness
- Retrograde amnesia for hours before and during the episode
- Resolves completely within 24 hours (by definition)
- **No delirium, no seizure activity**

Precipitants:

- Physical exertion
- Sexual intercourse
- Valsalva maneuver
- Cold water immersion
- Emotional stress
- Migraine

Pathophysiology: Unclear; hypotheses include:

- Transient ischemia to hippocampal-thalamic circuit (posterior circulation)
- Cortical spreading depression (migraine-like mechanism)
- Venous congestion with Valsalva → transient hippocampal ischemia

Investigations:

- MRI DWI: small diffusion restriction spots in CA1 region of hippocampus (seen on MRI 24–48 hours after; Sedlaczek phenomenon)
- EEG: normal (differentiates from transient epileptic amnesia)
- Duplex ultrasound: check for venous insufficiency

Prognosis: Recurrence ~6% per year; low risk of stroke; benign condition

No treatment required

Differential: Transient Epileptic Amnesia (TEA), shorter episodes (<1 hour), recurrent, associated with post-ictal confusion, responds to anticonvulsants

5.4 Hippocampal Pathology and Amnesia

Bilateral hippocampal damage → anterograde amnesia:

- Classic case: **HM (Henry Molaison)**, bilateral hippocampectomy for epilepsy; dense anterograde amnesia, intact procedural memory, intact remote memories
- Damage to CA1 subfield most critical (vulnerable to ischemia, excitotoxicity)

Unilateral hippocampal damage:

- Left hippocampus: verbal memory (story recall, word lists)
- Right hippocampus: non-verbal memory (faces, spatial routes)

Causes of bilateral hippocampal damage:

- Anoxia (cardiac arrest)
- Herpes simplex encephalitis (HSE), HSV-1; necrotizing encephalitis of medial temporal and orbitofrontal regions; MRI: bilateral temporal signal change; Treatment: acyclovir
- Status epilepticus
- Autoimmune encephalitis (anti-NMDAR, anti-LGI1)
- Thiamine deficiency (Korsakoff's, hippocampal and diencephalic)
- Severe hypoglycemia

5.5 Organic vs Dissociative Amnesia

FEATURE	ORGANIC AMNESIA	DISSOCIATIVE AMNESIA
Cause	Brain injury, metabolic, toxic	Psychological trauma/stress
Anterograde amnesia	Yes	No (usually)
Retrograde amnesia	Temporal gradient	Often selective (autobiographical)
Personal identity	Preserved	May be lost (fugue states)

FEATURE	ORGANIC AMNESIA	DISSOCIATIVE AMNESIA
Implicit memory	Preserved	Preserved
EEG / imaging	Abnormal (often)	Normal
Recovery	Partial (often permanent)	Usually complete
Suggestibility	No	Yes
Comorbid trauma	Not required	Often present
Onset	After physical event	After psychological trauma

SECTION 6: NEUROPSYCHIATRIC ASSESSMENT

6.1 Bedside Cognitive Testing

6.1.1 MINI-MENTAL STATE EXAMINATION (MMSE)

Total: 30 points

Domains: Orientation (10), Registration (3), Attention/Calculation (5), Recall (3), Language (8), Visuoconstructional (1)

Score interpretation:

- 24–30: Normal
- 18–23: Mild impairment
- 12–17: Moderate impairment
- <12: Severe impairment

Limitations: Ceiling effect for higher education; floor effect for severe dementia; poor sensitivity for frontal/subcortical deficits; language-dependent; not diagnostic

6.1.2 MONTREAL COGNITIVE ASSESSMENT (MOCA)

Total: 30 points (add 1 if <12 years education)

Domains: Visuospatial/executive (5), Naming (3), Memory (5), Attention (6), Language (3), Abstraction (2), Delayed recall (5), Orientation (6)

Cut-off: <26 = cognitive impairment

Advantages over MMSE: Better at detecting MCI; tests frontal/executive function; more sensitive for subtle deficits

6.1.3 ADDENBROOKE'S COGNITIVE EXAMINATION-III (ACE-III)

Total: 100 points

Cut-off: <82 for dementia screening; <88 if high education

Advantages: Better discrimination between dementia subtypes; high sensitivity; verbal fluency and visuospatial detail

6.2 Frontal Lobe Tests (Bedside)

GO-NO-GO TEST

Examiner taps once = patient taps once; Examiner taps twice = patient does NOT tap

Frontal impairment: Patient taps regardless of stimulus (response inhibition failure, OFC)

LURIA MOTOR SERIES (FIST-EDGE-PALM)

Patient sequences three hand positions repeatedly

Frontal impairment: Cannot maintain sequence; perseverates; simplifies

VERBAL FLUENCY (FAS / ANIMALS / PROFESSIONS)

- **Phonemic fluency (FAS):** Name words starting with F, A, S (1 minute each), normal >12–15 per letter
- **Semantic fluency (animals):** Name animals in 1 minute, normal >15
- Frontal impairment affects phonemic > semantic fluency

ALTERNATING SEQUENCES

Draw alternating MWMWMW on paper and ask patient to continue

Frontal impairment: perseverates on one shape (M or W repeatedly)

FRONTAL ASSESSMENT BATTERY (FAB): FULL SCORING

Already described in 2.1.4

6.3 Visuospatial Assessment

- **Clock Drawing Test (CDT):** Draw clock, set hands to 11:10, tests planning, visuospatial, executive; impaired in parietal, frontal, subcortical
 - **Rey Complex Figure Test (RCFT):** Copy complex figure; recall after 3 minutes and 30 minutes; tests visuospatial organization and memory
 - **Copying pentagons:** MMSE item; impaired in cortical dementias
 - **Trail Making Test A and B:** TMT-A = attention/processing speed; TMT-B = set-shifting/executive
-

6.4 Language Assessment

- **Spontaneous speech:** Fluent vs non-fluent (pitch, rate, effort, paraphasia)
- **Naming:** Boston Naming Test; bedside: name pen, watch, parts of pen
- **Repetition:** "No ifs, ands, or buts", tests arcuate fasciculus

- **Comprehension:** Follow 3-step command; point to objects named
- **Reading, Writing:** Alexia, agraphia

Aphasia types:

TYPE	FLUENCY	COMPREHENSION	REPETITION	LESION
Broca's	Non-fluent	Intact	Impaired	L inferior frontal (BA44,45)
Wernicke's	Fluent	Impaired	Impaired	L superior temporal (BA22)
Conduction	Fluent	Intact	Impaired	Arcuate fasciculus
Global	Non-fluent	Impaired	Impaired	Large perisylvian
Anomic	Fluent	Intact	Intact	Variable (temporal tip, angular gyrus)
Transcortical motor	Non-fluent	Intact	Intact	SMA, anterior to Broca's
Transcortical sensory	Fluent	Impaired	Intact	Posterior to Wernicke's

SECTION 7: BRAIN TUMORS AND PSYCHIATRY

7.1 General Principles

Brain tumors cause psychiatric symptoms via:

1. **Direct compression/infiltration** of brain regions (location-specific)
2. **Raised intracranial pressure (ICP)**, cognitive slowing, personality change
3. **Seizure activity**, ictal/postictal psychiatric symptoms
4. **Paraneoplastic effects**, autoimmune encephalitis
5. **Systemic effects**, metabolic, endocrine, medication-related

Important principle: New-onset psychiatric symptoms in middle-aged/elderly patients, especially atypical presentations or those with neurological signs, require neuroimaging.

7.2 Frontal Meningioma

Location: Parasagittal, convexity, sphenoidal, olfactory groove (anterior fossa)

Classic presentation:

Olfactory groove meningioma:

- Anosmia (unilateral, then bilateral), often not noticed by patient
- Frontal lobe psychiatric symptoms: personality change, apathy, disinhibition
- Foster Kennedy Syndrome: ipsilateral optic atrophy + contralateral papilledema (tumor compresses one optic nerve; raises ICP causing papilledema on other side)
- **Psychiatric presentation:** depression, personality change, early cognitive decline, can be mistaken for primary psychiatric illness or early dementia for years

Parasagittal/convexity meningioma:

- Often presents with seizures
- Contralateral motor deficit
- Personality change if near frontal lobe

Key exam scenario: Middle-aged woman (meningiomas are more common in females, F:M = 2:1) with gradual personality change, frontal release signs, anosmia → imaging reveals frontal meningioma

7.3 Temporal Glioma

Presentation:

- **Seizures**, temporal lobe seizures with automatisms, olfactory / gustatory auras, déjà vu, jamais vu
- **Psychiatric presentation:** anxiety, mood changes, psychosis (if temporal lobe dysfunction)
- **Memory impairment:** especially with dominant (left) temporal involvement
- **Personality changes:** if extending to medial temporal / amygdala

Low-grade glioma: may present with psychiatric symptoms years before mass effect (diagnosis often delayed)

7.4 Pituitary Tumors (Adenomas)

Location: Sella turcica; extends into suprasellar region

Neurological effects:

- **Bitemporal hemianopia** (compression of optic chiasm), tunnel vision
- Headache (dural stretch)
- Cavernous sinus involvement: cranial nerve palsies (III, IV, VI)

Psychiatric effects via hormonal excess:

- **Cushing's disease (ACTH-secreting):** Depression (most common), anxiety, cognitive impairment; frank psychosis in ~5%; cortisol toxicity to hippocampus → memory impairment

- **Prolactinoma:** Sexual dysfunction, depression (hyperprolactinemia → hypogonadism → mood effects); treated with dopamine agonists (cabergoline, bromocriptine)
- **Acromegaly (GH-secreting):** Depression, anxiety, fatigue
- **Non-functioning adenoma:** Cognitive slowing, depression from mass effect; hypogonadism from stalk compression → depression/fatigue

Treatment:

- Cushing's: surgery (transsphenoidal), ketoconazole, mifepristone; psychiatric symptoms often improve with cortisol normalization
- Prolactinoma: cabergoline first line; surgery if not responding
- Monitor: psychiatric symptoms may persist even after successful endocrine treatment (HPA axis normalization takes time)

SECTION 8: NEUROPSYCHIATRIC ASPECTS OF COVID-19

8.1 Acute Phase

CNS invasion pathways:

- Direct neurotropism (via ACE2 receptors on neurons/glia, limited evidence)
- Hematogenous spread
- Retrograde axonal transport via olfactory nerve (anosmia → direct brain access)
- **Neuroinflammation**, cytokine storm → blood-brain barrier disruption → microglial activation

Acute neuropsychiatric presentations:

- Delirium: most common in hospitalized/ICU patients; up to 50% in severe COVID ICU
- Stroke: coagulopathy (hypercoagulability), cardioembolism
- Encephalitis (rare): anti-NMDAR antibodies reported
- Acute disseminated encephalomyelitis (ADEM), rare
- Myelin oligodendrocyte glycoprotein antibody disease (MOGAD), rare

8.2 Post-COVID-19 Neuropsychiatric Syndrome ("Long COVID" / "Post-Acute Sequelae of COVID-19: PASC")

Prevalence: 10–30% of COVID-19 survivors experience prolonged symptoms

Neuropsychiatric symptoms:

- **"Brain fog":** Difficulty concentrating, word-finding problems, slowed processing
- **Fatigue**, most prevalent; can be disabling
- **Depression and anxiety**, both reactive and possibly neurobiologically mediated

- **Sleep disturbance**, insomnia, hypersomnia, circadian dysregulation
- **PTSD**, especially after ICU admissions; vivid nightmares, hyperarousal
- **Headache**, tension-type, migrainous
- **Anosmia/parosmia**, may persist months; linked to olfactory bulb damage

Mechanisms:

- **Neuroinflammation**, persistent microglial activation; cytokine dysregulation
- **Autoimmune**, autoantibodies against ACE2, GPCRs, platelet-activating factor
- **Vascular**, persistent microthrombi, endothelial dysfunction
- **Mitochondrial dysfunction**, reduced ATP production → fatigue, cognitive impairment
- **HPA axis dysregulation**, stress response
- **Gut-brain axis**, COVID impacts gut microbiome; dysbiosis → neuropsychiatric symptoms

Neuroimaging findings (research):

- Reduced gray matter in olfactory and parahippocampal cortex (Douaud et al., Nature 2022)
- White matter microstructure changes
- Hypometabolism on FDG-PET in fronto-parietal regions

Management:

- No disease-specific treatment proven
- Symptom-directed management
- Cognitive rehabilitation for brain fog
- CBT for fatigue, anxiety, PTSD
- Sleep hygiene, graded exercise (with caution in ME / CFS-like cases)
- Multidisciplinary approach (neurology, psychiatry, physiotherapy, occupational therapy)

SECTION 9: SPECIAL TOPICS

9.1 Neuropsychiatric Assessment: Integrated Approach

Structured approach to organic psychiatric presentations:

Step 1, History

- Onset: Acute (delirium, stroke, TBI) vs subacute (tumor, encephalitis) vs chronic (dementia, VCI)
- Course: Fluctuating (delirium), stepwise (VCI), progressive (dementia)
- Temporal relationship between neurological event and psychiatric symptoms

- Pre-morbid personality and cognitive level (crucial baseline)
- Medical/surgical history, medications, substance use
- Family history of neurological/psychiatric conditions

Step 2, Mental State Examination (modified for organic)

- Level of consciousness and arousal
- Orientation: time, place, person, date
- Attention: forward/reverse digit span; months of year backwards
- Memory: registration, recall (3-word or 5-word test)
- Executive function: verbal fluency, abstraction
- Frontal signs: FAB if time permits
- Perceptual disturbances: visual hallucinations (organic), auditory hallucinations (psychiatric but also organic)
- Speech and language

Step 3, Neurological Examination

- Cranial nerve examination
- Motor system: power, tone, reflexes (hyperreflexia = UMN)
- Primitive reflexes: grasp, palmomental, snout, glabellar tap
- Cerebellar: ataxia, nystagmus, dysarthria
- Gait: Parkinson's gait, normal pressure hydrocephalus gait (magnetic, broad-based, urinary incontinence, dementia)

Step 4, Investigations

- **Basic bloods:** FBC, CRP, ESR, U&E, creatinine, glucose, LFTs, TFTs, calcium, phosphate, B12, folate
- **Urinalysis:** UTI (common delirium cause in elderly)
- **Neuroimaging:** CT head (acute stroke, hemorrhage, mass); MRI (white matter disease, hippocampal atrophy, temporal lesions)
- **EEG:** Delirium (generalized slowing), epilepsy, encephalitis (PLEDS, FIRDA)
- **LP:** Encephalitis, meningitis, autoimmune encephalitis (CSF pleocytosis, oligoclonal bands)
- **Autoimmune panel:** Anti-NMDAR, anti-LGI1, anti-CASPR2, anti-AMPA antibodies
- **Neuropsychological testing:** Formal assessment if bedside screening insufficient

9.2 Normal Pressure Hydrocephalus (NPH)

Classic triad (Hakim's triad):

1. **Wet**, urinary incontinence

2. **Wobbly**, gait apraxia (magnetic gait: small steps, feet "stuck to floor," wide-based)
3. **Wacky**, cognitive impairment (subcortical: executive, memory)

Neuroimaging: CT/MRI, ventriculomegaly out of proportion to sulcal atrophy; Evans index >0.3

Diagnosis: LP with high-volume CSF removal (30–50 mL) → gait improvement (positive tap test)

Treatment: Ventriculoperitoneal (VP) shunting, most effective for gait and incontinence; cognitive improvement variable

9.3 Autoimmune Encephalitis

Key antibodies:

- **Anti-NMDAR encephalitis:** Most common; young women; associated with ovarian teratoma; psychiatric presentation first (psychosis, behavioral change) → seizures → movement disorders → autonomic instability → coma
- **Anti-LGI1 encephalitis:** Older males; faciobrachial dystonic seizures (FBDS); hyponatremia; memory problems
- **Anti-CASPR2:** Morvan's syndrome (neuromyotonia, encephalopathy); associated with thymoma
- **Anti-AMPA:** Limbic encephalitis; memory and mood disturbance
- **Anti-GABA-B:** Limbic encephalitis; seizures prominent

General presentation: Subacute onset; combination of psychiatric symptoms + seizures + movement abnormalities + autonomic features

Investigations: MRI (temporal lobe T2/FLAIR signal); EEG (delta brush pattern in anti-NMDAR); CSF (pleocytosis, protein elevation); serum and CSF antibodies

Treatment: Immunotherapy, first line: IV methylprednisolone + IVIG ± plasma exchange; second line: rituximab, cyclophosphamide; tumor removal if paraneoplastic

Psychiatric relevance: Anti-NMDAR presents as acute psychosis in young patients → often initially treated as schizophrenia → diagnosis delayed → outcomes worsened. Must consider autoimmune encephalitis in new-onset psychosis, especially with fever, seizures, movement abnormalities, or rapid progression.

9.4 Epilepsy and Psychiatry (Brief Overview: Detailed in NB-15)

Interictal psychosis (Schizophrenia-like psychosis of epilepsy, SLPE):

- Occurs in temporal lobe epilepsy
- Chronic psychosis with preserved affect (vs blunted affect in schizophrenia)

- Onset after 10–15 years of epilepsy
- Positive symptoms predominant

Postictal psychosis:

- After cluster seizures, lucid interval of 24–72 hours
- Then psychosis (often manic/mixed features, aggression)
- Resolves spontaneously in days to weeks

Forced normalization / Paradoxical normalization / Landolt's phenomenon:

- Psychiatric symptoms (psychosis, hypomania) emerge when seizures are controlled (EEG normalizes)
- Discontinuing anticonvulsant or reducing it may paradoxically help psychosis

Antipsychotics and seizure threshold: Clozapine and chlorpromazine lower seizure threshold most; risperidone, haloperidol relatively safe; quetiapine intermediate

SECTION 10: RAPID-FIRE EXAM POINTS

High-Yield One-Liners

- Robinson hypothesis: left anterior frontal lesion → highest rates of PSD
- PSD prevalence: 30–50% overall; peaks at 3–6 months post-stroke
- First-line PSD treatment: sertraline or fluoxetine
- PBA treatment: dextromethorphan/quinidine (Nuedexta), first FDA-approved treatment
- PBA mechanism: damage to corticobulbar pathways → release of brainstem motor-emotional circuits
- Anosognosia: right parietal lesion; patient unaware of left hemiplegia
- Post-stroke mania: right hemisphere; basal temporal, OFC, caudate
- Apathy vs depression: apathy = no distress, neutral mood; depression = distress, dysphoria
- CAM criteria: 1+2+(3 or 4), Acute onset, Inattention, Disorganized thinking, Altered arousal
- Hypoactive delirium: most common, most missed; worst prognosis
- Delirium pathophysiology: cholinergic deficit + neuroinflammation + dopamine excess
- Korsakoff's: mammillary body + medial dorsal thalamus lesions; confabulation
- Give thiamine BEFORE glucose in suspected Wernicke's
- TGA: repetitive questioning, lasts <24 hrs, no focal neurology, benign
- CTE: posthumous diagnosis; tau deposits perivascular; associated with repetitive TBI
- Moderate TBI: GCS 9–12; PTA 1–7 days

- Second impact syndrome: young athletes; catastrophic cerebral swelling; 50% mortality
- Propranolol: best evidence for aggression post-TBI
- OFC lesion = pseudopsychopathic syndrome (Phineas Gage)
- DLPFC lesion = pseudodepression (flat affect, executive dysfunction)
- Olfactory groove meningioma: anosmia + frontal psychiatric symptoms + Foster Kennedy syndrome
- Cushing's disease: depression most common psychiatric manifestation; cortisol toxic to hippocampus
- Anti-NMDAR encephalitis: young women, ovarian teratoma, psychiatric onset, NMDA receptor antibodies
- NPH triad: Wet + Wobbly + Wacky
- Gerstmann syndrome: finger agnosia, L-R disorientation, agraphia, acalculia → left angular gyrus
- CADASIL: NOTCH3 mutation; hereditary subcortical vascular dementia + migraine
- Long COVID neuropsychiatric: brain fog, fatigue, PTSD, depression; mechanism = neuroinflammation

Word count: ~15,500

Model Answers

KEY INSIGHT

Format guide: Each answer follows standard PG exams long-answer structure. Marks allocation shown in brackets. Bold = examinable points. Boxes = exam strategy tips.

Answer 1: Post-Stroke Depression: Etiology, Prevalence, and Management

[10 marks, Long Answer]

Introduction

Post-stroke depression (PSD) is the most common neuropsychiatric complication of stroke, affecting 30–50% of survivors. It is classified in DSM-5 as Depressive Disorder Due to Another Medical Condition (Stroke). PSD significantly worsens functional outcomes, delays rehabilitation, and increases mortality.

Prevalence

- Lifetime prevalence: 30–50% of stroke survivors
- Acute phase (0–2 weeks): ~25–30%
- Peak at 3–6 months post-stroke: ~35%
- Community studies suggest ~20–25% at one year
- Depression is more severe and more prevalent in hospital-based samples (selection bias)

Etiology: Multifactorial Model

1. Neurobiological (Robinson's Left Frontal Hypothesis)

Robinson and colleagues (1984, 1987) proposed that:

- Lesions of the **left anterior frontal cortex**, specifically left dorsolateral prefrontal cortex (DLPFC) and left basal ganglia, produce the highest rates and most severe depression after stroke.
- Mechanism: Left hemisphere damage disrupts descending serotonergic and noradrenergic projections from the frontal cortex through fronto-striato-thalamo-cortical circuits to the limbic system.

- The left hemisphere normally regulates approach-related positive affect. Its disruption results in unopposed negative affect (right hemisphere).
- **Lesion-to-frontal-pole distance** (on CT) inversely correlates with depression severity for left hemisphere strokes.
- Critiques: Meta-analyses found lateralization effect strongest in hospital-based, acute samples. Community studies less consistent. Current consensus: left frontal relationship is real but not absolute.

2. Neurochemical Factors

- Depletion of biogenic amines (serotonin, noradrenaline, dopamine) in fronto-limbic pathways disrupted by infarct
- HPA axis dysregulation, cortisol elevation with hippocampal atrophy
- Neuroinflammatory cascades (IL-1 β , IL-6) alter neurotransmitter turnover

3. Psychosocial Factors

- Pre-stroke depression or anxiety (strongest psychosocial predictor)
- Degree of functional disability (ADL dependence)
- Social isolation, poor social support
- Loss of occupational roles and identity
- Fear of recurrence, grief response to disability

4. Genetic/Premorbid Factors

- Personal/family history of depression
- Serotonin transporter gene polymorphisms (5-HTTLPR)
- Female sex
- Cognitive impairment

Clinical Features

- Overlaps with primary MDD but notable differences:
 - More prominent apathy (overlapping syndrome, must distinguish)
 - More neurovegetative features (fatigue, sleep disruption) confounded by stroke itself
 - Emphasis on cognitive-affective symptoms: anhedonia, hopelessness, worthlessness, suicidal ideation
 - Emotional lability frequently co-occurs
 - Assessment tools: MADRS (preferred, less somatic items), PHQ-9, GDS, HDRS
-

Management

A. Pharmacological

DRUG	EVIDENCE	STARTING DOSE
Sertraline	Strong RCT evidence; first choice	50 mg OD
Fluoxetine	FLAME trial, benefit for motor recovery + mood	20 mg OD
Citalopram	Good evidence; monitor QTc	10–20 mg OD
Nortriptyline	Outperformed fluoxetine in some trials	25 mg OD (titrate)
Mirtazapine	Insomnia + anorexia variant	15 mg at night
Methylphenidate	Rapid response in medically ill	5–10 mg BD (off-label)

- Duration: minimum 6–12 months after response; relapse common with early cessation
- Prophylaxis: Sertraline/escitalopram trial for high-risk patients (left frontal, prior depression), mixed evidence

B. Non-Pharmacological

- CBT (modified for cognitive deficits/aphasia), good evidence
- Problem-solving therapy
- Exercise (aerobic, 3–5× per week), RCT evidence
- Social support interventions
- Motivational interviewing for adherence
- Caregiver psychoeducation

Prognosis

- Untreated PSD doubles disability and mortality risk
- Treatment response is generally good (60–70% respond to antidepressants)
- Persistent PSD (>1 year) associated with worse functional outcomes
- Late-onset PSD (>6 months) more strongly linked to psychosocial factors

KEY INSIGHT

Exam Strategy Box: Robinson's hypothesis is a guaranteed examiner favourite. Know the neuroanatomy clearly: left DLPFC + left basal ganglia → serotonergic pathway disruption → depression. Mention critiques of the hypothesis to show analytical thinking. Always conclude with management, examiners want clinical relevance.

Answer 2: Delirium: Classification, Diagnosis, and Management

[10 marks, Long Answer]

Definition

Delirium is an acute, potentially reversible neuropsychiatric syndrome characterized by disturbances in attention, awareness, and cognition, with an acute onset and fluctuating course. It is always caused by an identifiable medical / toxic / metabolic etiology. It constitutes a neurological emergency.

DSM-5 Diagnostic Criteria

- Criterion A:** Disturbance in attention (reduced ability to direct, focus, sustain, shift attention) and awareness (reduced environmental orientation).
- Criterion B:** Acute onset (hours to days), change from baseline, tendency to fluctuate during the day.
- Criterion C:** Additional cognitive disturbance (memory deficit, disorientation, language, visuospatial, or perceptual disturbance).
- Criterion D:** Not explained by established NCD; not occurring during markedly reduced arousal (e.g., coma).
- Criterion E:** Direct physiological consequence of medical condition, substance intoxication / withdrawal, toxin exposure, or combination.

Classification by Subtype

Subtype	Key Features	Prevalence	Prognosis	Risk of Missing
Hyperactive	Agitation, combativeness, restlessness	25%	Better	Low
Hypoactive	Withdrawn, somnolent, quiet	50%	Worst	Very High
Mixed	Fluctuates between both	25%	Intermediate	Moderate

EXAM PEARL

Hypoactive delirium is the most common, least recognized, and carries the worst prognosis. Examiners frequently ask about this.

Bedside Diagnosis: CAM

Confusion Assessment Method (Inouye, 1990):

Delirium = Feature 1 AND Feature 2 AND (Feature 3 OR Feature 4)

1. **Acute onset + fluctuating course**
2. **Inattention** (digit span, months backwards)
3. **Disorganized thinking**
4. **Altered level of consciousness**

Sensitivity 94–100%; Specificity 90–95%

CAM-ICU: Non-verbal variant for intubated patients (uses RASS + visual attention tests)

Etiology

DELIRIUM Mnemonic:

- **D**, Drugs (opioids, benzodiazepines, anticholinergics, steroids)
 - **E**, Eyes / Ears (sensory deprivation)
 - **L**, Low oxygen (pneumonia, PE, cardiac failure)
 - **I**, Infection (UTI, sepsis, meningitis)
 - **R**, Retention (urinary retention, constipation) / Restraints
 - **I**, Intoxication or Injury (TBI, subdural hematoma)
 - **U**, Underhydration / electrolytes (Na, Ca, glucose, Mg)
 - **M**, Metabolic (hepatic failure, renal failure, thyroid)
-

Pathophysiology

1. Cholinergic Deficit Hypothesis:

- Acetylcholine critical for arousal, attention, REM regulation
- Anticholinergic drugs reliably cause delirium
- Physostigmine reverses anticholinergic delirium

2. Neuroinflammation:

- Systemic inflammation → activated microglia → pro-inflammatory cytokines (IL-1 β , IL-6, TNF- α) → BBB disruption → neurotransmitter dysregulation

3. Dopamine Excess:

- Relative excess of dopamine (vs acetylcholine) → hyperactive features
- Basis for antipsychotic (D2 blocker) use

4. Other neurotransmitters: GABA over-activity (benzodiazepines), glutamate excess (excitotoxicity)

Management

A. Non-Pharmacological (First Line)

HELP Program (Hospital Elder Life Program, Inouye):

- Orientation aids: clock, calendar, name boards
- Early mobilization; avoid restraints
- Sleep hygiene: dimmed lights at night, no nighttime vitals unless necessary
- Hydration: oral or IV
- Sensory aids: glasses, hearing aids
- Cognitive stimulation during daytime

Evidence: Reduces incidence by 33%, duration by 30–40%

B. Pharmacological (Adjunct, no FDA approval for delirium)

- **Haloperidol** 0.5–1 mg PO/IM q4h: Most evidence; parenteral option; risk EPS, QTc
- **Quetiapine** 12.5–25 mg: Preferred in elderly, Lewy body risk, Parkinson's; sedating
- **Olanzapine** 2.5–5 mg: IM available for acute agitation
- **Dexmedetomidine** (ICU): Alpha-2 agonist; better than benzodiazepines in ICU delirium (MENDS2, MIDEX trials)
- **Ramelteon** 8 mg at bedtime: Reduces incidence in at-risk patients (prevention)

AVOID: Benzodiazepines (except alcohol withdrawal); physical restraints

Delirium vs Dementia

FEATURE	DELIRIUM	DEMENTIA
Onset	Acute	Insidious
Course	Fluctuating	Progressive
Consciousness	Impaired	Intact (early)
Reversibility	Usually yes	Usually no
EEG	Diffuse slowing	Often normal (early)

KEY INSIGHT

Exam Strategy Box: In any MCQ on delirium, check whether it is asking about the most common subtype (hypoactive) vs the most clinically obvious (hyperactive). For long answers, structure as definition → DSM-5 criteria → subtypes → etiology → pathophysiology → management → prognosis.

Answer 3: Traumatic Brain Injury: Classification, Psychiatric Sequelae, and Management

[10 marks, Long Answer]

Definition

Traumatic brain injury (TBI) is defined as an alteration in brain function caused by an external mechanical force. It may be open (penetrating) or closed (blunt). Severity is classified by Glasgow Coma Scale (GCS) score.

GCS-Based Classification

SEVERITY	GCS	LOC	PTA
Mild	13–15	<30 min	<24 hrs
Moderate	9–12	30 min – 24 hrs	1–7 days
Severe	3–8	>24 hrs	>7 days

GCS = Eye (4) + Verbal (5) + Motor (6); Total 3–15

Additional markers: CT/MRI findings (contusion, DAI, hemorrhage), biomarkers (GFAP, S100B, NSE)

Psychiatric Sequelae

A. Acute Phase

- Post-traumatic delirium/confusion (universal in moderate-severe TBI)
- Agitation (up to 70% in ICU)
- Post-traumatic amnesia (PTA), duration predicts outcome

B. Subacute / Chronic

1. Post-Concussion Syndrome (PCS), Mild TBI

- Headache, dizziness, cognitive slowing, fatigue, irritability, sleep disturbance, anxiety
- ICD-10: F07.2; DSM-5: Mild NCD due to TBI
- Risk factors: Female, pre-existing anxiety/headache, prior concussion, health anxiety

- 80–90% resolve in 7–10 days; 10–20% develop PCS; <5% persist beyond 1 year
- Management: Graded return to activity; symptom-specific treatment; CBT for psychological component

2. Personality Change Due to TBI (DSM-5 Subtypes)

- Labile type: affective instability
- Disinhibited type: impulsivity, OFC damage
- Aggressive type: irritability, frontal + temporal
- Apathetic type: frontal/ ACC damage
- Prevalence: 50–80% of moderate-severe TBI

3. Depression Post-TBI

- Prevalence: 25–50%
- Associated with premorbid depression, left frontal damage, cognitive impairment
- Treatment: SSRIs (sertraline, citalopram); TCA caution (seizure risk)

4. Anxiety Post-TBI

- PTSD (15–25%): Re-experiencing, avoidance, hyperarousal
- GAD pattern common
- Treatment: Trauma-focused CBT (TF-CBT), EMDR, SSRIs

5. Psychosis Post-TBI

- 2–8% of moderate-severe TBI
- Temporal lobe damage, frontal-limbic disconnection
- Treat with low-dose atypical antipsychotics (avoid haloperidol, impairs recovery)

6. Chronic Traumatic Encephalopathy (CTE)

- Repetitive TBI → hyperphosphorylated tau accumulation (perivascular, sulcal depths)
- Posthumous diagnosis; stages I–IV
- Features: depression, explosivity, memory loss, Parkinsonism
- No specific treatment; posthumous pathological diagnosis

C. Aggression Post-TBI

- Pharmacological: Propranolol (best evidence), SSRIs, valproate, buspirone, amantadine
- Avoid benzodiazepines (paradoxical disinhibition) and haloperidol (impairs neuroplasticity)

Cognitive Rehabilitation

Principles: Neuroplasticity, specificity, intensity, meaningful goals

- Attention: Attention Process Training (APT-3)
- Memory: External aids, errorless learning, spaced retrieval
- Executive function: Goal Management Training
- Evidence: Strongest for attention training; moderate for memory strategies

KEY INSIGHT

Exam Strategy Box: Classify by GCS first, examiners always want this. For psychiatric sequelae, use a systematic temporal structure (acute → subacute → chronic). Include CTE, it is high-yield for modern exams. Always mention what to AVOID (haloperidol, benzodiazepines in TBI recovery), this shows clinical nuance.

Answer 4: Korsakoff's Syndrome: Etiology, Clinical Features, Pathology, and Treatment

[8 marks]

Introduction

Korsakoff's syndrome is a chronic amnestic disorder resulting from thiamine (Vitamin B1) deficiency, most commonly in the context of chronic alcohol use disorder. It often follows acute Wernicke's encephalopathy and constitutes the chronic pole of the Wernicke-Korsakoff continuum.

Etiology

- **Thiamine deficiency:** Primary cause; chronic alcoholism (impaired absorption + poor dietary intake + hepatic dysfunction)
- Non-alcoholic causes: Hyperemesis gravidarum, prolonged vomiting, bariatric surgery, total parenteral nutrition without thiamine supplementation, malnutrition, HIV / AIDS, refeeding syndrome

Neuropathology

Sites of hemorrhagic/necrotic lesions (bilateral):

- **Mammillary bodies**, atrophied; visible on MRI; pathognomonic; part of Papez circuit
- **Medial dorsal thalamus**, most critical site for amnesia (mediodorsal thalamic nuclei)
- **Anterior thalamic nuclei**
- Periaqueductal gray matter
- Floor of fourth ventricle
- Fornix white matter

Note: Hippocampus relatively spared in Korsakoff's (distinguishes from hypoxic amnesia)

Clinical Features

Core features:

1. **Dense anterograde amnesia**, cannot form new memories; inability to lay down episodic memories; implicit / procedural memory preserved
2. **Retrograde amnesia**, temporal gradient (Ribot's Law: recent memories lost first, remote memories preserved longer); variable severity
3. **Confabulation**, fabrication to fill memory gaps; patient has no awareness of falseness:
4. *Provoked confabulation*: In response to direct questions
5. *Spontaneous confabulation*: Unprompted false narratives (associated with additional frontal damage)
6. **Apathy and flatness of affect**, reduced emotional responsiveness
7. **Disorientation**, particularly temporal; cannot track date / day accurately
8. **Relatively preserved**: Social skills, procedural memory, working memory, remote memories (variable)

Wernicke's triad (acute preceding phase):

- **Confusion** (global confusional state)
 - **Ataxia** (cerebellar gait)
 - **Ophthalmoplegia** (nystagmus, lateral rectus palsy, conjugate gaze palsy)
 - Full triad present in only ~16%; any one component warrants thiamine treatment
-

Treatment

Acute Wernicke's:

- IV thiamine (Pabrinex): 200–500 mg TID for 3–5 days
- **CRITICAL: Thiamine BEFORE glucose administration** (glucose without thiamine precipitates acute WE in deficient patients)
- Subsequent oral thiamine supplementation

Chronic Korsakoff's:

- Continued thiamine supplementation
- Abstinence from alcohol
- Approximately 20–30% make full recovery; 50% partial recovery; 25% no improvement
- External memory aids (diaries, smartphones, structured timetables)
- Supervised / supported living arrangements
- Occupational therapy for functional independence

EXAM PEARL

The mammillary body + medial dorsal thalamus combination is the classic neuropathological answer. Confabulation is a high-yield clinical feature, explain both types. The thiamine-before-glucose rule is a patient safety point that examiners love to test.

Answer 5: Pseudobulbar Affect (Emotional Incontinence): Features, Mechanism, and Treatment

[6 marks]

Definition

Pseudobulbar affect (PBA) is a neurological condition characterized by involuntary, uncontrollable episodes of laughing or crying (or both) that are incongruent with the patient's subjective emotional state. Also termed: pathological laughing and crying (PLC), emotional lability, or emotional incontinence.

Clinical Features

- Episodes are sudden, brief (seconds to minutes), and self-terminating
- Often incongruent: patient may cry without feeling sad; laugh without amusement
- Patient is typically aware the reaction is excessive and feels embarrassed
- Episodes can be triggered by minor stimuli or occur spontaneously
- No alteration of consciousness
- Frequency: multiple times per day in severe cases

Associated neurological conditions:

- Stroke (most common)
 - Traumatic brain injury
 - Amyotrophic lateral sclerosis (ALS)
 - Multiple sclerosis
 - Parkinson's disease / Parkinsonism
 - Dementias (especially multi-infarct dementia)
-

Mechanism

- Loss of voluntary **cortical inhibition** over brainstem motor-emotional circuits (pontine-cerebellar pathways)
- Descending corticobulbar fibers normally exert tonic inhibition on brainstem emotional expression centers

- Damage to these fibers → involuntary release of emotional expression
 - **Neurotransmitter basis:** Serotonin (regulatory); glutamate / NMDA receptor dysregulation; sigma-1 receptor modulation
-

Differential Diagnosis

- **Labile mood (bipolar):** Full mood episodes; control is preserved
- **Ictal laughter (gelastic seizures):** Prolonged, stereotyped, associated with other ictal signs; EEG abnormal
- **Major depression with crying:** Congruent with sad mood; not involuntary
- **Adjustment disorder:** Congruent with stressor; voluntary control present

Assessment: CNS-LS (Center for Neurologic Study, Lability Scale)

Treatment

Pharmacological:

1. **Dextromethorphan/Quinidine (Nuedexta)**, FDA-approved 2010; first disease-specific treatment
2. Mechanism: Quinidine inhibits CYP2D6 → raises dextromethorphan levels
3. Dextromethorphan: sigma-1 receptor agonist + NMDA antagonist → reduces emotional dysregulation
4. Efficacy: Reduces episode frequency by ~50–75% in RCTs (PRISM I, PRISM II trials)
5. **SSRIs (sertraline, fluoxetine):** Often used first clinically; good evidence; low-cost
6. **Amitriptyline:** Older evidence; effective; anticholinergic burden a concern in stroke patients
7. **Nortriptyline:** Better tolerated TCA option

Non-pharmacological:

- Distraction during episode onset
 - Controlled breathing
 - Caregiver education and destigmatization
-

EXAM PEARL

Dextromethorphan / quinidine (Nuedexta) is the signature pharmacological answer here. Know the FDA approval year (2010) and the mechanism: CYP2D6 inhibition by quinidine → elevated dextromethorphan → sigma-1 + NMDA modulation. Many examiners ask about this precisely because it is often neglected in textbooks.

Answer 6: Chronic Traumatic Encephalopathy (CTE)

[6 marks]

Introduction

CTE is a progressive neurodegenerative disease resulting from repetitive traumatic brain injury (concussive and sub-concussive), characterized pathologically by accumulation of hyperphosphorylated tau in a perivascular distribution at the depths of cortical sulci.

Historical Context

- First described in boxers as "dementia pugilistica" or "punch-drunk syndrome" (Martland, 1928)
 - Term CTE proposed by Corsellis (1973)
 - Modern recognition in American football players, Dr. Bennet Omalu (2005)
 - Affects military veterans (blast TBI), rugby players, ice hockey players
-

Neuropathology

- **Hyperphosphorylated tau**, p-tau accumulates in neurons, astrocytes, and cell processes
 - **Distribution: perivascular, at depths of cortical sulci**, pathognomonic; distinguishes CTE from AD and other tauopathies
 - TDP-43 inclusions in later stages
 - Diffuse axonal injury background
 - Cavum septum pellucidum (seen on MRI in boxers, "punched out" appearance)
-

Clinical Staging (McKee et al.)

STAGE · DOMINANT FEATURES

I Headache, inattention, short-term memory deficits

II Depression, explosivity, impulsivity, executive dysfunction

III Memory loss, executive dysfunction, visuospatial impairment

IV Dementia, severe behavioral change, Parkinsonism, speech/swallow difficulties

Behavioral Profile

- Depression (60–80% in documented cases)
- Impulsivity and impulse control disorder
- Substance misuse (comorbid)

- Explosive aggression
 - Paranoia
 - Suicidality (elevated rates)
 - Progressive cognitive decline (memory, attention, executive)
-

Diagnosis

- **Currently a posthumous diagnosis**, requires brain autopsy
 - No validated in-vivo biomarker (research: tau-PET, plasma phospho-tau217, not yet clinical standard)
 - Brain MRI: cavum septum pellucidum, cerebral atrophy (non-specific)
 - Neuropathological criteria published by McKee et al. (2016)
-

Management

- No disease-modifying treatment
 - Symptomatic: antidepressants, mood stabilizers for behavioral features
 - Cognitive rehabilitation
 - Prevention: primary goal, return-to-play protocols, rule changes in contact sports, helmet technology
-

EXAM PEARL

Always state that CTE is a posthumous diagnosis, this differentiates it from all other neurodegenerative conditions. The perivascular sulcal-depth tau distribution is the pathognomonic neuropathological answer.

Answer 7: Frontal Lobe Syndromes: Neuroanatomy and Clinical Features

[8 marks]

Introduction

The frontal lobe constitutes approximately 30% of the cerebral cortex and is the substrate for the highest human cognitive functions including executive ability, impulse control, working memory, and social behavior. Three distinct functional divisions produce clinically recognizable syndromes when damaged.

Three Frontal Syndromes

1. Dorsolateral Prefrontal Cortex (DLPFC) Syndrome, "Pseudodepression"

Anatomy: BA 9, 10, 45, 46; projects to caudate (dorsal striatum) via fronto-striato-thalamic circuit

Functions: Working memory, planning, cognitive flexibility (set-shifting), verbal fluency, abstract reasoning

Lesion features:

- Apathy, reduced motivation (resembles depression but no dysphoric mood)
- Poor planning and organization (Tower of London)
- Impaired set-shifting (Wisconsin Card Sorting Test)
- Reduced verbal fluency (FAS test)
- Executive dysfunction
- Working memory failure

Named "pseudodepression" because: Flat affect + apathy without subjective depression

2. Orbitofrontal Cortex (OFC) Syndrome, "Pseudopsychopathy"

Anatomy: BA 11, 12, 13, 14; projects to amygdala, nucleus accumbens, mediodorsal thalamus

Functions: Reward processing, decision-making with emotional context (Somatic Marker Hypothesis, Damasio), response inhibition, social cognition

Lesion features:

- Disinhibition, socially inappropriate behavior
- Impulsivity, failure of response inhibition (Go-No-Go test failure)
- Grandiosity, euphoria (can mimic mania)
- Hypersexuality
- Iowa Gambling Task failure (cannot use emotional signals to guide decisions)
- Reduced concern for consequences

Classic case: Phineas Gage (1848), frontal pole damage from iron rod → responsible, capable man becomes irresponsible, impulsive

3. Medial PFC / Anterior Cingulate Cortex (ACC) Syndrome

Anatomy: BA 24 (ACC); projects to SMA, limbic structures, thalamus

Functions: Motivated behavior initiation, error monitoring, conflict detection, attention allocation

Lesion features:

- **Akinetic mutism** (severe bilateral): awake, eyes open, track objects, yet mute and motionless, extreme amotivation
- **Abulia** (moderate): diminished spontaneous activity, slow speech
- **Apathy** (mild): passivity, reduced initiation

- Preserved cognition when explicitly prompted (vs DLPFC dysfunction)
 - Classic cause: Bilateral ACA (anterior cerebral artery) infarct
-

Bedside Frontal Tests

TEST · FRONTAL DOMAIN ASSESSED

Frontal Assessment Battery (FAB) Broad frontal, 6 subtests, /18

Verbal fluency FAS DLPFC, phonemic generation

Go-No-Go OFC, response inhibition

Luria motor series (fist-edge-palm) SMA / pre-motor, programming

Proverb interpretation DLPFC, abstract reasoning

Trail Making B DLPFC, set-shifting

EXAM PEARL

Know the three syndromes with their eponymous names (pseudodepression, pseudopsychopathy, akinetic mutism) and link each to anatomy. The Phineas Gage case and the Iowa Gambling Task (Damasio) are frequent extras that signal depth of knowledge.

Answer 8: Anosognosia: Definition, Neuroanatomy, and Clinical Significance

[5 marks]

Definition

Anosognosia (from Greek: a = without, nosos = disease, gnosis = knowledge) is a neurological condition in which a patient with a neurological deficit fails to recognize or acknowledge that deficit. First described by Joseph Babinski (1914).

Clinical Spectrum

- **Anosognosia:** Explicit denial of the deficit
 - **Anosodiaphoria:** Acknowledges deficit but shows inappropriate indifference ("So what, it will pass")
 - **Hemispatial neglect:** Inattention to contralesional space (related but distinct)
 - **Anton's syndrome:** Denial of blindness in cortical visual loss (bilateral occipital)
-

Neuroanatomy

- **Right parietal lobe**, dominant for anosognosia of left hemiplegia
- Right supramarginal gyrus (inferior parietal lobule)
- Right somatosensory cortex integration areas
- Right temporoparietal junction
- Thalamus and right basal ganglia involvement in some cases
- Right frontal lobe, metacognitive awareness of deficits

Why right hemisphere?

- The right parietal lobe is dominant for body schema (awareness of the entire body including both sides)
- The left parietal lobe only represents the right side; the right represents bilateral space
- Right hemisphere lesions → impaired integrated body schema → anosognosia for left-sided deficits

Clinical Significance

1. **Rehabilitation:** Patient denies the deficit → refuses therapy → worsens outcome
2. **Safety risk:** Walking despite paralysis → falls, injury
3. **Caregiver conflict:** Family members frustrated by patient's apparent non-compliance
4. **Prognostication:** Persistent anosognosia predicts poor functional recovery

Management

- Direct confrontation (showing patient in mirror, video of deficits), variable success
- Prism adaptation therapy (for neglect component)
- Gradual insight may return as recovery progresses
- Involve caregiver in rehabilitation planning
- Goals-based rehabilitation rather than insight-dependent

EXAM PEARL

Link anosognosia explicitly to right parietal lesions, this is the most testable anatomical answer. Distinguish it clearly from hemispatial neglect (neglect = inattention; anosognosia = denial of deficit). Both often co-occur with right parietal damage.

Answer 9: Post-Concussion Syndrome: Diagnosis and Management

[6 marks]

Definition

Post-concussion syndrome (PCS) is a clinical syndrome following mild TBI (concussion) in which symptoms persist beyond the expected recovery period (>3 months after injury in ICD-10; >1–3 months clinically). DSM-5 classifies it as Mild Neurocognitive Disorder Due to Traumatic Brain Injury.

Symptom Triad

1. Somatic:

Headache (most common, tension-type pattern), dizziness, fatigue, sleep disturbance, photophobia, phonophobia, visual disturbance, nausea

2. Cognitive:

Memory problems, poor concentration, slowed information processing, word-finding difficulty

3. Affective/Behavioral:

Irritability, anxiety, depression, emotional lability, reduced frustration tolerance, personality change

Pathophysiology

- **Neurometabolic cascade** (Giza & Hovda): Ionic flux → glutamate excess → cellular energy crisis → mitochondrial dysfunction → period of neuronal vulnerability
 - Disrupted cerebrovascular autoregulation
 - Neuroinflammation
 - **Biopsychosocial model:** Biological injury + psychological response (health anxiety, catastrophizing) + social factors (litigation, secondary gain, maladaptive return-to-activity patterns)
-

Risk Factors for Prolonged PCS

- Female sex
 - Pre-existing headaches, anxiety, or depression
 - Prior concussion
 - Negative expectations at time of injury ("nocebo" effect)
 - Younger athletes
 - Delayed return to activity (over-resting paradox)
-

Management

Acute (first 24–48 hours):

- Cognitive and physical rest (brief; not prolonged)

Graduated Return to Activity (Stages, SCAT5 protocol):

1. Symptom-limited activity
2. Light aerobic exercise
3. Sport-specific exercise
4. Non-contact training
5. Full-contact practice
6. Return to competition

Symptom-specific:

- Headache: Amitriptyline (preventive), NSAIDs (acute), topiramate
- Sleep: Melatonin, trazodone, sleep hygiene
- Mood: SSRIs (sertraline), CBT
- Cognitive: Cognitive rehabilitation, graded return to school

Key principle: Avoid prolonged rest, **causes symptom perpetuation (active recovery principle)**

EXAM PEARL

The active recovery principle (avoid prolonged rest) is counterintuitive and thus exam-worthy. Also emphasize the biopsychosocial model, this distinguishes a sophisticated answer.

Answer 10: Transient Global Amnesia: Clinical Features and Differential Diagnosis

[5 marks]

Definition

Transient Global Amnesia (TGA) is a benign syndrome of sudden-onset, transient anterograde amnesia lasting up to 24 hours, in which the patient has intact personal identity and level of consciousness, with no other focal neurological deficits.

Clinical Features

- **Age:** Middle-aged to elderly (50–70 years)
- **Abrupt onset:** Often during or after a precipitant

- **Dense anterograde amnesia:** Cannot form new memories; no recall of the episode afterward
- **Stereotyped repetitive questioning:** "Where are we?" "What happened?", pathognomonic feature; same questions repeated every few minutes
- **Preserved personal identity:** Knows who they are, who family members are
- **Normal consciousness and affect**
- **Retrograde amnesia:** Covering hours before and during episode
- **Complete resolution within 24 hours** (by definition; average 4–6 hours)
- No focal neurological deficits

Common precipitants: Physical exertion, sexual intercourse, Valsalva maneuver, cold water immersion, emotional stress, migraine

Investigations

- **MRI DWI:** Small diffusion restriction spots in CA1 region of hippocampus, best seen 24–48 hours after onset (Sedlacek sign)
 - **EEG:** Normal, distinguishes from transient epileptic amnesia
 - **Vascular studies:** Jugular venous insufficiency may be found (Valsalva mechanism)
-

Differential Diagnosis

CONDITION · KEY DIFFERENTIATING FEATURES

Transient Epileptic Amnesia (TEA) Shorter episodes (<1 hour), recurrent, post-ictal, EEG abnormal, responds to anticonvulsants

TIA Focal neurological signs; imaging may show ischemia; risk factors

Dissociative amnesia Identity may be lost; preceded by psychological trauma; no imaging changes

Drug intoxication Drug history; other features of intoxication

Psychogenic fugue Prolonged; purposeful travel; identity change

Prognosis

- Recurrence rate: ~6% per year
 - No increased stroke risk
 - Completely benign condition, no treatment required
 - Reassurance and education for patient and family
-

EXAM PEARL

Repetitive stereotyped questioning is the pathognomonic clinical feature. The MRI DWI finding in CA1 hippocampus (Sedlacek sign) is a high-yield imaging question. TGA vs TEA is a classic differential exam question, distinguish by episode duration and EEG.

Answer 11: Vascular Cognitive Impairment: Classification and Management

[6 marks]

Definition

Vascular Cognitive Impairment (VCI) is an umbrella term encompassing the full range of cognitive impairment attributed to cerebrovascular disease, from vascular mild cognitive impairment (VaMCI) to vascular dementia (VaD).

Classification

TYPE · FEATURES

Vascular MCI (VaMCI) Cognitive decline in ≥ 1 domain; daily function intact; vascular etiology

Vascular Dementia (VaD) Cognitive decline impairing daily function; vascular etiology

Mixed Dementia VaD + AD pathology; most common type clinically

Subtypes of VaD:

1. **Multi-infarct dementia:** Multiple large cortical infarcts; stepwise decline
2. **Strategic infarct dementia:** Single critical-site infarct (thalamus, angular gyrus, basal forebrain); abrupt, profound but focal deficits
3. **Subcortical ischemic VaD / Binswanger's:** Small vessel disease, leukoariosis, lacunes; executive dysfunction + gait + urinary symptoms; insidious
4. **CADASIL:** NOTCH3 mutation; hereditary subcortical VaD; migraine with aura + recurrent strokes + psychiatric features + dementia

Clinical Profile

- Onset: Abrupt or stepwise (vs gradual in AD)
- Executive dysfunction > memory (vs memory-first in AD)
- Gait disturbance (early in VaD)
- Focal neurological signs present

- Recall improved with cuing (unlike AD where encoding is impaired)
- Prominent mood features: depression, apathy, emotional lability

Management

- **Vascular risk factor control:** Hypertension, diabetes, hyperlipidemia, atrial fibrillation, primary treatment
- **Antiplatelet therapy:** Aspirin 100 mg or clopidogrel
- **Statins**
- **Cholinesterase inhibitors** (donepezil, rivastigmine): Modest benefit for VaD; RCT evidence
- **Memantine:** Some evidence; approved for moderate-severe AD; used off-label in VaD
- Manage neuropsychiatric symptoms (depression, apathy, agitation)

EXAM PEARL

Know the four subtypes of VaD by name. CADASIL is high-yield, link NOTCH3 mutation to the diagnosis. Know that executive dysfunction precedes memory loss in VaD, which is the opposite pattern from AD.

Answer 12: Autoimmune Encephalitis: Clinical Features, Diagnosis, and Psychiatric Relevance

[6 marks]

Overview

Autoimmune encephalitis (AE) is a group of conditions in which antibodies target synaptic or neuronal cell-surface antigens, causing encephalitis. Psychiatric presentation is common, often preceding neurological features, making it critical for psychiatrists to recognize.

Key Antibodies and Clinical Profiles

ANTIBODY	TARGET	DEMOGRAPHICS	CLINICAL HALLMARKS
Anti-NMDAR	NMDA receptor (GluN1)	Young women; children	Psychiatric onset (psychosis, behavioral) → seizures → movement disorders → autonomic instability → coma

ANTIBODY	TARGET	DEMOGRAPHICS	CLINICAL HALLMARKS
Anti-LGI1	Leucine-rich glioma-inactivated 1	Older males	Faciobrachial dystonic seizures (FBDS), hyponatremia, memory loss
Anti-CASPR2	Contactin-associated protein-2	Older males; thymoma	Morvan's syndrome (neuromyotonia + encephalopathy)
Anti-AMPA	AMPA receptor	Middle-aged; often female	Limbic encephalitis; mood + memory
Anti-GABA-B	GABA-B receptor	Adults; associated with SCLC	Seizures + limbic features

Investigations

- MRI brain: Bilateral temporal FLAIR/T2 hyperintensity (limbic encephalitis pattern)
- EEG: **Delta brush pattern**, pathognomonic for anti-NMDAR encephalitis
- CSF: Pleocytosis, elevated protein; anti-NMDAR antibodies (positive CSF more sensitive than serum)
- Serum antibodies: Combined serum + CSF increases sensitivity
- Screen for occult tumor (anti-NMDAR → ovarian teratoma; anti-LGI1 → thymoma)

Psychiatric Relevance

- Anti-NMDAR presents as **acute psychosis** in young patients → frequently misdiagnosed as first-episode schizophrenia
- Red flags suggesting AE over primary psychosis:
- Fever during psychiatric presentation
- Seizures
- Movement abnormalities (orofacial dyskinesias, catatonia)
- Rapid progression over days-weeks
- Autonomic instability
- Decreased consciousness
- Memory failure disproportionate to psychosis
- No response to antipsychotics (or paradoxical worsening)

Treatment

- **First line:** IV methylprednisolone 1g/day × 3–5 days + IVIG 2g/kg over 3–5 days ± plasma exchange

- **Second line (refractory):** Rituximab (anti-CD20) or cyclophosphamide
- **Tumor removal** if paraneoplastic: Accelerates recovery in anti-NMDAR (ovarian teratoma removal)
- With treatment: 75–80% achieve good recovery; risk of relapse ~12–25%

EXAM PEARL

Anti-NMDAR encephalitis is likely to be the most tested autoimmune encephalitis. Lead with young woman + psychiatric onset + seizures + movement disorder + autonomic + ovarian teratoma. The delta brush EEG pattern is pathognomonic and often tested.

Answer 13: Delirium Superimposed on Dementia: Clinical Challenge and Management

[5 marks]

Introduction

Delirium superimposed on dementia (DSD) represents the most clinically complex scenario in hospital neuropsychiatry. Dementia is the single greatest risk factor for delirium (3–5× increased risk), and detecting delirium in a patient with existing cognitive impairment is diagnostically challenging.

Why DSD is Often Missed

- Hypoactive delirium (most common) mimics dementia progression
- No clear baseline cognitive state (especially in new patients)
- Fluctuation may be attributed to "sundowning"
- Staff assume confusion is the patient's baseline

Key Distinguishing Features

FEATURE	DSD	DEMENTIA PROGRESSION
Onset	Acute over hours-days	Gradual over weeks-months
Fluctuation	Marked, within hours	Absent or minimal
New somatic trigger	Present	Absent
Attention	Severely impaired	Relatively less affected
Arousal	Altered	Normal

Detection Tools for DSD

- **DOSS (Delirium Observation Screening Scale):** 13-item nursing-administered tool; validated in dementia
 - **Nu-DESC (Nursing Delirium Screening Scale):** 5 items; brief; practical
 - **SQID (Single Question in Delirium):** Ask family / caregiver: "Do you think your relative is more confused than usual?"
-

Long-term Consequences

- Accelerated cognitive decline (DSD → faster dementia progression)
 - Increased mortality (3–11× in hospitalized elderly)
 - Permanent institutionalization risk
 - Loss of functional independence
 - Persistent delirium in 30–40% at discharge
-

Management

1. Identify and treat precipitating cause (infection, dehydration, medication, constipation)
 2. Minimize anticholinergic medications
 3. Reorient frequently; familiar objects and faces
 4. Maintain sleep-wake cycle
 5. Low-dose quetiapine (12.5–25 mg) if behavioral disturbance severe
 6. **Avoid benzodiazepines**
 7. Family / caregiver involvement throughout
-

Answer 14: Neuropsychiatric Effects of Pituitary Tumors

[5 marks]

Introduction

Pituitary tumors (adenomas) produce neuropsychiatric effects via three mechanisms: mass effect on adjacent structures, hormonal excess from hyperfunctioning tumors, and hormonal deficiency from pituitary compression.

Neurological Effects (Mass Effect)

- **Bitemporal hemianopia:** Optic chiasm compression → loss of temporal visual fields bilaterally (tunnel vision)
- **Headache:** Dural stretching
- **Cranial nerve palsies:** Cavernous sinus invasion → III, IV, VI nerve palsies

Psychiatric Effects by Tumor Type

Cushing's Disease (ACTH-secreting):

- **Depression**, most common; often severe; melancholic features
- Anxiety
- Cognitive impairment (cortisol toxic to hippocampus → volume loss)
- Psychosis in ~5%
- Irritability, mood lability

Prolactinoma:

- Depression and anxiety (via hypogonadism, hyperprolactinemia → low testosterone/estrogen)
- Sexual dysfunction (libido loss, erectile dysfunction, amenorrhea)
- Treatment with dopamine agonists (cabergoline, bromocriptine), psychiatric symptoms often improve

Acromegaly (GH-secreting):

- Depression, anxiety, fatigue, quality-of-life impairment
- Sleep apnoea (common, worsens mood and cognitive function)

Non-functioning Adenoma:

- Subtle cognitive slowing from raised ICP and pituitary insufficiency
- Depression, fatigue from hypogonadism/hypothyroidism secondary to stalk compression

Principles of Management

- Cushing's: Surgery (transsphenoidal) first line; ketoconazole (cortisol synthesis inhibitor); mifepristone (glucocorticoid receptor antagonist) for psychosis
- Prolactinoma: Cabergoline first line; psychiatric symptoms track with prolactin normalization
- Psychiatric symptoms often improve with hormonal treatment but may persist, monitor
- Screen for depression and anxiety in all pituitary disease patients

Answer 15: Second Impact Syndrome: Mechanism and Prevention

[4 marks]

Definition

Second impact syndrome (SIS) is a catastrophic clinical event in which an individual sustains a second brain injury before fully recovering from an initial concussion, resulting in malignant, rapidly progressive cerebral edema.

Mechanism

- **Neurometabolic vulnerability window:** After the first concussion, the brain is in a state of ionic flux, mitochondrial dysfunction, and impaired cerebrovascular autoregulation
 - A second impact, even minor, causes dysregulation of cerebrovascular tone
 - **Massive cerebrovascular vasodilation** → rapid, bilateral cerebral swelling → herniation and death
 - The second injury does not need to be severe, a minor head bump can suffice
-

Clinical Features

- Typically affects young athletes (teenage to early adult)
 - Brief lucid interval after second impact
 - Rapid neurological deterioration (collapse within minutes)
 - Bilaterally dilated pupils; coma
 - Extremely high mortality (~50%) and severe morbidity in survivors
-

Prevention (Primary Goal)

- **Return-to-play (RTP) protocols:** Athlete must be completely asymptomatic before returning to contact sport
 - **SCAT5 (Sport Concussion Assessment Tool):** Standardized assessment; 6-stage RTP
 - **No same-day return to play after concussion**, absolute rule
 - Physician clearance mandatory before contact sport return
 - Education of coaches, parents, athletes
-

EXAM PEARL

The key mechanism answer is "dysregulation of cerebrovascular autoregulation → malignant cerebral edema." Emphasize that the second impact can be trivial, this is the clinically terrifying aspect. Prevention > treatment.

Mnemonics & Memory Tricks

KEY INSIGHT

Usage note: Each mnemonic includes the device, expansion, clinical anchor, and a brief recall hook. Star-rated for exam frequency: ★★★ = must-know, ★★ = high-yield, ★ = useful extra.

Mnemonic 1: DELIRIUM (Causes of Delirium) ★★★

Clinical anchor: The word itself = the condition. Anytime a patient is delirious, run through DELIRIUM top to bottom.

Recall hook: Delirium spells itself.

Mnemonic 2: CAM Criteria (Delirium Diagnosis) ★★★

Clinical anchor: Sensitivity 94–100%. In any exam question about delirium diagnosis bedside, CAM is the answer.

Recall hook: "AICA disrupts consciousness", just like delirium disrupts it.

Mnemonic 3: ROBINSON (Left Frontal Hypothesis for PSD) ★★★

Clinical anchor: Robinson → Left → Depression. Right → Mania.

Recall hook: "ROBinson → ROB the mood from the Left Front."

Mnemonic 4: GERSTMANN (Left Angular Gyrus Syndrome) ★★★

Clinical anchor: Left angular gyrus (BA 39). Dominant hemisphere. All four must be present for full syndrome.

Recall hook: "Gerstmann GAG-s on language": G=agraphia, A=acalculia, G=finger agnosia, ... plus L-R disorientation.

Mnemonic 5: WERNICKE'S TRIAD (Acute Thiamine Deficiency) ★★★

Clinical anchor: Full triad present in only ~16% of cases. Treat with thiamine if ANY one feature is present in an at-risk patient.

Recall hook: COA = "Caught Off Alert", Wernicke's catches you off guard with partial presentations.

Critical rule: Thiamine BEFORE glucose. "T before G, always."

Mnemonic 6: KORSAKOFF (Clinical Features) ★★★

Better device for differentiating confabulation:

Clinical anchor: Mammillary bodies + medial dorsal thalamus. Preserved procedural memory. Social skills relatively intact.

Recall hook: "Korsakoff MARC's memories, but they're all fabricated."

Mnemonic 7: NPH TRIAD (Normal Pressure Hydrocephalus) ★★★

Clinical anchor: Hakim's triad. Evans index >0.3 on CT. LP tap test (remove 30–50 mL CSF → gait improves). Treatment: VP shunt.

Recall hook: "Three W's = one confused, incontinent, shuffling patient."

Mnemonic 8: KLÜVER-BUCY Syndrome ★★

Clinical anchor: Bilateral anterior temporal lobe destruction (amygdala + anterior temporal pole). Causes: Herpes simplex encephalitis, trauma, Pick's disease.

Recall hook: "Klüver-Bucy patients HHPVAP themselves, they can't stop putting things in their mouths."

Mnemonic 9: FOSTER KENNEDY SYNDROME ★★

Clinical anchor: Olfactory groove meningioma. Middle-aged woman. Psychiatric symptoms for years before diagnosis.

Recall hook: "FOster Kennedy FOstered a brain tumor for years before anyone noticed."

Mnemonic 10: ANTI-NMDAR ENCEPHALITIS Red Flags ★★★

Clinical anchor: These are red flags that should trigger autoimmune encephalitis workup in a patient presenting as "first-episode psychosis."

Recall hook: "FARMS tell you it's NOT a farm-variety psychosis, it's autoimmune."

Mnemonic 11: CTE STAGES (McKee) ★★

Clinical anchor: CTE = posthumous diagnosis. Tau perivascular at sulcal depths. Repetitive TBI. Football, boxing, military.

Recall hook: "CTE beats you in the HEAD, four stages."

Mnemonic 12: TBI CLASSIFICATION (GCS) ★★★

Clinical anchor: Assess at 30 minutes post-injury (not immediately, confounded by hypoxia, hypotension).

Recall hook: "3-5-8: Mild is great (15), Severe is fate (3-8)."

Mnemonic 13: APHASIA TYPES ★★★

Recall hook: "Repetition intact = Trans or Anomic. Repetition impaired = everything else."

Mnemonic 14: FRONTAL LOBE SYNDROMES (Three Types) ★★★

Clinical anchor: Each maps to an anatomy and an eponymous syndrome.

Recall hook: "The front of your brain can either shut down (DLPFC), go wild (OFC), or go totally silent (Cingulate)."

Mnemonic 15: PSD TREATMENT (SSRIs for Post-Stroke Depression) ★★★

Clinical anchor: Sertraline = first choice for PSD. Fluoxetine = special status for motor recovery. Nortriptyline = older evidence, outperformed fluoxetine in some Robinson trials.

Recall hook: "FLAME lights up both motor and mood recovery, fluoxetine's double win."

Mnemonic 16: DELIRIUM SUBTYPES ★★★

Recall hook: "HYPOactive = HYPOthyroid, quiet, slow, deadly if missed."

Mnemonic 17: POST-STROKE PSYCHIATRIC SYNDROMES (DAMP) ★★

Recall hook: "Stroke leaves a DAMP MAP, navigate all of them."

Mnemonic 18: TGA DIAGNOSIS ★★

Recall hook: "TGA, 3 P's, 24 hours, benign. TEA, short, recurrent, EEG positive."

Mnemonic 19: AGGRESSION POST-TBI (Pharmacological) ★★

Recall hook: "Propranolol PRO-tects the TBI brain. Haloperidol HARMS it."

Mnemonic 20: AUTOIMMUNE ENCEPHALITIS ANTIBODIES ★★

Recall hook: "NLCAG, Navigate Limbic Circuits And Gaba, antibodies all attacking the synapse."

High-Yield Comparisons

EXAM STRATEGY

Comparison questions are among the most reliably asked in Indian PG psychiatry written exams. A clean table with 8–10 features earns full marks faster than prose. Each table here is formatted for direct exam use.

Table 1: Delirium vs Dementia

FEATURE	DELIRIUM	DEMENCIA
Onset	Acute (hours to days)	Insidious (months to years)
Course	Fluctuating (hallmark)	Progressive, relatively steady
Duration	Days to weeks	Months to years (chronic)
Level of consciousness	Always impaired	Preserved until late stages
Attention	Always impaired (core feature)	Relatively preserved early
Orientation	Grossly impaired	Impaired later
Memory	Impaired (anterograde + working)	Anterograde amnesia early (AD)
Psychomotor activity	Hyperactive, hypoactive, or mixed	Usually normal early
Hallucinations	Common (especially visual)	Variable; common in DLB, PDD
Sleep-wake cycle	Severely disrupted	Mildly disrupted early; sundowning
EEG	Diffuse slowing	May be normal (early); variable
Cause	Identifiable acute medical trigger	Neurodegenerative, vascular, etc.
Reversibility	Usually reversible with treatment	Usually irreversible
Onset of symptoms	Abrupt change from baseline	No clear break from baseline
Distress	Patient often distressed/agitated	Patient less distressed (early)

EXAM PEARL

Delirium superimposed on dementia (DSD) = most common and most missed combination.
Acute-on-chronic confusion: look for acute precipitant, fluctuation greater than baseline, worse attention.

Table 2: Hyperactive vs Hypoactive Delirium

FEATURE	HYPERACTIVE DELIRIUM	HYPOACTIVE DELIRIUM
Prevalence	~25%	~50% (most common)
Motor activity	Increased, restless, agitated	Decreased, withdrawn, slow
Speech	Loud, pressured, incoherent	Sparse, mumbled, minimal
Orientation	Markedly impaired	Markedly impaired
Hallucinations	Common (visual)	Less prominent
Delusions	Paranoid, persecutory	Less prominent
Pulling at IV lines	Yes	No
Recognizability	Easily recognized	Frequently missed
Common causes	Alcohol withdrawal, anti-cholinergic drugs, hypoxia	Sepsis, hepatic encephalopathy, hypoactive states, opioids
Prognosis	Better	Worse (higher mortality, longer hospital stay)
Misdiagnosis risk	Low	High, often mistaken for depression, fatigue, "being tired"
Treatment urgency	Often triggers intervention	Often undertreated

EXAM PEARL

"Hypo is Most, Missed, and Most Deadly." This single insight about hypoactive delirium generates exam marks repeatedly.

Table 3: Post-Stroke Depression vs Primary (Endogenous) Depression

FEATURE	POST-STROKE DEPRESSION (PSD)	PRIMARY MDD
Classification	Depressive Disorder Due to Another Medical Condition (DSM-5)	Major Depressive Disorder

FEATURE	POST-STROKE DEPRESSION (PSD)	PRIMARY MDD
Onset	Within weeks to months of stroke	Any time; no neurological trigger
Neuroanatomical basis	Yes, left anterior frontal, basal ganglia	Diffuse: PFC, amygdala, HPA, monoaminergic
Robinson's hypothesis	Directly applicable	Not applicable
Apathy	More prominent; often overlapping	Less prominent; can occur in severe MDD
Cognitive impairment	Common due to stroke itself	Present but secondary to mood
Somatic symptoms	Confounded by stroke deficits	More reliable markers
Emotional lability	Frequent co-occurrence (PBA)	Less common; not a feature
Suicidal ideation	Present but lower than primary MDD	Characteristic feature
Response to antidepressants	Good (60–70%); sertraline first choice	Good (60–70%); standard SSRIs
Non-pharmacological	CBT modified for cognitive deficits	Standard CBT
Course	May resolve as stroke recovers; some persist	Episodic or chronic
Premorbid history	Pre-stroke depression is strongest risk factor	Often positive family / personal history
Mortality impact	Doubles post-stroke mortality	Increases mortality (suicide, neglect)

Table 4: Mild vs Moderate vs Severe TBI

PARAMETER	MILD TBI	MODERATE TBI	SEVERE TBI
GCS Score	13–15	9–12	3–8
Loss of consciousness	<30 minutes	30 min – 24 hrs	>24 hours
Post-Traumatic Amnesia	<24 hours	1–7 days	>7 days
Imaging findings	Usually normal	May show structural injury	Structural abnormality common
Typical injury mechanism	Concussion; sports; falls	MVA; significant blow	High-energy trauma; falls from height

PARAMETER	MILD TBI	MODERATE TBI	SEVERE TBI
Acute management	Observation; discharge if stable	Admission; monitoring	ICU; neurosurgical intervention
Cognitive sequelae	Mild (usually resolves)	Moderate; may persist	Severe; often permanent
Psychiatric sequelae	Post-concussion syndrome (10–20%)	Depression, anxiety, personality change	Full range; high burden
CTE risk	Cumulative exposure risk	Moderate	Lower (often single severe event)
Biomarkers	S100B; GFAP may be elevated	GFAP elevated; NSE	All biomarkers elevated
Prognosis	Excellent (80–90% full recovery)	Good to fair	Variable; high mortality / disability

EXAM PEARL

GCS ≤ 8 = intubation threshold in clinical practice. Know all three GCS boundaries and their PTA correlates.

Table 5: Frontal Lobe Syndromes: Three Types Compared

FEATURE	DLPFC SYNDROME	OFC SYNDROME	MEDIAL PFC / ACC SYNDROME
Eponymous name	Pseudodepression	Pseudopsychopathy	Akinetic mutism / Apathy
Brodmann areas	BA 9, 10, 45, 46	BA 11, 12, 13, 14	BA 24 (ACC), medial surface
Primary projections	Caudate (dorsal striatum)	Amygdala, nucleus accumbens	SMA, limbic system, thalamus
Core deficit	Executive dysfunction, reduced output	Disinhibition, impulsivity	Loss of motivated behavior
Mood	Flat affect, apathy (no distress)	Euphoria, lability (may mimic mania)	Profound indifference
Impulse control	Relatively preserved	Severely impaired	N/A (reduced activity)
Social behavior	Withdrawn	Inappropriate, disinhibited, hypersexual	Mute, unresponsive
Classic bedside test	FAS verbal fluency, WCST, Trail B	Go-No-Go, Iowa Gambling Task	Initiation test; no spontaneous output

FEATURE	DLPFC SYNDROME	OFC SYNDROME	MEDIAL PFC / ACC SYNDROME
Classic case		Phineas Gage (1848)	Bilateral ACA infarct
Associated disorders	ADHD, schizophrenia (hypofrontality)	Antisocial PD, addiction, bipolar	Severe depression, Parkinson's (SMA)
Common cause	DLPFC stroke; TBI; FTD	OFC tumor; TBI; FTD (bvFTD)	ACA stroke; deep mid-line tumor

Table 6: Organic Amnesia vs Dissociative Amnesia

FEATURE	ORGANIC AMNESIA	DISSOCIATIVE AMNESIA
Etiology	Brain injury, metabolic, toxic, structural	Psychological trauma, extreme stress
Anterograde amnesia	Prominent (especially hippocampal)	Usually absent
Retrograde amnesia	Temporal gradient (Ribot's Law)	Selective autobiographical; islands of memory loss
Personal identity	Preserved	May be lost (fugue state)
Implicit memory	Preserved (HM case)	Preserved
Neuroimaging	Often abnormal (lesion, atrophy)	Normal
EEG	May be abnormal	Normal
Suggestibility	Not suggestible	Amenable to hypnosis, suggestion
Onset	After physical event / medical illness	After psychological trauma
Recovery	Partial; often permanent (anterograde)	Usually complete; spontaneous
Confabulation	Present (Korsakoff's)	Absent
Secondary gain	Absent	May be present
Comorbid trauma	Not required	Typically present
Psychotherapy response	Limited	Often responsive

Table 7: Vascular Dementia vs Alzheimer's Disease

FEATURE	VASCULAR DEMENTIA	ALZHEIMER'S DISEASE
Onset	Abrupt or stepwise	Gradual, insidious
Course	Stepwise or plateau-relapse	Slowly progressive
First cognitive domain	Executive function	Episodic memory (encoding)
Memory type	Recall deficits; cuing helps	Encoding deficits; cuing does NOT help
Gait disturbance	Early (small-vessel disease)	Late
Focal neurological signs	Present	Absent (early)
Mood disturbance	Depression, apathy, emotional lability common	Apathy, depression later
Vascular risk factors	Prominent	May co-exist but not causative
Neuroimaging	WMH, lacunes, cortical infarcts	Medial temporal atrophy, hippocampal volume loss
Cholinergic deficit	Less prominent	Primary (NBM degeneration)
Cholinesterase inhibitors	Modest benefit	Good evidence
Genetic risk	CADASIL (NOTCH3), APOE ε4	APOE ε4, APP, PSEN1, PSEN2
Neuropathology	Infarcts, WMH, lacunar changes	Amyloid plaques, neurofibrillary tangles
Mixed dementia	Common (VaD + AD co-exist in elderly)	Can have mixed pathology

Table 8: Post-Stroke Depression vs Post-Stroke Apathy

FEATURE	POST-STROKE DEPRESSION	POST-STROKE APATHY
Core symptom	Dysphoric mood, sadness	Reduced motivation, goal-directed behavior
Subjective distress	Present (patient suffers)	Absent (patient indifferent)
Mood	Depressed, sad, hopeless	Neutral, flat
Hedonic capacity	Anhedonia (cannot enjoy)	Reduced motivation (not the same as anhedonia)
Self-criticism	Present (guilt, worthlessness)	Absent
Response to prompting	Engages but remains sad	May show normal affect when engaged

FEATURE	POST-STROKE DEPRESSION	POST-STROKE APATHY
Neuroanatomy	Left frontal, basal ganglia (Robinson)	ACC, frontal-subcortical circuits
Prevalence post-stroke	30–50%	20–40%
Overlap	~50% of cases co-occur	~50% of cases co-occur
Assessment	MADRS, PHQ-9, HDRS	Apathy Evaluation Scale (AES), NPI apathy subscale
Treatment	SSRIs (sertraline), good evidence	Methylphenidate, rivastigmine (modest evidence)
Prognosis	Responds to antidepressants	Often persistent; no proven drug

Table 9: Transient Global Amnesia (TGA) vs Transient Epileptic Amnesia (TEA)

FEATURE	TGA	TEA
Episode duration	Up to 24 hours (average 4–6 hours)	Short (<1 hour, often minutes)
Frequency	Usually single episode (recurrence ~6% / yr)	Recurrent (multiple per year)
Repetitive questioning	Characteristic, pathognomonic	Less prominent
Personal identity	Preserved	Preserved
Consciousness	Fully alert	Brief impairment (post-ictal confusion)
Focal symptoms	Absent	May have aura (olfactory, epigastric)
Post-ictal confusion	Absent	Present
EEG	Normal	Abnormal (ictal / interictal)
MRI DWI	CA1 hippocampal dot (Sed-laczek sign)	Usually normal; may show epileptogenic focus
Treatment	None required	Anticonvulsants (lamotrigine, levetiracetam)
Prognosis	Benign; low stroke risk	Requires treatment; generally good
Pathophysiology	Hippocampal spreading depression / Valsalva-venous mechanism	Temporal lobe epilepsy

Table 10: Pseudobulbar Affect (PBA) vs Primary Emotional Disorders

FEATURE	PBA (EMOTIONAL INCONTINENCE)	BIPOLAR AFFECTIVE DISORDER	MAJOR DEPRESSION
Control of episodes	None, involuntary	Present	Present
Mood congruence	Incongruent (often crying without sadness)	Congruent	Congruent
Episode duration	Seconds to minutes	Days to weeks	Days to months
Patient awareness	Embarrassed; aware of inappropriateness	Variable insight in mania	Present
Underlying cause	Neurological (stroke, TBI, ALS, MS)	Idiopathic (genetic, neurobiological)	Idiopathic
Mechanism	Disrupted corticobulbar inhibitory pathways	Mood dysregulation (limbic-PFC circuits)	Monoamine deficiency model
EEG	Normal	Normal	Normal
Neuroimaging	Shows underlying stroke / lesion	Normal (usually)	May show PFC / limbic changes
Treatment	Dextromethorphan / quinidine (Nuedexta), SSRIs	Mood stabilizers, antipsychotics	Antidepressants, psychotherapy
Response to antidepressants	Good (SSRIs reduce episodes)	Caution (SSRIs may precipitate mania)	Good

Bonus Table: Aphasia Types: Quick Comparison

APHASIA	FLUENCY	COMPREHENSION	REPETITION	LESION LOCATION
Broca's	Non-fluent	Intact	Impaired	Left IFG (BA44/45)
Wernicke's	Fluent	Impaired	Impaired	Left STG (BA22)
Global	Non-fluent	Impaired	Impaired	Large left perisylvian
Conduction	Fluent	Intact	Impaired	Arcuate fasciculus
Transcortical Motor	Non-fluent	Intact	Intact	SMA / anterior to Broca

APHASIA	FLUENCY	COMPREHENSION	REPETITION	LESION LOCATION
Transcortical Sensory	Fluent	Impaired	Intact	Posterior to Wernicke
Anomic	Fluent	Intact	Intact	Variable (temporal tip, angular gyrus)

KEY INSIGHT

Rule: Repetition intact → Transcortical or Anomic. Repetition impaired → Broca, Wernicke, Global, or Conduction.

PYQ Frequency Analysis

KEY INSIGHT

Scope: Analysis covers question patterns from Indian MD Psychiatry exit examinations (PG exams, Exam pattern) over approximately 17 years. Questions reconstructed from pattern analysis, not verbatim reproductions. Frequency ratings and topic weights reflect cumulative exam data.

Section 1: Topic Frequency Heat Map

TOPIC	FREQUENCY	EXAM WEIGHT	PREDICTED 2026
Post-Stroke Depression (Robinson hypothesis, management)	★★★★★	Very High	Almost certain
Delirium, definition, DSM-5, CAM, subtypes, management	★★★★★	Very High	Almost certain
Korsakoff's syndrome, features, pathology, treatment	★★★★★	High	Very likely
TBI classification (GCS) + psychiatric sequelae	★★★★★	High	Very likely
Pseudobulbar affect / Emotional incontinence	★★★★★	High	Very likely
Frontal lobe syndromes	★★★★★	High	Very likely
Post-concussion syndrome	★★★★	Moderate-High	Likely
Anosognosia	★★★★	Moderate-High	Likely
Transient Global Amnesia	★★★★	Moderate	Likely
Vascular Dementia / VCI	★★★★	Moderate	Likely

TOPIC	FREQUENCY	EXAM WEIGHT	PREDICTED 2026
CTE (Chronic Traumatic Encephalopathy)	★★★	Moderate	Likely (recent trend)
Autoimmune encephalitis (anti-NMDAR)	★★★	Moderate	Likely (rising trend)
Gerstmann syndrome	★★	Moderate	Possible
Normal Pressure Hydrocephalus	★★	Moderate	Possible
Post-COVID neuropsychiatry	★★	Moderate	Possible
Second impact syndrome	★★	Low-Moderate	Possible
Brain tumors and psychiatry	★★	Low-Moderate	Possible
Klüver-Bucy syndrome	★★	Low	Unlikely but classic
CADASIL	★	Low	Low but targeted

Section 2: Question Pattern Classification

2.1 Long Answer Questions (10 marks each)

These questions require 4–5 pages of structured answer. The pattern consistently covers 3–4 sub-components.

Q1. "Discuss post-stroke depression. Include etiology, clinical features, and management."

Frequency: Asked in multiple exam sittings; virtually guaranteed across universities.

Expected sub-components:

- Definition + DSM-5 classification (1 mark)
- Prevalence data (1 mark)
- Robinson's left frontal hypothesis, detailed, with critique (3 marks)
- Risk factors, neurological + psychosocial (1 mark)
- Clinical features + assessment tools (2 marks)
- Management: pharmacological (sertraline, fluoxetine/FLAME, nortriptyline) + non-pharmacological (2 marks)

Key differentiator for high marks: Mention critiques of Robinson's hypothesis (community studies showed weaker lateralization; methodological heterogeneity). This shows analytical thinking rather than rote recall.

Examiner favourite additions: MADRS preferred over HDRS (less somatic item confounding); FLAME trial for fluoxetine; prophylactic sertraline evidence.

Q2. "Describe delirium, classification, pathophysiology, and management."

Frequency: One of the most reliably asked questions in Indian PG psychiatry.

Expected sub-components:

- Definition + DSM-5 criteria in full (2 marks)
- CAM criteria (1 mark)
- Classification by subtype: hyperactive / hypoactive / mixed with prevalence + prognosis (2 marks)
- Etiology (DELIRIUM mnemonic) (1 mark)
- Pathophysiology: cholinergic deficit + neuroinflammation + dopamine excess (2 marks)
- Management: HELP program (non-pharm) + pharmacological (haloperidol, quetiapine, dexmedetomidine) (2 marks)

Key differentiator: Naming hypoactive delirium as most common AND most missed AND worst prognosis consistently impresses examiners. Many candidates only describe hyperactive.

Q3. "Classify TBI. Discuss neuropsychiatric complications and their management."

Frequency: Regular across universities; especially strong in Exam pattern.

Expected sub-components:

- GCS classification table (mild / moderate / severe) + PTA duration (2 marks)
 - Acute psychiatric effects (delirium, agitation) (1 mark)
 - Post-concussion syndrome, symptoms, risk factors, management (2 marks)
 - Personality change due to TBI, DSM-5 subtypes (1 mark)
 - Depression, anxiety, psychosis post-TBI (1 mark)
 - CTE, definition, neuropathology, stages (1 mark)
 - Aggression management, propranolol, valproate, SSRIs; AVOID benzodiazepines and haloperidol (2 marks)
-

2.2 Short Answer Questions (5 marks each)

These appear in Section B or as "write short notes on." Average length: 1.5–2 pages.

Q4. "Korsakoff's syndrome."

Frequency: Very high; almost a fixture.

Expected content:

- Definition + etiology (thiamine deficiency, alcoholism)
- Neuropathology: mammillary bodies + medial dorsal thalamus (essential)
- Clinical features: anterograde amnesia, retrograde amnesia (Ribot's Law), confabulation (provoked + spontaneous), apathy
- Wernicke-Korsakoff continuum
- Treatment: thiamine IV before glucose; abstinence; external aids
- Prognosis

Key differentiator: Naming medial dorsal thalamus (not just mammillary bodies) as the critical lesion site for amnesia. Most candidates only mention mammillary bodies.

Q5. "Pseudobulbar affect (emotional incontinence)."

Frequency: High; asked as short note and as part of stroke complications.

Expected content:

- Definition: involuntary, uncontrollable laughing/crying incongruent with mood
- Mechanism: loss of corticobulbar inhibition of brainstem motor-emotional circuits
- Associated conditions (stroke, TBI, ALS, MS)
- Assessment: CNS-LS
- Treatment: dextromethorphan/quinidine (FDA-approved 2010; mechanism), SSRIs, amitriptyline

Key differentiator: Knowing the FDA-approved treatment by name (Nuedexta = dextromethorphan/quinidine) and its mechanism (CYP2D6 inhibition → elevated DM → sigma-1 receptor + NMDA modulation).

Q6. "Frontal lobe syndromes."

Frequency: High; asked as short note and within neuroanatomy questions.

Expected content:

- Three syndromes: DLPFC (pseudodepression), OFC (pseudopsychopathy), medial PFC/ACC (akinetism)
- Anatomy of each
- Clinical features of each
- Classic cases: Phineas Gage (OFC)

- Bedside tests: FAB, Go-No-Go, Luria, FAS fluency
-

Q7. "Anosognosia."

Frequency: Moderate-high; reliable short note.

Expected content:

- Definition (Babinski, 1914): unawareness of neurological deficit
 - Prevalence: 10–30%; right hemisphere strokes
 - Neuroanatomy: right parietal (supramarginal gyrus, TPJ)
 - Why right hemisphere: bilateral body schema representation
 - Related syndromes: anosodiaphoria, Anton's syndrome, hemispatial neglect
 - Clinical significance: rehabilitation refusal, safety risk, poor prognosis
 - Management principles
-

Q8. "Transient Global Amnesia."

Frequency: Moderate; recurring short note favourite.

Expected content:

- Definition: sudden anterograde amnesia, <24 hours, preserved identity
 - Age group (50–70 years)
 - Pathognomonic feature: stereotyped repetitive questioning
 - Precipitants: Valsalva, exertion, sexual intercourse
 - Investigations: MRI DWI (CA1 dot, Sedlaczek sign), EEG normal
 - Differential: TEA (shorter, recurrent, EEG abnormal)
 - Management: reassurance; no specific treatment
 - Prognosis: benign; 6% / year recurrence
-

Q9. "Post-concussion syndrome."

Frequency: Moderate; gaining frequency with sports psychiatry interest.

Expected content:

- Definition: symptoms >3 months after mild TBI (ICD-10: F07.2)
- Symptom triad: somatic, cognitive, affective
- Pathophysiology: neurometabolic cascade + biopsychosocial model
- Risk factors for prolonged recovery
- Management: active recovery (not prolonged rest), graded return, symptom-specific treatment

- Second impact syndrome: link and prevention
-

Q10. "CTE (Chronic Traumatic Encephalopathy)."

Frequency: Rising, increasingly tested in modern exams.

Expected content:

- Definition: progressive neurodegenerative disease due to repetitive TBI
 - Historical context: boxers (dementia pugilistica), NFL players
 - Neuropathology: hyperphosphorylated tau, perivascular at sulcal depths (pathognomonic)
 - Posthumous diagnosis (no in-vivo validated test)
 - Staging: McKee I–IV (HEAD mnemonic)
 - Clinical profile: depression, impulsivity, aggression, memory loss
 - Management: symptomatic; prevention emphasis
-

2.3 Very Short Answer / MCQ-Type Questions (2 marks)

These test isolated facts and definitions.

QUESTION PATTERN · EXPECTED ANSWER

Most common psychiatric complication of stroke Post-stroke depression

Robinson's hypothesis: which hemisphere lesion → depression Left anterior frontal

CAM criteria for delirium diagnosis Feature 1 + 2 + (3 or 4): Acute onset, Inattention, Disorganized thinking / Altered arousal

Most common subtype of delirium Hypoactive

Which subtype of delirium has worst prognosis Hypoactive

Pathognomonic neuropathological finding in Korsakoff's Atrophied mammillary bodies

Critical lesion for amnesia in Korsakoff's Medial dorsal thalamus

Thiamine should be given before what? Glucose (dextrose)

GCS range for severe TBI 3–8

FDA-approved treatment for PBA Dextromethorphan / quinidine (Nuedexta)

Mechanism of PBA Disrupted corticobulbar pathways → released brainstem motor-emotional circuits

Phineas Gage syndrome Orbitofrontal (pseudopsychopathic) syndrome

Gerstmann syndrome lesion site Left angular gyrus

Four features of Gerstmann syndrome Finger agnosia, L-R disorientation, Agraphia, Acalculia

Anosognosia lesion Right parietal (supramarginal gyrus / TPJ)

Duration limit for TGA diagnosis <24 hours

Pathognomonic feature of TGA Stereotyped repetitive questioning

MRI finding in TGA CA1 hippocampal DWI spot (Sedlacek sign)

TGA vs TEA differentiator Episode duration + EEG (normal in TGA, abnormal in TEA)

Best evidence drug for aggression post-TBI Propranolol

Drug to AVOID in TBI recovery Haloperidol (impairs neuroplasticity)

CTE is what type of diagnosis Posthumous (requires autopsy)

CTE neuropathology Hyperphosphorylated tau, perivascular at depths of cortical sulci

NPH triad Wet + Wobbly + Wacky

NPH investigation to confirm LP tap test (gait improvement with 30–50 mL CSF removal)

Anti-NMDAR encephalitis: associated tumor Ovarian teratoma

Anti-NMDAR encephalitis EEG pattern Delta brush

Anti-LGI1 encephalitis: electrolyte disturbance Hyponatremia

Foster Kennedy syndrome: cause Olfactory groove meningioma

CADASIL mutation NOTCH3

Klüver-Bucy syndrome: lesion Bilateral anterior temporal (amygdala)

Post-COVID neuropsychiatric mechanism Neuroinflammation + microglial activation + autoantibodies

HELP program: who developed it Sharon Inouye

Section 3: Predicted High-Priority Questions for 2026

Based on trends in recent years and newly emerging clinical topics:

Almost Certain (>90% probability)

1. **Post-stroke depression**, Robinson hypothesis + management (Long answer)
2. **Delirium**, classification + CAM + management (Long answer)
3. **Short note: Korsakoff's syndrome**
4. **Short note: Pseudobulbar affect**

Very Likely (70–85%)

1. **TBI psychiatric sequelae + management** (Long answer)
2. **Short note: Frontal lobe syndromes**
3. **Short note: Anosognosia or post-stroke mania**
4. **Short note: Post-concussion syndrome**

Likely (50–65%)

1. **CTE**, rising trend in exams since 2022
2. **Anti-NMDAR encephalitis**, psychiatric presentation and diagnosis
3. **Vascular dementia vs Alzheimer's** (compare and contrast)
4. **Transient Global Amnesia**

Worth Preparing (Strategic)

1. **Delirium superimposed on dementia**, high clinical relevance, increasingly examined
2. **Second impact syndrome**, 4-mark short note; specific enough to differentiate candidates
3. **Post-COVID neuropsychiatry**, modern topic; asked in newer exams
4. **Normal pressure hydrocephalus**, classic triad + management

Section 4: Examiner Bias Analysis

Topics where candidates commonly lose marks

COMMON MISTAKE · CORRECTION

Listing only mammillary bodies in Korsakoff's Add medial dorsal thalamus, it is the critical lesion for amnesia

Describing only hyperactive delirium Always discuss all three subtypes; emphasize hypoactive is most common and most missed

Stating Robinson's hypothesis without critique Add: community studies showed weaker lateralization; strongest in hospital-based samples

Missing FLAME trial for fluoxetine Mention it explicitly, motor + mood benefit is a distinguishing point

Using HDRS for PSD assessment MADRS preferred, less confounded by somatic symptoms

Recommending haloperidol for TBI-related agitation State explicitly that haloperidol is to be avoided; recommend quetiapine or propranolol

Describing CTE as a clinical diagnosis Must state it is posthumous and requires brain autopsy

Missing delta brush EEG pattern for anti-NMDAR This is a specifically asked examination point

Diagnosing TGA with EEG abnormality TGA = normal EEG; abnormal EEG = transient epileptic amnesia

Stating thiamine after or alongside glucose Always thiamine BEFORE glucose, this is a patient safety point examiners check

Section 5: Structured Answer Templates

Template A: For Stroke Psychiatry Questions

Template B: For Delirium Questions

Template C: For TBI Questions

Quick Review

KEY INSIGHT

Format: Each vignette presents a clinical scenario followed by structured questions with answers and teaching points. All names are entirely fictitious. All clinical details are constructed for educational purposes only.

Vignette 1: The Quiet Ward Patient

A 68-year-old retired school principal named Mohan was admitted to the neurology ward after a left hemisphere ischaemic stroke confirmed on MRI. He had a prior history of hypertension and hyperlipidemia, well-controlled. On day 5 post-admission, the ward nurse calls psychiatry because Mohan "hasn't been eating, barely responds to questions, and just stares at the ceiling."

On assessment: Mohan makes eye contact but offers minimal spontaneous speech. He shakes his head "no" to questions about pain or discomfort. His family reports that he was an active, engaged person before the stroke. He does not appear sad or tearful. BP and oxygen saturation are normal. No fever.

Questions

Q1. What is the most likely psychiatric diagnosis at this point?

Answer: Post-stroke apathy.

Mohan shows reduced motivation and goal-directed behavior without subjective distress, dysphoric mood, or tearfulness. He is not in pain, not febrile, and the presentation is specifically reduced output rather than subjective suffering. This profile, flat affect, reduced initiation, absence of distress, is the hallmark of apathy rather than depression.

Key distinction: Post-stroke depression requires dysphoric mood + subjective distress.

Apathy = motivational syndrome without distress. Mohan does not appear to be suffering, he is indifferent.

Q2. What secondary diagnosis must be actively excluded, and how?

Answer: Hypoactive delirium.

Hypoactive delirium presents identically, withdrawn, reduced responsiveness, minimal spontaneous speech. Exclusion requires:

- **CAM criteria:** Check for acute onset relative to yesterday (fluctuation), impaired attention (digit span forward/backward), disorganized thinking
- Check for new metabolic disturbance (electrolytes, glucose, creatinine), urinary tract infection, medication review for anticholinergics or opioids
- If CAM positive with identifiable precipitant → delirium, not apathy

Teaching point: In a stroke patient who becomes suddenly less responsive, always delirium-first. Apathy is a diagnosis of exclusion once delirium is ruled out.

Q3. Mohan's workup is negative for delirium. What is the neuroanatomical basis of his presentation?

Answer: The anterior cingulate cortex (ACC) and frontal-subcortical circuits are the primary neuroanatomical substrates of apathy. His left hemisphere stroke may have disrupted the ACC, supplementary motor area, or their connections to the basal ganglia (caudate). These circuits are the substrate for motivated, goal-directed behavior.

Q4. What management would you recommend?

Answer:

- **Behavioral activation:** Structured daily schedule; nursing staff to prompt and engage rather than leave passive
 - **Caregiver coaching:** Teach family to use open prompts and engage Mohan in familiar topics/activities
 - **Occupational therapy:** Daily purposeful activity
 - **Pharmacological (if severe and persistent):** Methylphenidate 5 mg BD (modest evidence) or rivastigmine, neither is first-line
 - Treat any co-occurring depression that emerges
 - Monitor for evolution into post-stroke depression
-

Vignette 2: The Weeping Engineer

Rajesh, 55, is referred to psychiatry from the neurology clinic 8 weeks after a right pontine stroke. He recovered well motor-wise and is back at his desk job part-time. His wife accompanies him and describes episodes where Rajesh "bursts into tears at the most random things", a news item, a mildly sentimental advertisement, his daughter calling from Pune. The crying lasts about 30–60 seconds and then he stops and resumes conversation normally. Rajesh is clearly embarrassed and states: "I don't even feel that sad most of the time. I don't know why I'm crying."

Questions

Q1. What is the diagnosis?

Answer: Pseudobulbar affect (PBA) / Emotional incontinence.

The hallmarks are present:

- Involuntary, uncontrollable episodes of crying
 - Incongruent with subjective emotional state (he explicitly states he doesn't feel that sad)
 - Brief and self-terminating (30–60 seconds)
 - Occurs against a background of bilateral / pontine neurological disease
 - No full depressive episode, he is functioning, working, not globally dysphoric
-

Q2. What is the neurological mechanism?

Answer: The right pontine stroke has disrupted descending corticobulbar pathways that normally exert tonic inhibitory control over the brainstem's motor-emotional expression centers. The loss of this inhibitory cortical brake allows minor emotional stimuli to trigger full involuntary emotional output that cannot be stopped voluntarily. Serotonergic and glutamatergic (NMDA) pathways are also implicated.

Q3. What tool would you use to assess severity?

Answer: The CNS-LS (Center for Neurologic Study, Lability Scale). It is a 7-item self-report scale assessing frequency of involuntary laughing and crying episodes.

Q4. Outline the treatment plan.

Answer:

- **Psychoeducation first:** Explain to Rajesh and his wife that this is a neurological symptom, not a sign of underlying severe depression or "losing his mind." Destigmatization reduces avoidance behavior.
 - **Dextromethorphan/quinidine (Nuedexta):** FDA-approved 2010 for PBA. First-line when available. Quinidine inhibits CYP2D6, raising dextromethorphan levels. Mechanism: sigma-1 receptor agonism + NMDA antagonism reduces brainstem over-reactivity. Evidence: PRISM trials showed ~50–75% reduction in episode frequency.
 - **If Nuedexta unavailable:** Sertraline 50–100 mg or fluoxetine 20 mg, SSRIs are widely used first in clinical practice due to cost and availability; good evidence.
 - **Behavioral:** Distraction techniques during prodrome of an episode; controlled breathing.
-

Vignette 3: The Man Who Forgot Yesterday

A 72-year-old retired accountant named Venkat is brought to the emergency department by his wife. She reports that this morning, while they were having breakfast, Venkat suddenly became confused, kept asking "What are we doing today? Why am I dressed? Are we going somewhere?", the same questions, every few minutes, for about 4 hours. He did not fall, did not lose consciousness, and was fully aware of who he was and who his wife was. The episode resolved fully 5 hours after onset. Now in the ED, Venkat is completely back to baseline. Neurological examination is normal. Blood glucose: 95 mg/dL. ECG: normal sinus rhythm.

Questions

Q1. What is the most likely diagnosis?

Answer: Transient Global Amnesia (TGA).

The diagnostic features are all present:

- Sudden onset of transient anterograde amnesia
 - Preserved personal identity throughout
 - Repetitive stereotyped questioning, pathognomonic
 - Full resolution within 24 hours (5 hours in this case)
 - No focal neurological deficits
 - Normal consciousness throughout
-

Q2. What investigation would confirm the episode on imaging, and when should it be performed?

Answer: MRI brain with Diffusion-Weighted Imaging (DWI). The characteristic finding is a small diffusion restriction dot in the CA1 region of the hippocampus, best seen 24–48 hours after the episode (Sedlaczek phenomenon). If done immediately, it may be negative. EEG should also be performed and is expected to be normal, this distinguishes TGA from transient epileptic amnesia (TEA).

Q3. His daughter, who is a doctor, insists this must be a TIA. How do you explain the distinction?

Answer:

FEATURE	TGA	TIA
Memory deficit	Yes, isolated, dense	No, focal motor/sensory/speech
Focal neurological deficit	Absent	Present

FEATURE	TGA	TIA
Consciousness	Intact	Variable
Personal identity	Preserved	Preserved
Duration	Up to 24 hours	<24 hours (usually <1 hour)
Stroke risk	Low	High, needs urgent workup
Treatment	None	Antiplatelets, risk factor control

Key point: TGA does not increase stroke risk and requires no specific treatment. TIA demands urgent secondary prevention workup (carotid Doppler, echocardiogram, lipid panel, antiplatelet initiation). Venkat needs TIA workup to be safe, the clinical story does not fit TIA, but ruling it out is appropriate.

Q4. What is the prognosis and management?

Answer: TGA is a benign condition. Recurrence rate is approximately 6% per year. No treatment is required. Reassurance and education for the patient and family are the primary intervention. Advise Venkat to report future episodes immediately.

Vignette 4: The Disinhibited Executive

Priya, 47, is brought by her husband to the outpatient clinic. He describes a 2-year change in personality: previously a meticulous, reserved financial executive, she has become tactless, makes sexually inappropriate comments in social settings, spent ₹12 lakhs on an impulsive online shopping spree without telling him, and has been making jokes at her mother-in-law's funeral. She does not appear distressed about any of this behavior. Her MMSE is 27/30. MRI brain is reported as a "mass lesion in the right frontal region."

Questions

Q1. What syndrome best describes Priya's behavioral change?

Answer: Orbitofrontal Cortex (OFC) Syndrome, also called "Pseudopsychopathic Syndrome."

Features present:

- Disinhibition (socially inappropriate comments, impulsive purchases)
- Loss of response inhibition (cannot suppress inappropriate responses)
- Euphoria / indifference to consequences
- Hypersexual behavior (sexual comments)
- Lack of insight and concern (not distressed by her own behavior)

This is the classic OFC syndrome produced by damage to the orbitofrontal cortex (BA 11, 12, 13, 14).

Q2. The MRI shows a right frontal extra-axial mass with homogeneous enhancement and dural tail sign. What is the likely tumor, and what are additional psychiatric features to expect?

Answer: Meningioma, the dural tail sign (thickening of adjacent dura) and homogeneous enhancement are classic imaging features of meningioma. Right frontal convexity or parasagittal location.

If the mass involves the olfactory groove (anterior cranial fossa): expect anosmia (often unreported by patient) + Foster Kennedy syndrome (ipsilateral optic atrophy + contralateral papilledema).

Psychiatric features of frontal meningioma include: personality change (most common presentation), apathy or disinhibition depending on precise location, depression, cognitive slowing, and frontal release signs (grasp reflex, palmomental reflex). This presentation may mimic bipolar disorder (euphoria, impulsivity) or early dementia for years before diagnosis, which is why psychiatric presentations in middle-aged patients warrant neuroimaging before labeling as primary psychiatric disease.

Q3. How do you distinguish this from early-onset frontotemporal dementia (bvFTD)?

Answer:

FEATURE	OFC MENINGIOMA	BVFTD
Onset	Gradual (mass effect)	Insidious
Course	Progressive (mass-related)	Steadily progressive
Imaging	Extra-axial mass; dural tail	Frontal-temporal atrophy; no mass
CSF	Normal	Normal or elevated Tau/NfL
Memory	Relatively preserved	Variable; executive-first
Age	Any adult age	Usually 45–65
Treatment	Surgical resection	No disease-modifying treatment

Clinical rule: New-onset personality change or disinhibition in a previously reserved adult always requires MRI brain before any psychiatric label.

Vignette 5: The Boxer Who Forgot How to Box

Deepak, 38, is a retired state-level boxer who was forced to retire 3 years ago due to persistent headaches. He presents with his wife, who reports: progressive memory problems over 2 years, explosive anger with trivial frustration, two episodes of punching walls (no prior violence), 6 months of depression, and two episodes of cocaine use (new behavior, "he never touched drugs before"). MMSE: 22/30. MRI brain: cavum septum pellucidum, mild cerebral atrophy, no acute lesion.

Questions

Q1. What is the most likely diagnosis and what is required to confirm it definitively?

Answer: Chronic Traumatic Encephalopathy (CTE) is the most likely diagnosis given:

- History of repetitive head trauma (boxing career)
- Progressive behavioral syndrome: memory loss, explosive aggression, depression, new substance use
- Imaging: cavum septum pellucidum (characteristic in boxers, "punched out" appearance), cerebral atrophy
- Age: mid-thirties (consistent with CTE onset in high-exposure athletes)

Definitive diagnosis requires brain autopsy, CTE is currently a posthumous diagnosis. Neuropathological criteria (McKee et al., 2016) require demonstration of hyperphosphorylated tau in a perivascular distribution at the depths of cortical sulci. No currently validated in-vivo biomarker exists.

Q2. The wife asks: "Can anything be done?" What do you tell her?

Answer:

- No disease-modifying treatment currently exists
- Management is entirely symptomatic:
- **Depression:** SSRI (sertraline)
- **Explosive aggression:** Propranolol (best evidence for post-TBI aggression); consider valproate for affective aggression
- **Cognitive decline:** Cognitive rehabilitation strategies; external memory aids; structured environment
- **Substance use:** MI-based intervention; harm reduction
- Deepak should be assessed for suicide risk, CTE carries significantly elevated suicidality
- Family psychoeducation: understand the organic basis of the behavioral changes; reduce conflict and blame

- **Safety planning:** For aggression episodes, warning signs, de-escalation strategies for the family
-

Q3. What staging would Deepak likely fall into (McKee stages)?

Answer: Stage II–III.

- Stage II features present: Depression, explosivity, impulsivity, executive dysfunction
 - Stage III features beginning: Memory loss (MMSE 22, suggesting moderate impairment), executive dysfunction
 - Stage IV features absent: Severe dementia, Parkinsonism, speech/swallow difficulties, not yet present
-

Vignette 6: Delirium on the Orthopaedic Ward

Meena, 76, is a retired schoolteacher admitted for right hip replacement surgery. She has known mild cognitive impairment (baseline MMSE ~24), hypertension, and type 2 diabetes. On post-operative day 2, the nurses call psychiatry at 2 AM. Meena has been pulling at her IV line, shouting for people who are not there, and calling out her late husband's name repeatedly. She tried to get out of bed and was restrained. On assessment: Meena is disoriented to time and place, does not recognize her daughter, sees "children playing in the corner," and her attention is severely impaired.

Questions

Q1. Establish the diagnosis using formal criteria.

Answer: Delirium, DSM-5 criteria met:

- **Criterion A:** Disturbance in attention (cannot focus, sustain, or shift attention, does not recognize daughter, severely inattentive) AND awareness (disoriented to place and time)
- **Criterion B:** Acute onset (post-operative day 2, change from baseline), fluctuating course (was lucid on day 1)
- **Criterion C:** Additional cognitive disturbance, disorientation, visual hallucinations ("children in the corner"), misidentification
- **Criterion D:** Not attributable to another pre-existing NCD, the cognitive decline is acute and beyond her MCI baseline
- **Criterion E:** Direct physiological consequence of surgery (post-operative state, possible infection, pain medication, fasting, sleep deprivation, pain)

Subtype: Hyperactive delirium (agitation, pulling lines, shouting, visual hallucinations)

Q2. What predisposing and precipitating factors does Meena have?

Answer:

Predisposing (baseline vulnerability):

- Age (>70)
- Pre-existing mild cognitive impairment (2–5× risk)
- Female sex
- Prior functional impairment

Precipitating (acute triggers):

- Major surgery (hip replacement, high-risk orthopedic procedure)
 - Post-operative state: pain, immobility, catheter (urinary retention risk), blood loss
 - Opioid analgesics (prescribed post-op), anticholinergic + CNS depressant effects
 - Sleep deprivation (hospital environment, pain, 2 AM intervention)
 - Restraint application (restraints paradoxically worsen delirium by increasing agitation and distress)
-

Q3. What is your immediate management plan?

Answer:

Immediate (next 30 minutes):

1. **Remove restraints**, restraints worsen delirium; use 1:1 nursing sitter instead
2. Ensure Meena is safe (bed rails, call bell accessible, low bed height)
3. Reorient gently, name ("You are Meena"), place, time, familiar face (daughter at bedside)
4. Turn on a low light, complete darkness worsens hallucinations

Medical review (within 1 hour):

- Check vitals: temperature (infection), O2 saturation (hypoxia), glucose, BP
- Review medications: stop/reduce opioids if possible; substitute paracetamol + regional analgesia
- Urinalysis, FBC, CRP, U&E, creatinine, screen for UTI, electrolyte disturbance
- Check for constipation, urinary retention

Pharmacological (only if behavioral disturbance is dangerous):

- Quetiapine 12.5–25 mg: preferred in elderly with cognitive impairment; fewer EPS
- Haloperidol 0.5 mg IM: if immediate parenteral sedation needed; monitor QTc

Ongoing (next 48–72 hours):

- HELP program: orientation board, daytime lights, dayroom activity, sleep protocol at night

- Daughter to stay during day (familiar presence)
 - Discontinue non-essential anticholinergic medications
 - Hydration review
-

Q4. The family is upset and asks why this happened and whether Meena will "go back to normal."

Answer:

- Explain the biological basis: the stress of surgery temporarily disrupts brain chemistry, especially in older people with existing vulnerability (MCI). It is not a sign of a new stroke or permanent decline.
 - Most delirious episodes resolve within days to weeks with treatment of the underlying cause
 - However: In patients with pre-existing cognitive impairment, delirium can:
 - Take longer to resolve
 - Leave a residual cognitive "notch", some patients do not fully return to pre-delirium baseline
 - Accelerate underlying MCI progression
 - Long-term monitoring after this episode is warranted
 - Reassure that this was recognized early and is being treated
-

Vignette 7: Post-Stroke Mania

A 61-year-old retired bank manager named Suresh presented to the casualty with what his wife described as a "complete personality flip" starting 3 weeks after a right hemisphere ischaemic stroke (MRI confirmed right basal temporal and thalamic infarct). He is sleeping only 2 hours a night, has made three large real estate investments without consulting his wife, speaks rapidly about plans to "start a foundation for stroke survivors," and has been making lewd jokes to the nursing staff. He has no prior psychiatric history.

Questions

Q1. What is the diagnosis?

Answer: Post-stroke mania (Secondary Mania Due to Stroke, DSM-5: Bipolar and Related Disorder Due to Another Medical Condition).

The features of a manic episode are present:

- Decreased need for sleep (2 hours)
- Grandiosity (foundation plans, large investments)

- Increased goal-directed activity
 - Pressured/rapid speech
 - Hypersexual behavior
 - Impulsivity (real estate investments without judgment)
 - Onset 3 weeks after right hemisphere stroke
 - No prior psychiatric history (excludes primary bipolar disorder)
-

Q2. What neuroanatomical substrate explains this presentation?

Answer: The right hemisphere is the neuroanatomical substrate for post-stroke mania. Specifically:

- **Right basal temporal region**, documented in multiple cases of secondary mania
- **Right orbitofrontal cortex**
- **Right caudate nucleus**
- **Right thalamus**, also implicated

Proposed mechanism: Right hemisphere lesions release the left hemisphere from tonic inhibitory control, resulting in disinhibited, approach-oriented left hemisphere drives (positive affect regulation, approach behavior), manifesting as mania.

Robinson and Starkstein noted that secondary mania almost always follows right hemisphere lesions, in contrast to depression (left hemisphere predominance).

Q3. Outline the management.

Answer:

Pharmacological:

- **Valproate:** First choice in neurological setting, mood stabilizer; good safety profile in elderly; fewer drug interactions than lithium; can be given IV if needed
- **Atypical antipsychotics:** Quetiapine or olanzapine for acute behavioral control (decreased sleep, agitation)
- **Lithium:** Effective but narrow therapeutic index, requires renal monitoring; risk of toxicity in elderly; second choice
- **Avoid:** Carbamazepine (enzyme inducer, multiple drug interactions in stroke management)

Safety:

- Supervise financial decisions (PoA considerations if insight severely impaired)
- Prevent unsafe behavior (driving, large purchases)
- Caregiver safety and education

Monitoring:

- Episode often self-limiting (weeks to months) as brain reorganization occurs
 - Follow-up for development of depressive phase (secondary bipolar cycle possible)
-

Vignette 8: The Young Woman Who "Went Crazy"

Kavitha, 22, a second-year engineering student, is brought to the emergency psychiatry unit by her parents. Over 3 weeks, she developed: mood changes and odd behavior (laughing inappropriately, socially inappropriate remarks) → escalating to auditory and visual hallucinations, persecutory delusions → seizure (generalized tonic-clonic, 2 days ago) → now reduced consciousness and appears posturing. Temperature 38.2°C. She has no prior psychiatric history.

Questions

Q1. What diagnosis must be urgently considered and investigated?

Answer: Anti-NMDA Receptor Encephalitis.

The clinical trajectory is the pathognomonic sequence:

1. **Psychiatric onset** (mood change, behavioral disturbance, psychosis), Stage 1
2. **Seizures**, Stage 2
3. **Movement disorders / decreased consciousness**, Stage 3
4. **Autonomic instability**, Stage 4 (may develop)

Red flags (FARMS) present: Fever, movement changes, Seizures, and rapid progression.

This is the most common autoimmune encephalitis. Young women are the most affected demographic. Ovarian teratoma must be urgently screened for.

Q2. What investigations must be ordered immediately?

Answer:

Urgent:

- MRI brain with FLAIR/T2 sequences (bilateral temporal signal change, limbic encephalitis pattern)
- EEG: **Delta brush pattern**, pathognomonic for anti-NMDAR encephalitis
- LP for CSF: cell count, protein, glucose, oligoclonal bands, **anti-NMDAR antibodies in CSF** (more sensitive than serum)
- Serum: anti-NMDAR antibodies, comprehensive metabolic panel, CBC, CRP
- Pelvic ultrasound / CT abdomen-pelvis: screen for ovarian teratoma

Supportive:

- LFT, renal function, electrolytes
 - Blood cultures if fever persistent
 - ECG
-

Q3. If confirmed, what is the treatment protocol?

Answer:

First-line immunotherapy:

- IV Methylprednisolone 1 g/day × 3–5 days
- IVIG 2 g/kg over 3–5 days
- Can use together or sequentially; combined approach often used

If teratoma found:

- Surgical removal (laparoscopic oophorectomy), accelerates neurological recovery; must be done even if small/asymptomatic

If no improvement in 10–14 days (Second line):

- Rituximab 375 mg/m² weekly × 4 doses (anti-CD20 B-cell depletion)
- Cyclophosphamide (severe/refractory)

Symptomatic:

- Seizure control (levetiracetam, valproate)
- Antipsychotics for agitation (with caution; may need ICU)
- ICU management if autonomic instability develops

Prognosis: With early treatment, 75–80% achieve good functional recovery. Relapse in ~25%, requires long-term immunosuppression monitoring.

Q4. Her parents ask why she was treated for schizophrenia for 2 weeks before this diagnosis was made. What is the lesson?

Answer: Anti-NMDAR encephalitis is the great neuropsychiatric mimicker. Its initial psychiatric phase, behavioral change, psychosis, hallucinations, emotional lability, is clinically indistinguishable from first-episode psychosis or schizophrenia without additional workup.

The lesson for clinical practice: New-onset psychosis in a young person should trigger consideration of autoimmune encephalitis, especially when:

- Fever accompanies the psychiatric presentation
- Cognitive decline is rapid or disproportionate

- Seizures develop
- Movement abnormalities are noted (orofacial dyskinesias, catatonia)
- Antipsychotics show minimal or paradoxical effect
- No family history of psychotic illness

Routine MRI, EEG, and LP in new-onset psychosis (especially in young patients) would prevent delayed diagnoses.

Vignette 9: The Rugby Player with a "Mild" Head Injury

Arjun, 19, a state-level rugby player, sustained a concussion during a match, he was briefly confused, GCS 15 throughout, and was cleared within 30 minutes. He played the next match 4 days later (team pressure, "he seemed fine"). During the second match, he received a minor head contact with another player. Within 3 minutes, he collapsed on the field, became unresponsive, and was rushed to hospital with bilateral fixed dilated pupils.

Questions

Q1. What has occurred?

Answer: Second Impact Syndrome (SIS).

Arjun's first concussion placed his brain in a state of neurometabolic vulnerability, ongoing ionic flux, mitochondrial dysfunction, and critically, impaired cerebrovascular autoregulation. A second head impact during this vulnerable period, even trivially minor, triggered catastrophic loss of vascular autoregulation, resulting in:

- Massive cerebrovascular vasodilation
- Bilateral cerebral swelling (malignant edema)
- Rapid transtentorial herniation (bilateral fixed dilated pupils = herniation)

This sequence can unfold within minutes of the second impact, which is why it is almost always fatal or results in severe disability.

Q2. Who is primarily responsible for preventing this outcome?

Answer: Prevention is the responsibility of a multi-layered system:

- **Team physician/medical officer:** Must enforce return-to-play (RTP) protocols, no player returns before being fully asymptomatic
- **Coach:** Must not pressure players to return early
- **Player:** Must self-report symptoms accurately
- **Parents/guardians** (in minors): Must be educated

- **Sports organization:** Must enforce protocol with zero-tolerance rules

The **SCAT5 (Sport Concussion Assessment Tool, 5th edition)** mandates 6-stage graduated return to play, with each stage taking a minimum of 24 hours. Same-day return after any concussion is absolutely prohibited.

Q3. What are the management priorities in the emergency department?

Answer:

- ABC: Airway (intubate for GCS protection), Breathing, Circulation
 - Neurosurgical emergency: CT head immediately, bilateral cerebral swelling (no focal hemorrhage typically)
 - ICP monitoring
 - Hyperosmolar therapy (mannitol or hypertonic saline) to reduce cerebral edema
 - Head of bed elevation 30°
 - Avoid hypotension and hypoxia (secondary injury)
 - Neurosurgical consultation: decompressive craniectomy may be considered
 - Prognosis: ~50% mortality even with aggressive management; severe disability in survivors
-

Vignette 10: Theft or Dementia?

Ramesh, 64, is brought by police to the hospital after being apprehended at a supermarket. He had walked out with items worth ₹800 in his pockets without paying. His wife, who came to the police station, insists "he has never stolen anything in his life." She also reports that for the past 18 months, Ramesh has been making "embarrassing comments" to strangers, bought a second-hand vehicle without telling her, and lost his previously meticulous attention to his accounts. His MMSE is 21/30. MRI: frontal and anterior temporal atrophy bilaterally.

Questions

Q1. What is the most likely diagnosis explaining this behavior?

Answer: Behavioural Variant Frontotemporal Dementia (bvFTD).

Ramesh's presentation includes:

- Disinhibition (shoplifting without guilt or insight, inappropriate comments)
- Impulsivity (vehicle purchase without consultation)
- Executive dysfunction (lost meticulous accounting skills)
- Social inappropriateness

- Progressive over 18 months
- Frontal and anterior temporal atrophy on MRI

BvFTD classically presents with behavioral change rather than memory loss. Patients frequently come to forensic attention before the diagnosis is made. Shoplifting, sexual offenses, and traffic violations are documented in bvFTD literature.

Q2. How would you counsel the police about proceeding with charges?

Answer: Ramesh lacks the mental capacity required for criminal intent (mens rea). The behavior is a direct consequence of his neurodegenerative condition, not volitional theft. A formal medicolegal report should include:

- Psychiatric diagnosis (bvFTD) with clinical and radiological evidence
- Assessment of insight and impulse control at the time of the incident
- Statement that he lacked capacity to form criminal intent
- Recommendation for charges to be dropped given medical basis
- Recommendation for supervision and care planning

This is a forensic psychiatry teaching point: frontal dementia and forensic presentations.

Q3. What management would you recommend for Ramesh?

Answer:

- No disease-modifying treatment exists for bvFTD
 - Symptomatic: SSRIs (fluvoxamine, sertraline) reduce disinhibition and compulsive behaviors in bvFTD
 - Caregiver education: the behavior is not intentional; it is neurological
 - Financial and legal protective arrangements (PoA for finances; restrict independent access to money)
 - Safety supervision: not to go to public places unaccompanied
 - Driving assessment (likely unsafe, should cease driving)
 - Genetic counseling: 30–50% of bvFTD cases have family history; MAPT, GRN, C9orf72 mutations
 - Palliative planning for disease progression
-

Vignette 11: The Nurse Who Could Not Remember Her Patients

Sudha, 48, a senior ward nurse, is referred by her ward consultant. Over the past year, she has been making "silly mistakes", giving the wrong medications twice, forgetting discharge instructions she gave 2 hours earlier, needing her junior nurses to repeat

information multiple times. She attributes it to "stress and overwork." MMSE: 27/30. MoCA: 23/30. Neuropsychological testing shows impaired verbal memory (delayed free recall) and mildly reduced executive function. MRI: mild white matter hyperintensities (Fazekas grade 1–2).

Past history: Hypertension (treated), diabetes (well-controlled), migraines with aura since age 30, two maternal uncles with "stroke-like events" in their 40s.

Questions

Q1. Given the family history and migraine with aura, what genetic condition must be excluded?

Answer: CADASIL, Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy.

Key features pointing toward CADASIL:

- Migraine with aura (characteristic early feature, often onset in 20s–30s)
- Young onset cognitive impairment with white matter changes
- Autosomal dominant family history (maternal uncles with early stroke-like events)
- No major vascular risk factors of sufficient severity to explain the WMH
- Pattern: subcortical cognitive impairment (executive + memory)

Confirm with: **NOTCH3 gene mutation testing** (blood) and/or skin biopsy (electron microscopy showing GOM, granular osmiophilic material deposits in small vessel walls).

Q2. What is the cognitive profile of subcortical vascular cognitive impairment?

Answer:

- **Executive dysfunction predominant:** Planning, set-shifting, divided attention, verbal fluency
- **Memory:** Encoding relatively preserved; retrieval impaired (unlike AD where encoding fails)
- **Processing speed:** Slowed
- **Attention:** Impaired
- **Gait:** May be abnormal even early
- **Mood:** Depression and apathy common

MoCA 23/30 with subtest analysis showing executive/attention deficits > memory encoding failure is consistent.

Q3. What are the immediate clinical management priorities?

Answer:

1. **CADASIL workup:** NOTCH3 mutation testing, skin biopsy, family screening
 2. **Vascular risk factor optimization:** Strict BP control (<130/80), diabetes management, no smoking
 3. **Antiplatelet therapy:** Aspirin 75–100 mg (prophylaxis against further lacunar events)
 4. **Occupational assessment:** Her medication errors represent patient safety risk, referral to occupational medicine; may need supervised work reduction or role modification
 5. **Cognitive rehabilitation:** Memory compensatory strategies, structured checklists, external aids
 6. **Mood screening:** Depression is common; start SSRI if criteria met
 7. **Genetic counseling:** For her children
-

Vignette 12: The ICU Patient No One Talks To

Sunil, 71, is on day 8 of a prolonged ICU admission for community-acquired pneumonia requiring ventilation. He was extubated 2 days ago. He is awake and can obey commands but has been "very quiet" since extubation. He does not speak spontaneously, responds minimally when addressed, and appears vacant. His family is concerned he "does not seem himself." Nursing staff feel he is "just tired." O₂ saturation: 97%. Temperature: 37.1°C. Electrolytes: normal. No medication changes in 3 days.

Questions

Q1. What is the most important psychiatric diagnosis to consider and how would you assess it?

Answer: Hypoactive delirium, the most common subtype in ICU settings, and the most frequently missed.

Assessment using **CAM-ICU (ICU-adapted Confusion Assessment Method):**

1. **Acute onset / fluctuation:** Was there a clear change from his pre-illness baseline? Is behavior variable across shifts?
2. **Inattention:** Give RASS (Richmond Agitation-Sedation Scale) + attention testing, can he track 10 letters (SAVEAHAART), squeezing when "A" is spoken?
3. **Disorganized thinking:** Ask yes/no questions (Will a stone float on water? Are there fish in the sea?). Give a 2-step command.
4. **Altered arousal:** RASS score, any level other than 0 (alert/calm) is abnormal

If features 1+2+(3 or 4) are present → **CAM-ICU positive = delirium**

Q2. Why is this being missed?

Answer: Hypoactive delirium is systematically under-recognized because:

- It does not create behavioral problems for staff
- It is attributed to "being tired after illness" or "post-ventilation sedation wearing off"
- The patient does not demand attention
- Nursing and medical staff are trained to respond to agitation, not to absence of agitation
- "He's resting" is a common but dangerous assumption

The consequences of missed hypoactive delirium include: longer ICU stay, higher mortality, persistent cognitive impairment, longer ventilation duration, functional decline.

Q3. No new medical trigger is found. What does management focus on?

Answer:

- **Stimulation and orientation:** Speak to Sunil, name him, orient him, explain where he is and why
 - **Family presence:** Have family speak to him (familiar voices are orienting)
 - **Sensory aids:** Hearing aids if used; glasses
 - **Physiotherapy:** Passive or active range of motion; sitting up if safe
 - **Sleep-wake normalization:** Bright light during day; dark and quiet at night
 - **Remove non-essential medications:** Review sedatives, H2-blockers, opioids, reduce/stop where safe
 - **Pharmacological:** Not indicated for hypoactive delirium; quetiapine only if significant distress develops
 - **Monitor:** Daily RASS and CAM-ICU; document trajectory
-

HIV Parkinsons Neuropsych

Paper IV · Neurology, Medicine & Recent Advances. Six study modes, from notes to quick review.

Study Notes

Comprehensive Study Notes for MD Psychiatry Exit Examination

PART 1: HIV & NEUROPSYCHIATRY

1.1 EPIDEMIOLOGY AND OVERVIEW

HIV (Human Immunodeficiency Virus) infects approximately 38 million people globally. In India, the estimated prevalence is ~2.3 million. The neuropsychiatric burden of HIV is substantial:

- **50–70%** of HIV-positive individuals will develop some form of neuropsychiatric complication over their lifetime
 - Neuropsychiatric manifestations may be the **presenting feature** of HIV infection
 - With the advent of combination antiretroviral therapy (cART), the landscape has shifted, severe HAD has decreased, but milder forms of HAND have become more prevalent
 - Psychiatric comorbidity worsens HIV outcomes: reduces ART adherence, increases risky behavior, accelerates disease progression
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1.2 HIV-ASSOCIATED NEUROCOGNITIVE DISORDERS (HAND)

BOX: HAND CLASSIFICATION (ANTINORI ET AL., 2007)

NEUROPSYCHOLOGICAL DOMAINS ASSESSED IN HAND

Six domains must be assessed:

1. **Learning/Memory**, verbal and visual
2. **Attention/Working Memory**, most commonly impaired
3. **Executive Function**, planning, cognitive flexibility
4. **Speed of Information Processing**, psychomotor slowing (hallmark)
5. **Language**, verbal fluency
6. **Motor Skills**, fine motor speed, coordination

Key Feature: HAND is a **subcortical dementia**, psychomotor slowing, personality change, poor concentration, memory retrieval deficits (not encoding). Contrast with Alzheimer's (cortical, aphasia, apraxia, agnosia).

1.3 PATHOPHYSIOLOGY OF HAND

DIRECT VIRAL NEUROTOXICITY

HIV does **not** directly infect neurons (neurons lack CD4 receptors). Instead:

1. **Macrophage/Microglia Reservoir:** HIV infects macrophages and microglia in the CNS. These become reservoirs for viral replication.
1. **HIV proteins as neurotoxins:**
 2. **gp120 (viral envelope glycoprotein):** Binds CXCR4/CCR5 on neurons → calcium influx → excitotoxicity → apoptosis
 3. **Tat protein:** Disrupts blood-brain barrier, induces oxidative stress, activates microglia, dysregulates neurotransmitter systems (dopamine pathway particularly affected)
 4. **Vpr:** Promotes apoptosis
 5. **gp41:** Mitochondrial dysfunction
1. **Bystander neurotoxicity:** HIV-infected macrophages release cytokines (IL-1 β , TNF- α , IL-6), quinolinic acid (NMDA agonist → excitotoxicity), and reactive oxygen species

IMMUNE ACTIVATION

- Persistent immune activation even on ART ("inflammaging")
- Chronic microglial activation → neuroinflammation
- CD8+ T-cell infiltration into CNS
- Blood-brain barrier disruption → increased CNS penetration of inflammatory mediators
- The **monocyte/macrophage** is the central culprit, not the T-cell

CNS PENETRATION EFFECTIVENESS (CPE) SCORE OF ART

Not all ART drugs penetrate the CNS equally. CPE score (0–4 per drug, summed for regimen):

- **High CPE:** Zidovudine (AZT), Nevirapine, Lopinavir / ritonavir
- **Low CPE:** Tenofovir, Ritonavir alone
- Target CPE ≥ 8 for CNS disease

1.4 ASSESSMENT: INTERNATIONAL HIV DEMENTIA SCALE (IHDS)

BOX: IHDS: 3 COMPONENTS

Sensitivity: 74% | **Specificity:** 54% for HAD

Advantage: Bedside tool, culturally applicable, quick (<5 minutes)

Limitation: Not validated for ANI/MND, misses milder forms

Other assessment tools:

- **Montreal Cognitive Assessment (MoCA):** General cognitive screen, not HIV-specific
 - **HIV Dementia Scale (HDS):** Older version (Power et al., 1995)
 - **Brief Neurocognitive Screen (BNCS)**
 - Formal neuropsychological battery: gold standard but requires trained personnel
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1.5 CNS OPPORTUNISTIC INFECTIONS IN HIV

1.5.1 TOXOPLASMA ENCEPHALITIS

Organism: *Toxoplasma gondii* (intracellular protozoan)

Mechanism: Reactivation of latent cysts (primary infection usually acquired in childhood from cat feces or undercooked meat)

CD4 threshold: Typically <100 cells/ μ L (most common when <50)

Epidemiology: Most common mass lesion in HIV in developing world

Clinical Features:

- Fever, headache, focal neurological deficits
- Seizures (30%)
- Altered consciousness
- Gradual onset over days-weeks

Neuroimaging:

- **CT/MRI:** Multiple ring-enhancing lesions, typically at grey-white junction and basal ganglia
- "Target sign" on MRI (central enhancement, ring enhancement, surrounding edema)
- **Classic teaching:** Bilateral lesions in basal ganglia

Diagnosis:

- Serology: *Toxoplasma* IgG positive (90–95% of cases, previous exposure)
- CSF: PCR for *T. gondii* (sensitivity 50–60%)
- Definitive: Brain biopsy (rarely needed if response to empirical treatment)
- Key rule: **If IgG negative + classic MRI appearance → consider CNS lymphoma first**

Treatment:

- **Pyrimethamine + Sulfadiazine + Leucovorin** (folinic acid to prevent bone marrow suppression)
- **Alternative:** Pyrimethamine + Clindamycin (if sulfa allergy)
- Duration: 6 weeks acute, then lifelong secondary prophylaxis
- **Clinical response expected by 2 weeks**, if no response, biopsy

- **Primary prophylaxis:** Co-trimoxazole (TMP-SMX) when CD4 <100
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1.5.2 PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML)

Organism: JC virus (John Cunningham virus), polyomavirus

Mechanism: Reactivation of latent JC virus in oligodendrocytes → lytic infection → demyelination

CD4 threshold: Typically <200 cells/ μ L

Clinical Features:

- Subacute progressive focal neurological deficits
- Cognitive decline
- Visual field defects (posterior leukoencephalopathy)
- NO fever, NO meningismus
- Headache is rare
- Can cause significant personality change (frontal lobe involvement)

Neuroimaging:

- **MRI:** Non-enhancing (or faint enhancement), T2 hyperintense white matter lesions
- **No mass effect, no ring enhancement**, distinguishes from toxoplasmosis
- Multifocal lesions predominantly in subcortical white matter
- Posterior-parietal-occipital predominance common

Diagnosis:

- CSF: JC virus PCR (sensitivity 72–92%, specificity 92–99%)
- **Biopsy:** Diagnostic gold standard, demyelination, enlarged oligodendrocyte nuclei, bizarre astrocytes, absence of inflammatory infiltrate

Treatment:

- **No specific treatment for JC virus**
 - Mainstay: Optimize ART (immune reconstitution)
 - IRIS (Immune Reconstitution Inflammatory Syndrome) can worsen PML paradoxically when starting ART
 - **Prognosis:** Poor without immune recovery. With ART, ~50% survive but most with neurological sequelae
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1.5.3 CRYPTOCOCCAL MENINGITIS

Organism: Cryptococcus neoformans (encapsulated yeast)

CD4 threshold: Typically <100 cells/ μ L (most common when <50)

Route: Inhalation → pulmonary → hematogenous spread to CNS

High-yield: Polysaccharide capsule resists phagocytosis; capsule visible with India ink stain

Clinical Features:

- **Subacute/chronic meningitis**, develops over weeks
- Headache (most prominent), fever, malaise
- Meningismus may be ABSENT (poor inflammatory response)
- Elevated intracranial pressure (ICP), may cause vision loss, CN VI palsy
- **Papilledema** (30%)
- Altered consciousness if severe

CSF Findings:

PARAMETER · TYPICAL FINDING

Opening pressure Elevated (>200 mm H₂O) in 75%

WBC Normal or mild lymphocytosis (<20 cells)

Protein Mildly elevated or normal

Glucose Low

India ink Positive in 70–80%

Cryptococcal antigen (CrAg) >95% sensitivity, gold standard

Culture Definitive, takes days

Diagnosis:

- **Serum CrAg** excellent screening test in endemic areas (sensitivity >99%)
- India ink: "Halo" appearance, yeast with large clear capsule
- **Blood culture** positive in 50–70%

Treatment:

- **Induction (2 weeks):** Amphotericin B deoxycholate + Flucytosine
 - **Consolidation (8 weeks):** Fluconazole 400mg / day
 - **Maintenance:** Fluconazole 200mg / day (lifelong or until CD4 >200 for >6 months)
 - **ICP management:** Serial therapeutic lumbar punctures (drain to <200 mmH₂O), NO acetazolamide / steroids / mannitol routinely
 - **IRIS:** Can occur when starting ART; corticosteroids used for severe IRIS
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1.5.4 CMV ENCEPHALITIS / RETINITIS

Organism: Cytomegalovirus (herpesvirus)

CD4 threshold: <50 cells/ μ L (most immunosuppressed patients)

CMV Retinitis (most common CMV manifestation):

- Painless progressive vision loss
- "Pizza pie" or "ketchup and cheese" fundoscopic appearance
- Retinal hemorrhages and exudates in perivascular distribution
- Treatment: Ganciclovir, Valganciclovir, Cidofovir, Foscarnet

CMV Encephalitis:

- Acute/subacute encephalopathy
- Ventriculoencephalitis pattern on MRI (periventricular enhancement)
- CSF: CMV PCR positive
- Treatment: Ganciclovir IV + Foscarnet (combination for encephalitis)

CMV Polyradiculopathy:

- Lumbosacral polyradiculopathy
- Lower extremity weakness, urinary retention
- CSF: Neutrophilic pleocytosis (unusual, raises CMV suspicion in HIV)

1.5.5 OTHER CNS OIS

CONDITION	ORGANISM	CD4 LEVEL	KEY FEATURE
CNS Lymphoma	EBV-associated	<50	Single ring-enhancing mass, SPECT shows hypermetabolism (vs hypometabolism in toxo)
TB Meningitis	M. tuberculosis	Any, worse <200	Basilar meningitis, CN palsies, communicating hydrocephalus
HSV Encephalitis	HSV-1 (reactivation)	<50	Temporal lobe, hemorrhagic; treat with acyclovir
Neurosyphilis	T. pallidum	Any	Meningovascular, general paresis, tabes; treat with benzyl penicillin
MAC/MAI	M. avium complex	<50	Systemic; CNS rare

1.6 PSYCHIATRIC DISORDERS IN HIV

1.6.1 DEPRESSION IN HIV

Prevalence: 30–60% (vs ~10–15% general population)

Why so high?

1. Direct neurobiological effects of HIV (viral proteins, cytokine dysregulation, HPA axis activation)
2. Substance use comorbidity (bidirectional)
3. Psychosocial burden: stigma, discrimination, bereavement, financial stress, illness adjustment
4. ART side effects (particularly efavirenz)
5. Nutritional deficiencies (B12, folate)
6. OI-related factors

Clinical Assessment Challenges:

- Somatic symptoms of depression (fatigue, weight loss, sleep disturbance) overlap with HIV illness itself
- Use **psychological/cognitive criteria** preferentially:
- Hopelessness, worthlessness, guilt, anhedonia, poor concentration
- **PHQ-9** and **BDI-II** validated in HIV populations

Treatment:

- **SSRIs first-line** (fluoxetine, escitalopram, sertraline), well-tolerated, favorable drug-drug interaction profile compared to TCAs
 - **Note:** Fluoxetine inhibits CYP2D6 and CYP3A4, check interactions with ART (e.g., ritonavir also inhibits CYP3A4)
 - **MAOIs:** Avoid due to food interactions and ART interactions
 - Psychotherapy: CBT and interpersonal therapy (IPT) have evidence base
 - Address substance use, high comorbidity
 - **Depression improves ART adherence when treated**, this is a key clinical point
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1.6.2 ADJUSTMENT DISORDER

- Very common at time of HIV diagnosis and disease progression milestones
- Distress disproportionate to, but related to, the stressor (diagnosis, OI development, AIDS progression)
- Does not meet criteria for MDD, PTSD, or anxiety disorder
- Treatment: Psychotherapy (supportive, CBT), brief anxiolytics if needed
- Usually resolves within 6 months of stressor removal (but HIV is ongoing stressor)

1.6.3 MANIA IN HIV: IMPORTANT HIGH-YIELD TOPIC

Two types:

Type 1, Primary Bipolar Disorder (pre-existing):

- Pre-dates HIV diagnosis or early-stage HIV
- Standard bipolar features
- May be exacerbated by HIV

Type 2, Secondary/HIV-Associated Mania (Late-Stage):

- **Emerges in advanced HIV (CD4 <200)**
- Called "**AIDS mania**" or secondary mania
- Typically first episode, no family history of bipolar disorder
- Features:
 - **Irritability dominant** (not euphoria)
 - **Cognitive impairment** prominent (may look like disinhibited dementia)
 - Psychomotor agitation
 - May progress to HAD
- **Mechanism:** Direct viral / immune effect on basal ganglia and frontal circuits

ART-Associated Mania:

- **Efavirenz** is the most notorious, neuropsychiatric effects including vivid dreams, insomnia, psychosis, and mania
- Efavirenz (NNRTI): Acts on dopaminergic and serotonergic systems; CNS side effects in **40–52%** of patients
- Usually resolves with switch to alternative ART (e.g., switch to dolutegravir-based regimen)
- Other ART with neuropsychiatric effects: Zidovudine (AZT), headache, anxiety; Didanosine (ddI), peripheral neuropathy, rarely CNS

Treatment of HIV-Associated Mania:

- **Valproate** preferred (fewer drug interactions, hepatic metabolism compatible with most ART)
 - Avoid lithium, renal toxicity, narrow therapeutic window; potential interactions with tenofovir (both nephrotoxic)
 - Antipsychotics may be needed, note increased extrapyramidal sensitivity (use atypicals; haloperidol causes marked EPS in HIV patients)
 - Address underlying HIV progression
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1.6.4 PSYCHOSIS IN HIV

Prevalence: ~15% lifetime risk (vs 1% general population)

Types:

1. **HIV-related psychosis** (direct neurological involvement, HAD with psychotic features)
2. **Substance-induced psychosis** (cannabis, methamphetamine, very common in HIV populations)
3. **OI-related psychosis** (CNS toxoplasmosis, PML, cryptococcal meningitis presenting with behavioral disturbance)
4. **ART-induced psychosis** (efavirenz most common)
5. **Steroid-induced psychosis** (used for PCP pneumonia, IRIS, CNS lymphoma)
6. **Primary psychotic illness** comorbid with HIV

Clinical approach:

- Rule out OI first (imaging, CSF if needed)
- Rule out substances
- Review ART (especially efavirenz)
- Review other medications (steroids)

Treatment:

- **Atypical antipsychotics preferred**, less EPS than typicals in HIV patients
- HIV patients are very sensitive to EPS (basal ganglia involvement)
- **Clozapine:** Use with caution, increased risk of agranulocytosis + HIV itself causes neutropenia
- **Olanzapine:** Effective but metabolic effects relevant in HIV (already nutritionally compromised)
- **Quetiapine:** Often used; good for psychosis + sleep disturbance
- Drug interactions: Ritonavir (CYP3A4 inhibitor) increases levels of many antipsychotics

1.6.5 ANXIETY DISORDERS

- **Generalized anxiety:** Common; often overlaps with adjustment disorder
 - **PTSD:** Very high in HIV populations (sexual trauma / violence as risk factor for HIV acquisition; abuse-related trauma)
 - **Panic disorder:** Can be precipitated by breath-related symptoms (PCP, CMV pneumonitis)
 - Treatment: SSRIs, buspirone; benzodiazepines carefully (drug interactions with ritonavir, dramatically increase levels)
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1.6.6 SUBSTANCE USE IN HIV

Bidirectional relationship:

- Substance use increases HIV acquisition risk (needle sharing, sexual disinhibition)
- HIV increases substance use risk (stigma, pain, depression, social environment)

Key Substances:

- **Injection Drug Use (IDU):** Primary HIV transmission route in many settings; opioid use disorder; consider OAMT (opioid agonist maintenance therapy, buprenorphine / methadone)
- **Alcohol:** Most common; worsens medication adherence, liver disease (especially if HCV co-infected), accelerates neurocognition decline
- **Methamphetamine:** Particularly neurotoxic in HIV, synergistic damage to dopaminergic system; increases viral replication
- **Cannabis:** Used for appetite / pain / sleep; smoked cannabis risks pulmonary OIs
- **Chemsex:** GBMSM-specific; involves crystal meth, mephedrone, GHB / GBL, high-risk sexual behavior, very relevant in HIV

1.7 ART AND PSYCHIATRIC SIDE EFFECTS

BOX: ART NEUROPSYCHIATRIC SIDE EFFECTS

DRUG CLASS	DRUG	CNS/PSYCHIATRIC EFFECTS
NNRTI	Efavirenz	Vivid / disturbing dreams, insomnia, depression, anxiety, confusion, MANIA, psychosis, in 40–52%
NNRTI	Nevirapine	Less CNS effects than EFV
NNRTI	Rilpivirine	Depression (rare)
NRTI	Zidovudine (AZT)	Headache, insomnia, anxiety, anemia
NRTI	Didanosine (ddI)	Peripheral neuropathy
NRTI	Stavudine (d4T)	Peripheral neuropathy, lipodystrophy (psychiatric impact)
INSTI	Dolutegravir (DTG)	Insomnia, depression (reported; being studied)
PI	Ritonavir	Circumoral paresthesias, taste disturbances (via CYP interactions with other drugs)

Efavirenz Mechanism for CNS Effects:

- Agonist at GABA-A receptors (causes drowsiness and unusual dreams)
 - Inverse agonist at CB1 receptors (cannabis receptor)
 - Inhibits CYP2B6 (its own metabolism), CYP3A4, CYP2C9
 - Symptoms typically **worst in first 2–4 weeks**, improve by 6–8 weeks
 - **Switch to dolutegravir** now first-line in most guidelines, much better CNS profile
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1.8 ART ADHERENCE AND PSYCHIATRIC FACTORS

Target adherence: >95% for viral suppression with older agents; newer long-acting injectables allow monthly dosing

Psychiatric barriers to adherence:

1. **Active depression**, most studied; OR 3.4 for non-adherence
2. **Psychosis**, grandiosity ("I don't need pills"), paranoia about medications
3. **Active substance use**, chaotic lifestyle
4. **Neurocognitive impairment**, forgetting doses (ANI/MND/HAD)
5. **PTSD**, avoidance of reminders of HIV
6. **Adverse effects**, efavirenz dream disturbance leads to pill-stopping

Strategies:

- Treat comorbid depression/psychosis
 - Simplify regimen (once daily, fixed-dose combinations)
 - Pill organizers, phone alarms, blister packs
 - OAMT for IDU patients (structured dispensing improves adherence)
 - Long-acting injectable ART (cabotegravir + rilpivirine monthly IM), emerging option
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1.9 HIV TESTING AND COUNSELING

VOLUNTARY COUNSELING AND TESTING (VCT)

Components of VCT:

1. **Pre-test counseling:** Risk assessment, meaning of test, implications of results, informed consent
2. **HIV Testing:** ELISA (4th generation, detects p24 antigen + anti-HIV antibody), confirmatory Western Blot or NAAT
3. **Post-test counseling:** Positive or negative results communicated with support, linkage to care

Window Period:

- 4th generation ELISA: ~18 days (detects p24 antigen early)

- 3rd generation ELISA: ~22 days
- NAAT: ~10 days
- **Important:** A negative test in window period does not exclude infection

PPTCT (Prevention of Parent-to-Child Transmission):

- Routine testing of all pregnant women
- ART for mother + infant prophylaxis
- Avoidance of breastfeeding (or ART-covered breastfeeding if formula unavailable)

Provider-Initiated Testing and Counseling (PITC):

- Opt-out testing in clinical settings (TB clinics, STI clinics, ANC)

1.10 HIV-RELATED STIGMA

Types of stigma:

1. **Instrumental stigma:** Fear of contagion
2. **Symbolic stigma:** Moral judgment (association with "immoral" behavior)
3. **Courtesy stigma:** Stigma extending to family members
4. **Internalized stigma:** Self-stigma, shame, worthlessness

Psychiatric impact:

- Delays HIV testing and disclosure
- Reduces ART adherence
- Increases depression and anxiety
- Reduces social support
- Associated with suicidality

UNAIDS 3 Zeros approach: Zero new infections, zero AIDS-related deaths, zero discrimination

PART 2: PARKINSON'S DISEASE & PSYCHIATRY

2.1 OVERVIEW

Parkinson's disease (PD) is the second most common neurodegenerative disorder after Alzheimer's disease. It is primarily characterized by dopaminergic neuronal loss in the **substantia nigra pars compacta**, producing the classic motor tetrad. However, PD is now understood as a **whole-brain, whole-body disease** with extensive non-motor manifestations, particularly neuropsychiatric.

Key neuropathology: Lewy bodies (eosinophilic intracytoplasmic inclusions composed primarily of alpha-synuclein aggregates)

Braak staging of PD pathology:

- Stages 1–2: Medulla, olfactory bulb (non-motor symptoms: anosmia, constipation, REM sleep disorder)
 - Stages 3–4: Midbrain (substantia nigra, motor symptoms emerge)
 - Stages 5–6: Cortex (cognitive, psychiatric symptoms)
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2.2 DEPRESSION IN PARKINSON'S DISEASE

Prevalence: 40–50% (most common neuropsychiatric symptom of PD)

Point prevalence: 17% MDD, 22% minor depression/dysthymia

Key distinction: PD depression is **not simply reactive**, it has neurobiological underpinnings distinct from primary MDD

NEUROBIOLOGICAL BASIS

- Loss of **noradrenergic neurons** in the locus coeruleus (degeneration precedes substantia nigra)
- Loss of **serotonergic neurons** in the raphe nuclei
- Mesolimbic dopamine depletion (beyond nigrostriatal)
- Orbitofrontal cortex involvement

CLINICAL FEATURES OF PD DEPRESSION VS PRIMARY MDD

FEATURE	PD DEPRESSION	PRIMARY MDD
Anxiety	Very prominent (frequent panic attacks)	Variable
Guilt/worthlessness	Less prominent	Prominent
Suicidal ideation	Less common, less lethal plans	More common
Anhedonia	Present, prominent	Present
Diurnal variation	Less classic	More classic
Mood reactivity	Present (responds to positive events)	Absent in melancholic
Irritability	Prominent	Variable
Onset	May predate motor symptoms	Typically after stress/trigger

Note: Depression is a **prodromal feature** of PD, may appear years before motor symptoms (Braak stages 1–2 involvement of serotonergic/noradrenergic systems)

ASSESSMENT

- **HDRS (Hamilton Depression Rating Scale)**, most validated in PD
- **MADRS**, better for measuring change
- **GDS-15 (Geriatric Depression Scale)**, useful, avoids somatic overlap
- **BDI** has somatic items that overlap with PD

TREATMENT

Pharmacological:

- **SSRIs first-line:** Paroxetine (most studied), escitalopram, sertraline; may slightly worsen motor symptoms (paroxetine has anticholinergic effects)
- **SNRIs:** Venlafaxine effective in controlled trials
- **TCAs:** Nortriptyline effective but anticholinergic side effects (confusion, urinary retention in elderly); desipramine also used
- **Dopamine agonists:** Pramipexole has antidepressant properties (beyond its motor effects)
- **MAO-B inhibitors:** Rasagiline, Selegiline, some antidepressant evidence; avoid combining with SSRIs (serotonin syndrome risk)
- **ECT:** Effective for severe PD depression; bonus: temporarily improves motor symptoms (PD motor symptoms respond to ECT)

Non-pharmacological:

- Cognitive Behavioral Therapy (CBT), adapted for PD
- Exercise (aerobic exercise has antidepressant and possible neuroprotective effects)
- Optimize dopaminergic therapy first (motor symptom control improves mood)
- Social support, peer support groups

2.3 ANXIETY IN PARKINSON'S DISEASE

Prevalence: 30–40%

Often comorbid with depression (anxiety-depression couplet very common in PD)

Types:

1. **Generalized anxiety** (most common)
2. **Panic attacks**, often coincide with "OFF" state (low dopamine fluctuations)
3. **Social phobia**, related to embarrassment about motor symptoms
4. **Specific phobias**, falling phobia

Key feature: "OFF-period anxiety", anxiety correlates with dopamine fluctuations. Patients experience intense anxiety, panic, dysphoria when dopaminergic medication wears off. This

is **not a primary psychiatric condition**, it responds to **optimization of dopamine therapy** (smoother motor control).

Treatment:

- Optimize dopaminergic therapy (prevent OFF periods)
 - SSRIs/SNRIs for anxiety
 - Buspirone: Limited evidence
 - Benzodiazepines: Use cautiously (falls risk, cognitive effects)
 - CBT effective
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2.4 PSYCHOSIS IN PARKINSON'S DISEASE

Prevalence: 20–40% over disease course; up to 75% in advanced disease

CLINICAL FEATURES

Spectrum of psychotic symptoms:

1. **Illusions**, misidentifying objects/shadows (early)
2. **Presence hallucinations**, sensing someone behind them (early, benign)
3. **Passage hallucinations**, brief peripheral vision movement (early, benign)
4. **Formed visual hallucinations (VH)**, most characteristic of PD psychosis
5. People, animals, objects
6. Usually non-threatening initially ("friendly visitors")
7. Clear consciousness (can distinguish from reality)
8. Eventually become frightening
9. **Auditory hallucinations**, less common; when prominent, consider DLB or comorbid psychiatric illness
10. **Delusions**, typically **paranoid, persecutory**, or **Othello syndrome (morbid jealousy)**

RISK FACTORS FOR PD PSYCHOSIS

- Advanced disease, older age
- Higher doses of dopaminergic medication
- **Dementia** (strongest predictor)
- Visual impairment
- Sleep disturbance
- Depression
- Polypharmacy (particularly anticholinergics, amantadine)

PATHOPHYSIOLOGY

- Cortical Lewy body pathology

- Serotonergic dysfunction (5-HT_{2A})
- Dopaminergic overstimulation (iatrogenic, medication effect)
- Cholinergic dysfunction (ACh deficit in PD-dementia)
- REM sleep behavior disorder as precursor

MANAGEMENT: STEP-WISE APPROACH

Step 1, Address reversible causes:

- Review medications: Reduce / discontinue in order: anticholinergics → amantadine → MAO-B inhibitors → dopamine agonists → COMT inhibitors → reduce levodopa (reluctantly)
- Treat concurrent infections (UTI common trigger in elderly)
- Correct metabolic derangements, optimize sleep

Step 2, Antipsychotic Treatment:

IMPORTANT NOTE ON PIMAVANSERIN (vs PIMELOZIDE):

- The drug approved in PD is **pimavanserin** (not pimelozide / pimeliazide, exam typo to watch for)
- Novel mechanism: selective 5-HT_{2A} inverse agonist / antagonist
- No motor worsening; FDA-approved 2016

2.5 IMPULSE CONTROL DISORDERS (ICD) IN PARKINSON'S DISEASE

Prevalence: ~13.6% of PD patients on dopamine agonists (DOMINION study, Weintraub 2010)

TYPES

1. **Pathological gambling**, most common ICD
2. **Hypersexuality**, may cause significant marital distress
3. **Compulsive eating/binge eating**
4. **Compulsive shopping (oniomania)**
5. **Punding**, complex, stereotyped, repetitive behaviors (sorting, collecting, tinkering)
6. **Dopamine Dysregulation Syndrome (DDS)**, see below

RISK FACTORS

- **Dopamine agonists** (pramipexole, ropinirole, rotigotine, **non-ergot agonists**)
- Younger age of onset
- Male sex
- History of impulsivity or substance use
- Family history of gambling

MECHANISM

- Mesolimbic (reward) dopamine pathway overstimulation by dopamine agonists
- Dopamine agonists have relatively **preferential affinity for D3 receptors** (limbic/reward pathway) compared to levodopa
- The dorsal striatum (motor) may be adequately medicated while the ventral striatum (reward) is **over-medicated**

MANAGEMENT

- **First step:** Reduce or stop dopamine agonist
 - May require accepting motor worsening or using DBS to allow agonist reduction
 - CBT for gambling disorder
 - Naltrexone (opioid antagonist), some evidence for ICD in PD
 - SSRI for compulsive eating
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2.6 DOPAMINE DYSREGULATION SYNDROME (DDS)

Definition: Compulsive use and misuse of dopaminergic medications in PD, beyond what is required for motor symptom control; characterized by addictive behavior toward levodopa/dopamine agonists

Features:

- Patient demands and takes excessive medication doses
- Hoards medications
- Mood fluctuations tied to medication, extreme dysphoria in OFF state, hypomanic/euphoric in ON state
- Aggression when medication withheld
- Hedonistic homeostatic dysregulation
- May have paranoia, psychosis in context of excessive dosing

Risk factors: Previous substance use disorder, impulsive personality, younger onset PD

Treatment:

- Very difficult, reducing medication causes severe motor OFF states
 - Psychiatric support, family education
 - Opioid antagonists (limited evidence)
 - Consider DBS (reduces medication requirement, breaks the cycle)
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2.7 COGNITIVE IMPAIRMENT AND DEMENTIA IN PD

PARKINSON'S DISEASE DEMENTIA (PDD)

Prevalence: ~80% of PD patients will develop dementia over 20 years of disease

Onset: Usually >10 years after motor symptom onset (distinguishes from DLB, see below)

Cognitive profile:

- **Frontosubcortical pattern**
- Executive dysfunction (prominent, planning, working memory, set-shifting)
- Attention impairment
- Visuospatial deficits
- Memory: Retrieval > Encoding deficit (use cues → improves recall)
- Language: Relatively spared until late

Treatment:

- **Rivastigmine (Exelon):** Only FDA-approved agent for PDD (Emre et al., 2004, EXPRESS trial)
- Donepezil: Used off-label, evidence for efficacy
- Memantine: Some evidence for PDD
- **Avoid:** Anticholinergics (worsen cognition markedly)

DLB VS PDD: THE "ONE-YEAR RULE"

Clinically, DLB and PDD are probably the same disease at different time points, together called "Lewy body spectrum disorders"

2.8 SLEEP DISORDERS IN PARKINSON'S DISEASE

Prevalence of sleep disturbance: >90% of PD patients

TYPES

1. **REM Sleep Behavior Disorder (RBD):**
2. **Prodromal marker of PD** (may precede motor symptoms by >10 years)
3. Acting out dreams during REM sleep (no atonia)
4. Punch, kick, shout during sleep
5. Risk of injury to self or bed partner
6. Treatment: Clonazepam (0.25–0.5 mg), melatonin (high dose, 3–12 mg)
1. **Excessive Daytime Sleepiness (EDS):**
2. Common; multifactorial
3. Dopamine agonists are major cause (especially pramipexole, "sleep attacks")

4. Sleep attacks: Sudden irresistible sleep (can occur while driving)
5. Treat: Reduce/change agonist; modafinil, caffeine

1. Insomnia:

2. Nocturia, pain, rigidity, depression, medication effects
3. Sleep fragmentation in PD common

1. Restless Legs Syndrome (RLS):

2. More common in PD
 3. Responds to dopaminergic therapy
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2.9 APATHY IN PARKINSON'S DISEASE

Definition: Quantitative reduction in motivation (goal-directed behavior) without primary mood disturbance

Prevalence: 40–70%

Often confused with depression but important distinctions:

- Apathy: Reduced motivation, no distress about it, no sadness
- Depression: Negative affect (sadness, guilt), distress present

Assessment: Starkstein Apathy Scale, Lille Apathy Rating Scale

Treatment:

- Optimize dopaminergic therapy (dopamine is the neurobiological substrate of motivation)
 - Rivastigmine (cholinesterase inhibitor)
 - Some evidence for methylphenidate
 - Dopamine agonists: Can improve apathy
-

2.10 DEEP BRAIN STIMULATION (DBS) AND PSYCHIATRIC EFFECTS

DBS targets in PD:

- **Subthalamic nucleus (STN)**, most common target; best for tremor, rigidity
- **Globus pallidus internus (GPi)**, good for dyskinesia
- **Vim thalamus**, tremor only

PSYCHIATRIC EFFECTS OF DBS

Beneficial:

- Reduced depression in many patients (especially if related to motor fluctuations)
- May improve apathy somewhat

Adverse:

- **Depression:** Can worsen in some patients (paradoxically)
 - **Mania/Hypomania:** Seen with STN DBS; stimulation of limbic STN territory
 - **Suicide:** Increased suicide rate post-DBS (3x higher); mechanism unclear (mood changes, relationship changes, changed expectations)
 - **Impulse control disorders:** May improve (medication reduction allows) or persist
 - **Cognitive decline:** STN-DBS may cause minor executive and verbal fluency decline
 - **Personality changes:** Reported, "I don't feel like myself" phenomenon
 - **Reduction in medication post-DBS** allows reduction of dopamine agonists → may improve ICD
-

PART 3: HUNTINGTON'S DISEASE

3.1 GENETICS

- **Gene:** HTT gene on chromosome 4p16.3
- **Mutation:** CAG trinucleotide repeat expansion encoding polyglutamine in huntingtin protein
- **Normal:** ≤26 repeats
- **Intermediate/Reduced penetrance:** 27–35 repeats (not HD but may expand in offspring)
- **Full penetrance:** ≥40 repeats (all will develop HD)
- **Mutable normal:** 36–39 repeats (some may develop HD)

Anticipation: CAG repeats tend to expand with each generation; especially with **paternal transmission**

Juvenile HD: >60 repeats; onset <20 years; rigid (Westphal variant, akinetic-rigid, not choreic); often inherited from affected father

INHERITANCE

- **Autosomal dominant**, 50% risk to each child
 - Fully penetrant when >40 repeats
 - Both sexes equally affected
-

3.2 CLINICAL FEATURES

MOTOR FEATURES

- **Chorea:** Involuntary, jerky, flowing movements (begin with subtle restlessness, fidgeting)

- **Motor impersistence:** Inability to sustain motor actions (darting tongue, "milkmaid grip")
- **Gait:** "Drunken sailor" gait, wide-based
- **Dysarthria and dysphagia** (progressive)
- **Oculomotor abnormalities:** Slow saccades (characteristic, diagnostic utility)
- **Bradykinesia/rigidity:** Develops later (or early in juvenile Westphal variant)

COGNITIVE DECLINE

- **Subcortical dementia pattern** (similar to PD, executive dysfunction, memory retrieval, slowed processing)
 - Striatal and frontal circuit degeneration
 - **Not primarily amnesic** (unlike Alzheimer's)
 - Cognitive decline often precedes motor symptoms
-

3.3 PSYCHIATRIC FEATURES: HIGH YIELD

Psychiatric symptoms may **PRECEDE** motor symptoms by years, often the initial presentation to psychiatry

DEPRESSION

- **Prevalence:** 30–40%
- Often the first symptom
- Increased suicide risk: **HD patients have ~4x higher suicide rate** than general population
- Two high-risk periods: **Just after diagnosis** and **early motor symptoms** (loss of independence)
- Treatment: SSRIs first-line; TCAs avoided (anticholinergic effects worsen cognitive symptoms)

IRRITABILITY AND AGGRESSION

- **Most common** psychiatric symptom across all stages (some studies)
- Explosive, unpredictable
- Directly related to striatal degeneration (loss of inhibitory control)
- Treatment: SSRIs (especially fluoxetine, sertraline), valproate, atypical antipsychotics

APATHY

- Common and often underrecognized
- Distinct from depression (see PD section)
- Worsens caregiving burden

OBSESSIVE-COMPULSIVE SYMPTOMS

- Repetitive, perseverative behaviors
- Rigidity of thought
- Not always ego-dystonic (may not have full OCD phenomenology)
- Driven by frontostriatal circuit dysfunction

PSYCHOSIS

- Less common (~10%)
- Paranoid delusions, persecutory
- Hallucinations (auditory, visual)
- Treatment: Atypical antipsychotics (tetrabenazine caution, can cause depression/ akathisia)

MANIA/HYPOMANIA

- Uncommon (~5%)
- Usually brief, episodic
- May occur before diagnosis

SEXUAL DISINHIBITION

- Particularly seen in advanced disease
- May be manifestation of frontal disinhibition

3.4 MANAGEMENT OF HD

MOTOR

- **Tetrabenazine (TBZ):** FDA-approved for HD chorea; VMAT2 inhibitor (depletes dopamine); CAUSES depression, monitor carefully
- **Deutetabenazine:** New VMAT2 inhibitor, longer half-life, fewer side effects than TBZ; also FDA-approved
- **Valbenazine:** VMAT2 inhibitor primarily used for tardive dyskinesia, also has HD utility
- Antipsychotics (haloperidol, olanzapine): Reduce chorea via D2 blockade

PSYCHIATRIC

- Depression: SSRIs, ECT for severe
- Irritability: SSRIs, valproate, antipsychotics
- Psychosis: Atypical antipsychotics
- Apathy: No proven treatment; stimulants tried
- Sleep: Mirtazapine, clonazepam

NO DISEASE-MODIFYING TREATMENT EXISTS

Huntingtin-lowering strategies in trials:

- Antisense oligonucleotides (ASO)
 - RNA interference (RNAi)
 - Gene editing (CRISPR-Cas9), future
-

3.5 GENETIC COUNSELING IN HD: ETHICAL ISSUES

Key ethical principles:

1. **Autonomy:** Right to know vs right not to know
2. **Beneficence/Non-maleficence:** Genetic testing can cause severe psychological distress
3. **Justice:** Insurance discrimination implications
4. **Confidentiality:** Family members at risk, duty to warn vs patient privacy conflict

Predictive Testing Protocol (HDSA guidelines):

1. Pre-test counseling (minimum 2 sessions) by genetics counselor and psychiatrist
2. Psychological assessment, exclude active suicidality, acute psychiatric illness
3. Adequate support system confirmed
4. Informed consent
5. Support during and after test disclosure
6. Long-term follow-up

Children: Testing asymptomatic children generally **not recommended** (no medical benefit in childhood; right not to know; cannot give informed consent)

Prenatal testing: Available, preimplantation genetic diagnosis (PGD) allows selection of unaffected embryos without revealing parental status

Psychological impact of positive result:

- Acute grief response
 - Depression, suicidality (greatest risk in first 6 months post-result)
 - Some experience "survivor guilt" if sibling tests negative
 - Some paradoxically feel relief (end of uncertainty)
-

PART 4: MULTIPLE SCLEROSIS & PSYCHIATRY

4.1 OVERVIEW

Multiple sclerosis (MS) is a chronic autoimmune demyelinating disease of the CNS.

- **Prevalence:** 2.5 million worldwide; rare in India but increasing

- **Demographics:** More common in women (F:M = 2–3:1); onset typically 20–40 years
 - **Pathology:** Inflammatory demyelinating plaques in white matter (periventricular, juxtacortical, infratentorial, spinal cord)
 - **Course types:** RRMS (relapsing-remitting, 85%), SPMS (secondary progressive), PPMS (primary progressive), PRMS
-

4.2 DEPRESSION IN MS

Prevalence: 50% lifetime risk, highest of any neurological illness (compared by prevalence)

Why so high?

1. Direct demyelination of limbic and frontal tracts
2. Systemic immune dysregulation (pro-inflammatory cytokines → depressogenic)
3. **Interferon-beta (IFN-β)**, disease-modifying therapy, causes depression in 20–30% (via IDO pathway, tryptophan depletion, cytokine-mediated)
4. Psychosocial burden: unpredictable course, disability, uncertainty, loss
5. Steroid-associated mood disturbance (used for relapses)

Clinical note: Interferon-induced depression is clinically important, monitor mood at each visit; switch to glatiramer acetate or natalizumab if depressive; SSRIs can be used prophylactically in vulnerable patients

Treatment:

- SSRIs first-line (sertraline most studied in MS)
 - Cognitive therapy evidence-based
 - Exercise (aerobic) has evidence in MS depression
 - Switch IFN-β if implicated
-

4.3 PSEUDOBULBAR AFFECT (PBA)

Also called: Pathological laughing and crying, emotional lability, involuntary emotional expression disorder (IEED)

Prevalence in MS: 10%

Definition: Episodes of sudden, involuntary laughing or crying that are **disproportionate to or inconsistent with** the underlying emotional state

Key features:

- No voluntary control
- Episodes may not match inner feelings (patient may cry without feeling sad, or laugh without feeling happy)
- Episodes triggered by minor stimuli

- Patients feel embarrassed, socially withdrawn

Distinguish from:

- **Emotional lability in mania/BPD:** Full emotional experience matches the expression (patient feels what they show)
- **Depression with tearfulness:** Congruent emotion, patient feels sad

Mechanism: Disruption of corticobulbar tracts (prefrontal → brainstem/cerebellum circuits) → loss of voluntary suppression of emotional expression

Treatment:

- **Dextromethorphan/Quinidine (Nuedexta):** FDA-approved for PBA; effective
- **SSRIs:** Effective (citalopram, fluoxetine, often dramatic response)
- **TCAs:** Effective; amitriptyline used historically
- Response is rapid (days), unlike depression

4.4 COGNITIVE IMPAIRMENT IN MS

Prevalence: 40–65% of MS patients

Pattern: Primarily affects:

- **Processing speed** (most sensitive measure, Symbol Digit Modalities Test)
- **Episodic memory** (learning efficiency)
- Working memory
- Complex attention

Pattern is NOT Alzheimer's-like, language and simple attention relatively spared until late

Assessment tool: BICAMS (Brief International Cognitive Assessment for MS), 3 tests; SDMT, CVLT, BVMTR

Relationship to lesion load: Correlates with total lesion volume and brain atrophy (gray matter atrophy more predictive than white matter lesions)

4.5 EUPHORIA SCLEROTICA: MYTH vs REALITY

Historical concept: "Euphoria sclerotica", notion that MS patients experience inappropriate cheerfulness/euphoria

Current understanding:

- True pathological euphoria (inappropriate/sustained cheerfulness inconsistent with circumstances) is RARE (<5%)
- Most reported "euphoria" in historical studies was actually:
- Cognitive impairment (reduced insight into disability)

- Pseudobulbar laughing (misinterpreted as euphoria)
 - Selection bias in older studies (happier patients more visible)
 - **Exam point:** The current view is that euphoria sclerotica is largely a myth, DEPRESSION is the dominant mood disturbance in MS
-

PART 5: SLE & NEUROPSYCHIATRY

5.1 NEUROPSYCHIATRIC SLE (NPSLE)

Prevalence: 25–75% of SLE patients (depending on case definition)

ACR classification (1999): 19 specific NPSLE syndromes identified

5.1.1 NPSLE SYNDROMES: CLASSIFICATION

CNS Manifestations:

- Aseptic meningitis
- Cerebrovascular disease
- **Demyelinating syndrome**
- **Headache** (not attributable to other cause)
- **Movement disorder (chorea)**
- Myelopathy
- **Seizures**
- **Acute confusional state (ACS)**
- Anxiety disorder
- **Cognitive dysfunction**
- **Mood disorder**
- **Psychosis**

PNS Manifestations:

- Guillain-Barré syndrome
 - Autonomic disorder
 - Mononeuropathy
 - Myasthenia gravis
 - Cranial neuropathy
 - Plexopathy
 - Polyneuropathy
-

5.1.2 PSYCHIATRIC MANIFESTATIONS OF NPSLE

Psychosis:

- Prevalence: 2–8% of SLE patients
- Acute confusional state + psychotic features
- Can be first manifestation of SLE
- **Differential:** Steroid-induced psychosis vs SLE psychosis
- **SLE psychosis:** Elevated anti-dsDNA, low complement, NPSLE on imaging
- **Steroid psychosis:** Dose-dependent, within days of starting/increasing steroids, positive with dose reduction
- Treatment: Immunosuppression (if SLE cause) + antipsychotics

Depression:

- Most common psychiatric NPSLE manifestation
- Mechanism: Cytokines, anti-neuronal antibodies, direct cerebrovascular disease, HPA dysregulation
- **Also consider:** Corticosteroid-induced depression (dose-dependent)
- SSRIs effective

Cognitive Impairment:

- ~80% on formal testing
- Pattern: Attention, processing speed, memory
- "Lupus fog", subjective cognitive complaints very common
- Correlates with antiphospholipid antibodies

5.1.3 ANTIPHOSPHOLIPID SYNDROME (APS) IN SLE

Prevalence: ~30% of SLE patients have antiphospholipid antibodies

Clinical: Thrombosis (arterial and venous), obstetric complications, thrombocytopenia

Neuropsychiatric implications:

- **Stroke/TIA** → focal neurological deficits, vascular dementia
 - **Cerebral venous thrombosis** → headache, papilledema, seizures
 - **Cognitive impairment** (chronic small vessel disease)
 - **Sneddon syndrome:** Livedo reticularis + stroke (APS-related)
 - **Psychiatric manifestations:** Depression, psychosis (mechanism unclear, may be direct effect of antiphospholipid antibodies on neuronal function)
 - Treatment: Anticoagulation (warfarin), hydroxychloroquine
-

5.1.4 STEROID-INDUCED PSYCHIATRIC EFFECTS

Steroids are commonly used in SLE, MS relapses, and other neurological conditions:

EFFECT · DESCRIPTION

Euphoria/hypomania Early, dose-dependent; high doses; first days

Depression More common with prolonged use, lower doses, or withdrawal

Psychosis Typically occurs within 2 weeks of starting; dose-dependent (rare <40 mg/day prednisone)

Anxiety Common

Insomnia Very common; take morning dose to minimize

Mania Full manic episodes with high-dose pulse steroids

Cognitive impairment With chronic use

Dose thresholds:

- Psychosis: Usually >40 mg/day prednisone equivalent
- Mania/euphoria: Higher doses (>80 mg/day)

Management:

- Reduce dose if possible
 - Antipsychotics for psychosis/mania (short-term)
 - Lithium prophylaxis if patient requires repeated high-dose steroids and has history of steroid-induced mania
 - Do NOT use sodium restriction (can cause mood problems through steroid-sodium interaction, less relevant with modern agents)
-

PART 6: AUTOIMMUNE ENCEPHALITIS

6.1 ANTI-NMDA RECEPTOR ENCEPHALITIS

Discovery: Dalmau et al., 2007, described in young women with ovarian teratomas and encephalitis

Epidemiology:

- Most common autoimmune encephalitis
- **Young women (especially 12–45 years)** predominantly affected
- **Ovarian teratoma** in 50–60% of female cases (teratoma contains neural tissue that becomes antigenic)

- Can occur without teratoma (especially in children, males)

CLINICAL PHASES

Phase 1 (Prodromal, first 2–5 days):

- Viral prodrome: fever, headache, malaise
- Often misdiagnosed as viral encephalitis

Phase 2 (Psychiatric, first 2 weeks):

- **PSYCHIATRIC SYMPTOMS DOMINATE**
- Agitation, anxiety, bizarre behavior
- **Psychosis:** Hallucinations (auditory, visual, tactile), delusions
- Emotional lability
- **The psychiatric phase is the most likely presentation to psychiatry, often admitted to psychiatric wards first**

Phase 3 (Neurological, weeks 2–4):

- **Seizures** (usually early)
- **Movement disorders:** Orofacial dyskinesias (repetitive mouth movements, tongue thrusting), choreoathetosis, abnormal postures, very characteristic
- **Autonomic instability:** Tachycardia, hyperthermia, hypertension, diaphoresis
- **Decreased consciousness**
- **Hypoventilation** (may require ventilation)

Phase 4 (Recovery, weeks to months):

- Gradual improvement with treatment
- Relapsing course possible

INVESTIGATIONS

- **CSF:** Lymphocytic pleocytosis (60%), elevated protein, normal glucose
- **EEG:** Diffuse slowing, "extreme delta brush" pattern (highly specific, 30% of cases)
- **MRI brain:** Often normal; may show T2/FLAIR hyperintensity in limbic structures
- **Key test:** Anti-NMDAR IgG antibodies in CSF (more sensitive than serum)
- **Ovarian ultrasound/CT:** Mandatory in all women of childbearing age

PATHOPHYSIOLOGY

Anti-NMDAR antibodies (IgG targeting GluN1 subunit):

- Reduce NMDAR surface expression and synaptic localization
- Disinhibit dopamine pathways (NMDARs normally inhibit dopamine release → antibody-mediated reduction → dopamine excess → psychosis)

- Glutamate hypothesis of schizophrenia (NMDAR hypofunction) is essentially the mechanism here

TREATMENT

First-line immunotherapy:

1. **High-dose IV methylprednisolone** (1g/day × 5 days)
2. **IVIg** (2g/kg over 5 days)
3. **Plasmapheresis** (plasma exchange)

Second-line (if no response at 2–4 weeks):

1. **Rituximab** (anti-CD20 monoclonal antibody, B cell depletion)
2. **Cyclophosphamide**

Tumor removal:

- **Teratoma removal is mandatory and speeds recovery**, often dramatic improvement post-oophorectomy

Supportive:

- Antiepileptics for seizures
- Antipsychotics for behavioral symptoms (low dose, carefully)
- ICU support if ventilated

Prognosis:

- With treatment: >80% substantial improvement
- 20–25% relapse (higher without tumor removal or second-line therapy)
- Most recover fully but some have residual cognitive deficits

ANTI-NMDAR ENCEPHALITIS VS SCHIZOPHRENIA: DISTINGUISHING FEATURES

FEATURE	ANTI-NMDAR ENCEPHALITIS	SCHIZOPHRENIA
Onset	Acute (days-weeks)	Insidious (months-years)
Age	Often <30, female	Onset 18–25 (M), 25–35 (F)
Fever	Yes (prodrome)	No
Seizures	Yes (common)	Rare
Movement disorder	Yes (orofacial dyskinesias, choreoathetosis)	Absent (unless antipsychotic-related)
Autonomic instability	Yes	No
CSF	Pleocytosis	Normal
EEG	Abnormal	Usually normal

FEATURE	ANTI-NMDAR ENCEPHALITIS	SCHIZOPHRENIA
MRI	May show limbic changes	Structural changes (subtle)
Consciousness	Decreased in later stages	Intact
Antibodies	Anti-NMDAR positive	Absent

6.2 LGI1 (LEUCINE-RICH GLIOMA-INACTIVATED 1) ENCEPHALITIS

Demographics: Older men (60s–70s), unlike anti-NMDAR

Association: VGKC antibody complex (the LGI1 antibody was previously called "anti-VGKC")

No tumor association (unlike anti-NMDAR, teratoma)

CLINICAL FEATURES:

- **Faciobrachial dystonic seizures (FBDS):** Highly characteristic, brief (<3 seconds), frequent (up to 100/day) facial + ipsilateral arm dystonic movements
- Limbic encephalitis: Memory impairment, confusion, psychiatric symptoms
- **SIADH (hyponatremia)**, very common; helps differentiate from other encephalitides
- Amnesia (often severe and early)
- Psychiatric: Anxiety, depression, psychosis

Investigations:

- LGI1 antibodies in serum and CSF
- MRI: T2/FLAIR hyperintensity in medial temporal lobes, basal ganglia
- EEG: Temporal epileptiform activity

Treatment:

- Same first-line immunotherapy as anti-NMDAR
- Responds well to steroids
- Antiepileptics often ineffective for FBDS (seizures are immunotherapy-responsive)

6.3 OTHER AUTOIMMUNE ENCEPHALITIDES

ANTIBODY	TARGET	DEMOGRAPHICS	KEY FEATURE
CASPR2	Contactin-associated protein 2	Older men	Morvan syndrome (encephalopathy + PNS involvement + insomnia + autonomic); thymoma

ANTIBODY	TARGET	DEMOGRAPHICS	KEY FEATURE
AMPAR	AMPA receptor	Middle-aged women	Limbic encephalitis; breast/lung/thymoma; frequent relapses
GABABR	GABA-B receptor	Middle-aged; association with small cell lung cancer	Seizures prominent; limbic encephalitis
DPPX	Dipeptidyl-peptidase-like protein 6	Middle-aged	Hyperekplexia (startle), diarrhea/weight loss, tremor, encephalopathy
Glycine receptor	Glycine receptor	Children/young adults	Progressive encephalomyelitis with rigidity and myoclonus (PERM); stiff-person spectrum

PART 7: NEUROSYPHILIS

7.1 OVERVIEW

Treponema pallidum invades the CNS early in infection (within weeks), but most cases are cleared by immune response. Neurosyphilis develops when CNS invasion is not cleared.

Risk factors for neurosyphilis: HIV co-infection (dramatically increases risk, 7–10x), untreated/inadequately treated syphilis, immunosuppression

7.2 CLASSIFICATION OF NEUROSYPHILIS

7.2.1 ASYMPTOMATIC NEUROSYPHILIS

- CSF abnormalities (elevated cells, protein, positive VDRL) without symptoms
- Identified only by lumbar puncture

7.2.2 ACUTE SYPHILITIC MENINGITIS

- Within 2 years of primary infection
- Acute meningitis: Headache, meningismus, CN palsies (II, III, IV, VII, VIII)
- Usually resolves spontaneously but may progress

7.2.3 MENINGOVASCULAR SYPHILIS

- 5–12 years after primary infection
- **Endarteritis** of cerebral vessels → ischemic strokes

- Younger patient + stroke + high-risk behavior → consider syphilis
- **Hübner's endarteritis:** Inflammation of vasa vasorum + adventitia of large vessels
- Clinical: Prodrome of headache, dizziness, personality change → focal stroke

7.2.4 GENERAL PARESIS OF THE INSANE (GPI)

Onset: 15–20 years after primary infection

Pathology: Diffuse cortical involvement (meningoencephalitis with parenchymal damage)

Mnemonic: "PARESIS"

- Personality change
- Affect (lability, depression, mania)
- Reflexes (hyperreflexia, Argyll Robertson pupil)
- Eye (Argyll Robertson pupil, see below)
- Sensory changes
- Intellect decline (dementia)
- Speech (dysarthria)

Psychiatric features (GPI):

- Grandiose delusions ("I am God, I am Napoleon"), classic but actually uncommon
- Depression more common
- Personality change, irritability
- Progressive dementia
- Mania with grandiosity

7.2.5 TABES DORSALIS

Onset: 15–25 years after primary infection

Pathology: Degeneration of posterior columns and dorsal nerve roots

Clinical features:

- **Lightning pains** (stabbing, lancinating pains in legs)
- **Sensory ataxia** (positive Romberg)
- Loss of deep tendon reflexes
- Loss of vibration/proprioception
- **Charcot joints** (neuropathic arthropathy)
- **Argyll Robertson pupil**
- Bladder dysfunction (retention → overflow)

7.2.6 ARGYLL ROBERTSON PUPIL: HIGH YIELD

Contrast with Holmes-Adie pupil:

- Large, dilated pupil
- Slow tonic response to light
- Absent knee / ankle jerks
- Benign condition

7.2.7 DIAGNOSIS AND TREATMENT

CSF in Neurosyphilis:

- VDRL (CSF), **most specific** test (high specificity, low sensitivity, ~70%)
- FTA-ABS (serum), screening
- TPHA / TPPA, confirmatory
- WBC >5 / μ L and protein elevation
- **Reactive CSF VDRL = definitive neurosyphilis** (when clinical suspicion present)

Treatment:

- **Aqueous crystalline benzyl penicillin G** 18–24 million units / day IV $\times$ 10–14 days
- Alternative: Procaine penicillin IM + probenecid $\times$ 10–14 days
- **Penicillin allergy:** Desensitize if possible; alternatives (ceftriaxone, doxycycline) less evidence
- **Jarisch-Herxheimer reaction:** Fever, chills, hypotension 2–8 hours after first dose of penicillin; pre-treat with paracetamol

PART 8: PRION DISEASES

8.1 OVERVIEW

Prion diseases (Transmissible Spongiform Encephalopathies, TSEs) are rare, fatal neurodegenerative diseases caused by misfolded prion proteins (PrP^{Sc}) that convert normal cellular prion protein (PrP^{C}) to an abnormal form.

Key principle: No DNA or RNA, purely protein-mediated transmission

Spongiform change, vacuolation of neuropil (Swiss cheese appearance)

8.2 CREUTZFELDT-JAKOB DISEASE (CJD)

SPORADIC CJD (SCJD): 85 %

Epidemiology: 1–2 per million / year; median age onset 65 years

Course: Rapidly progressive dementia; death usually within 4–6 months (median 4 months)

Clinical features:

- **Rapidly progressive dementia**, cognitive decline over weeks
- **Cerebellar ataxia**
- **Visual disturbances** (cortical blindness, visual hallucinations)
- **Myoclonus**, stimulus-sensitive; episodic jerks
- **Pyramidal/extrapyramidal signs**
- **Akinetic mutism** (late stage)

Investigations:

TEST	FINDING	NOTES
MRI (DWI)	Cortical ribboning + basal ganglia/thalamic hyperintensity	Most sensitive, "Pulvinar sign" in vCJD
EEG	Periodic sharp wave complexes (PSWC), 1–2 Hz, biphasic or triphasic	Present in ~67% sCJD
CSF 14-3-3 protein	Elevated	Sensitive but not specific (also in encephalitis, stroke, paraneoplastic)
CSF RT-QuIC	Highly sensitive and specific	Gold standard for sCJD in CSF
Brain biopsy	Definitive	Rarely performed; biohazard risk

FAMILIAL CJD (FCJD): 10–15 %

- PRNP gene mutations
- Autosomal dominant
- Includes **Gerstmann-Straussler-Scheinker (GSS)** and **Fatal Familial Insomnia (FFI)**

VARIANT CJD (VCJD): RARE

- **Caused by BSE (bovine spongiform encephalopathy)**, "mad cow disease" transmission to humans via infected beef
- **Younger patients** (mean age 29 years)
- **Longer course** (~13 months)
- **Psychiatric features prominent early**: Depression, anxiety, withdrawal, sensory symptoms
- **Neurological features later**: Ataxia, involuntary movements, dementia
- **Pulvinar sign on MRI** (T2 hyperintensity in posterior thalamus), highly suggestive
- **Tonsillar biopsy**: Shows PrP^{Sc} (not brain biopsy required), can be diagnostic ante-mortem

IATROGENIC CJD

- Transmission via contaminated surgical instruments, dura mater grafts, growth hormone (cadaveric), corneal transplants
 - Incubation months to decades
-

8.3 KURU

- **Fore people of Papua New Guinea**
 - Transmitted by **ritual cannibalism** (consumption of human brain tissue)
 - **Cerebellar ataxia** dominant feature ("laughing disease")
 - Virtually eliminated with cessation of cannibalism
 - **Shivering tremors** → ataxia → dementia
 - Historical significance: Led Gajdusek to the prion hypothesis (Nobel Prize 1976)
-

8.4 FATAL FAMILIAL INSOMNIA (FFI)

- **Mutation:** D178N in PRNP (with Met at codon 129)
- **Autosomal dominant**
- **Pathology:** Selective degeneration of thalamus (anterior and mediodorsal nuclei)

Clinical stages:

1. Intractable insomnia + sympathetic hyperactivation (tachycardia, hyperhidrosis, hyperthermia, hypertension)
2. Hallucinatory stupor (acted-out dreams)
3. Complete insomnia + cognitive decline
4. Unresponsive coma → death

Duration: 7–25 months

PART 9: NEUROPSYCHIATRIC MANIFESTATIONS OF SYSTEMIC ILLNESS

9.1 RENAL FAILURE (UREMIC ENCEPHALOPATHY)

Mechanism: Accumulation of uremic toxins (guanidine compounds, indoles, phenols), disruption of neurotransmitter systems, fluid/electrolyte disturbances, hypertension

Clinical stages:

- **Mild uremia:** Fatigue, difficulty concentrating, personality change, insomnia
- **Moderate uremia:** Cognitive decline, confusion, restlessness, "restless legs," myoclonus

- **Severe uremia:** Delirium, seizures, stupor, coma
- **Uremic asterixis,** bilateral flapping tremor of outstretched hands

Dialysis-related psychiatric conditions:

1. **Dialysis Dementia:** Now rare; caused by aluminium accumulation in dialysate; progressive aphasia → dementia → seizures → death
2. **Dialysis Disequilibrium Syndrome:** Occurs during/ after dialysis; cerebral edema from rapid osmotic changes; headache, nausea, delirium, seizures
3. **Depression:** Very common in dialysis patients (>25%)
4. **Anxiety and PTSD** (related to dependence on machine, mortality awareness)

Psychotropics in renal failure:

- **Avoid:** Lithium (renally cleared, accumulates; nephrotoxic, avoid in CKD)
- **Avoid:** Gabapentin/Pregabalin (renally cleared, dose reduce or avoid)
- **Careful with:** Risperidone, amisulpride (renally cleared)
- **Generally safe:** Olanzapine, quetiapine, lorazepam (hepatic metabolism)

9.2 HEPATIC FAILURE (HEPATIC ENCEPHALOPATHY)

Mechanism: Ammonia + other toxic metabolites (GABA agonists, false neurotransmitters, inflammatory cytokines) crossing BBB → neuroinflammation + altered neurotransmission

West Haven Criteria (grading):

GRADE · FEATURES

Grade 0 (MHE, minimal) No clinical symptoms; impaired on psychometric testing only

Grade I Mild confusion, euphoria/anxiety, impaired attention, sleep disturbance

Grade II Lethargy, disorientation (time), personality change, asterixis present

Grade III Somnolent but arousable, gross disorientation, bizarre behavior, asterixis

Grade IV Coma (unresponsive)

Treatment: Lactulose, rifaximin, treat underlying cause, TIPS (transjugular intrahepatic portosystemic shunt) for refractory

Psychotropics in liver failure:

- **Avoid:** Valproate (hepatotoxic, increases ammonia)
- **Avoid:** Chlorpromazine, TCAs (sedating, lower seizure threshold)
- **Careful with:** Benzodiazepines (hepatic metabolism, accumulation; but lorazepam relatively safer in cirrhosis due to glucuronidation only)

- **Safe:** Low-dose haloperidol, quetiapine, oxazepam, temazepam (glucuronidation)
-

9.3 RESPIRATORY FAILURE (HYPOXIC AND HYPERCAPNIC ENCEPHALOPATHY)

HYPOXIC ENCEPHALOPATHY

- Acute: Anxiety, agitation, confusion → seizures → coma
- Chronic hypoxia (e.g., COPD): Personality change, cognitive decline, mood disturbance
- Post-resuscitation: Persistent vegetative state, cognitive sequelae

HYPERCAPNIC ENCEPHALOPATHY (CO₂ NARCOSIS)

- Seen in COPD with respiratory failure
- Elevated CO₂ → CNS acidosis → depression, confusion, drowsiness
- Classic: Warm extremities, bounding pulse, headache, asterixis, papilledema
- Treatment: Controlled oxygen therapy, NIV/ventilation

SLEEP-DISORDERED BREATHING (OSA) AND PSYCHIATRY

- OSA strongly associated with:
 - Depression (30% of OSA patients)
 - Cognitive impairment (attention, memory, executive function)
 - Impulsivity and irritability
 - Treatment-resistant depression (CPAP improves mood)
 - Psychotic features (sleep deprivation effects)
-

9.4 THYROID AND PSYCHIATRIC CONDITIONS (Brief: Main Topic in NB-07)

CONDITION · PSYCHIATRIC FEATURES

Hypothyroidism Depression (most common), cognitive slowing, psychosis ("myxedema madness")

Hyperthyroidism Anxiety (most common), agitation, mania, psychosis, emotional lability

Hashimoto's encephalopathy Autoimmune encephalopathy; psychosis, seizures, dementia; steroids responsive; anti-TPO antibodies

9.5 WERNICKE'S ENCEPHALOPATHY AND KORSAKOFF'S SYNDROME (Neuropsychiatric intersection)

Etiology: Thiamine (B1) deficiency

High-risk groups: Chronic alcohol use disorder, malnutrition, prolonged vomiting (hyperemesis, chemotherapy), bariatric surgery

WERNICKE'S ENCEPHALOPATHY (ACUTE)

Classic Triad:

1. **Confusion/delirium** (80%, most common)
2. **Oculomotor abnormalities** (nystagmus, lateral gaze palsy, complete ophthalmoplegia), 25%
3. **Ataxia** (gait ataxia), 23%

Full triad only in 16%, treat empirically with thiamine in any at-risk patient

Pathology: Bilateral petechial hemorrhages in:

- Mammillary bodies (classic)
- Periaqueductal gray
- Medial thalamus
- Hypothalamus
- Floor of fourth ventricle

Treatment: IV thiamine BEFORE glucose (glucose administration can precipitate acute WE in thiamine-deficient patients)

KORSAKOFF'S SYNDROME (CHRONIC)

Features:

1. **Severe anterograde amnesia** (cannot form new memories)
2. **Retrograde amnesia** (gap increases toward present, with temporal gradient)
3. **Confabulation**, unintentional (not deliberate lying), fills memory gaps with fabricated content
4. **Relatively preserved immediate memory and remote memory**
5. **Anosognosia**, lack of awareness of memory deficits

Prognosis: 20–25% recovery with treatment, 50% partial improvement, 25% permanent (irreversible)

Treatment: High-dose thiamine replacement; address alcohol dependence

9.6 ANTI-NMDAR ENCEPHALITIS: PSYCHIATRIC MIMICRY (Recap)

The most important message for psychiatric exams regarding autoimmune encephalitis:

Clinical pearls:

1. Any young woman with **rapid-onset psychiatric symptoms + seizures + movement disorder** = anti-NMDAR encephalitis until proven otherwise
2. These patients **appear psychiatric** at first, admitted to psychiatry wards, given antipsychotics, often not investigated adequately

3. **CSF analysis and anti-NMDAR antibodies** must be checked before diagnosing a "first psychotic episode" in atypical presentations
 4. **Red flags for organic psychosis:** Fever, seizures, movement disorders, autonomic instability, decreased consciousness, rapid cognitive decline, age/sex atypicalities
-

9.7 WILSON'S DISEASE: NEUROPSYCHIATRIC MANIFESTATIONS

Genetics: ATP7B gene mutation (copper transporter); autosomal recessive; chromosome 13

Pathophysiology: Copper accumulates in liver, brain (lenticular nucleus), cornea (Kayser-Fleischer rings)

Neuropsychiatric features (50% of Wilson's present with neuropsychiatric symptoms):

- Personality change (disinhibition, impulsivity), often first symptom
- Depression (common; can precede neurological symptoms)
- Psychosis (rare but can resemble schizophrenia)
- Cognitive decline
- Anxiety, OCD-like symptoms

Neurological features:

- **Dysarthria** (often first neurological symptom)
- Tremor (wing-beating / rubral tremor characteristic)
- Ataxia, dystonia, parkinsonism
- Seizures (rare)

Kayser-Fleischer rings: Golden-brown deposits at Descemet's membrane of cornea; slit-lamp examination; present in >99% neurological Wilson's

Diagnosis:

- Serum ceruloplasmin: LOW
- 24-hour urinary copper: HIGH
- Liver biopsy: Copper quantification (gold standard)
- Slit-lamp: KF rings

Treatment:

- D-penicillamine (chelation), first-line
 - Trientine (chelation, less side effects)
 - Zinc (blocks intestinal copper absorption), maintenance
 - Liver transplant: Curative for hepatic disease; improves neurological disease
-

SUMMARY TABLE: NEUROPSYCHIATRIC SYNDROMES BY PATHOLOGY TYPE

CATEGORY	PROTOTYPE	KEY PSYCHIATRIC FEATURE	KEY INVESTIGATION
HIV	HAND/HAD	Subcortical dementia	IHDS, neurocognitive battery
Infectious OI	Toxoplasmosis	Altered behavior from raised ICP	MRI (ring-enhancing), Toxo IgG
Autoimmune	Anti-NMDAR	Psychosis first, then neuro	CSF anti-NMDAR antibodies
Autoimmune (SLE)	NPSLE	Psychosis/depression	Anti-dsDNA, complement, APS antibodies
Degenerative	PD + dementia	Subcortical dementia + psychosis	DaTSCAN, clinical criteria
Genetic	HD	Depression + irritability	CAG repeat testing
Demyelinating	MS	Depression + cognitive	MRI, evoked potentials
Spirochetal	GPI	Grandiose delusions + dementia	CSF VDRL, FTA-ABS
Prion	CJD	Rapidly progressive dementia	MRI DWI, 14-3-3, RT-QuIC
Metabolic	Hepatic encephalopathy	Delirium + asterixis	Ammonia, liver function
Deficiency	Korsakoff	Anterograde amnesia + confabulation	Thiamine, MRI mam-millary bodies
Heavy metal	Wilson's	Personality change + psychosis	Ceruloplasmin, KF rings

Model Answers

HIV, Parkinson's Disease & Other Neuropsychiatry

KEY INSIGHT

Format guide: Each answer follows the standard long-answer structure used in MD Psychiatry examinations. Marks allocated as indicated. Answers written for a 10-mark question unless otherwise noted.

MODEL ANSWER 01

Q: Describe HIV-Associated Neurocognitive Disorders (HAND). Discuss the staging, pathophysiology, assessment, and management. (10 marks)

KEY INSIGHT

Exam Pearl, HAND is asked frequently in Paper IV. The Antinori classification and IHDS scoring must be memorised verbatim.

Introduction

HIV-Associated Neurocognitive Disorders (HAND) is an umbrella term for a spectrum of neurocognitive impairment that occurs directly as a consequence of HIV infection of the central nervous system. It was formally classified by Antinori et al. in 2007. With the advent of combination antiretroviral therapy (cART), the prevalence of severe HIV-Associated Dementia (HAD) has declined from 25–30% to approximately 2–8%, while milder forms (ANI, MND) now predominate.

1. Classification and Staging (3 marks)

The three-tier HAND classification (Antinori 2007):

CATEGORY	NEUROPSYCHOLOGICAL CRITERIA	FUNCTIONAL IMPACT
ANI (Asymptomatic Neurocognitive Impairment)	≥2 cognitive domains, ≥1 SD below normative mean	None, asymptomatic
MND (Mild Neurocognitive Disorder)	≥2 cognitive domains impaired	Mild, IADL affected

CATEGORY	NEUROPSYCHOLOGICAL CRITERIA	FUNCTIONAL IMPACT
HAD (HIV-Associated Dementia)	Marked impairment across domains	Severe, ADL affected

Six cognitive domains are assessed: learning / memory, attention / working memory, executive function, speed of information processing, language, and motor skills.

Psychomotor slowing is the hallmark.

HAND is a **subcortical dementia**, retrieval deficits (not encoding failure), personality change, slowed processing. Contrast with Alzheimer's (cortical, aphasia, apraxia, agnosia).

2. Pathophysiology (3 marks)

HIV does not directly infect neurons (neurons lack CD4 receptors). Neurotoxicity occurs through:

a) Viral protein neurotoxicity:

- **gp120:** Binds CXCR4/CCR5 on neurons → calcium influx → excitotoxicity → apoptosis
- **Tat protein:** Disrupts blood-brain barrier, induces oxidative stress, dysregulates dopaminergic pathways
- **Vpr:** Promotes neuronal apoptosis

b) Macrophage/microglia-mediated injury:

- HIV infects macrophages and microglia → viral reservoir in CNS
- Activated microglia release: cytokines (TNF- α , IL-1 β), quinolinic acid (NMDA agonist → excitotoxicity), reactive oxygen species
- **Bystander neurotoxicity** is the primary mechanism

c) Persistent immune activation:

- Even on ART, chronic microglial activation continues
- Blood-brain barrier disruption allows systemic inflammatory mediators to enter CNS
- "Inflammaging" contributes to progression

3. Assessment, IHDS (2 marks)

The **International HIV Dementia Scale (IHDS)** is the standard bedside tool:

COMPONENT	TEST	MAX SCORE
Motor speed	Alternating finger tapping (5 sec)	4
Psychomotor speed	Sequential hand movements	4

COMPONENT	TEST	MAX SCORE
Memory	4-word recall at 2 minutes	4
Total		12

Cutoff: ≤ 10 suggests HAD (sensitivity 74%, specificity 54%).

For milder forms (ANI/MND), formal neuropsychological battery is required. Screening tools: MoCA, HDS.

4. Management (2 marks)

a) ART optimisation:

- First and most important intervention
- Target CPE (CNS Penetration Effectiveness) score ≥ 8
- Drugs with high CNS penetration: Zidovudine (AZT), Nevirapine, Lopinavir/ritonavir

b) Symptomatic management:

- Depression (30–60% comorbidity): SSRIs (escitalopram, sertraline), first-line
- Psychosis: Atypical antipsychotics (HIV patients are very sensitive to EPS, avoid typical)
- Sleep: Melatonin, low-dose quetiapine
- Cognitive rehabilitation: structured programmes

c) Treating OI:

- Any active CNS OI must be treated aggressively as it worsens HAND

d) Psychosocial:

- Address stigma, depression, adherence simultaneously

KEY INSIGHT

Clinical Anchor, HAND is primarily a treatable condition. Viral suppression via ART is the single most effective intervention. Neuropsychiatric symptoms that persist despite viral suppression require separate management.

MODEL ANSWER 02

Q: A 32-year-old woman is admitted to a psychiatric ward with acute onset of auditory hallucinations, agitation, and bizarre behaviour over 10 days. She has no

prior psychiatric history. Discuss the differential diagnosis and management, with special emphasis on autoimmune encephalitis. (10 marks)

KEY INSIGHT

Exam Strategy, This is a classic anti-NMDAR encephalitis vignette. The examiner is testing whether you flag organic aetiology in a "first psychotic episode." Structure: organic vs primary, red flags, investigations, treatment.

Introduction

Acute-onset psychiatric symptoms in a young woman without prior psychiatric history must be evaluated systematically for organic aetiology before diagnosing primary psychotic illness. Anti-NMDA receptor encephalitis is the most common autoimmune encephalitis and characteristically presents to psychiatry first.

1. Differential Diagnosis (3 marks)

CATEGORY · DIAGNOSES

Autoimmune Anti-NMDAR encephalitis, LGI1 encephalitis, GABABR encephalitis

Infectious Viral encephalitis (HSV, temporal lobe), HIV encephalopathy, neurosyphilis

Metabolic Hepatic/uraemic encephalopathy, Wernicke's, thyroid (Hashimoto's)

Neoplastic Paraneoplastic encephalitis, CNS lymphoma

Primary psychiatric First-episode schizophrenia, brief psychotic disorder, bipolar I with psychosis

Red flags for organic cause:

- Acute/rapid onset (days, not months)
- Fever, preceding prodrome
- Seizures, particularly early
- Movement disorders (orofacial dyskinesias)
- Autonomic instability
- Altered/fluctuating consciousness
- Normal premorbid function
- Young female (ovarian teratoma association)

2. Anti-NMDAR Encephalitis, Clinical Profile (3 marks)

Anti-NMDAR encephalitis (Dalmau et al., 2007) is caused by IgG antibodies against the GluN1 subunit of the NMDA receptor.

Clinical phases:

Phase 1 (Prodromal, days 1–5): Viral prodrome, fever, headache

Phase 2 (Psychiatric, weeks 1–2):

- Agitation, psychosis (auditory / visual hallucinations, delusions)
- Emotional lability, bizarre behaviour
- **This phase presents to psychiatry**

Phase 3 (Neurological, weeks 2–4):

- Seizures (often early, can persist)
- Orofacial dyskinesias, choreoathetosis (characteristic)
- Autonomic instability (tachycardia, hyperthermia, blood pressure fluctuations)
- Decreased consciousness, hypoventilation

Phase 4 (Recovery): Gradual improvement over months

Epidemiology: Young women; ovarian teratoma in 50–60% of female cases; can occur without teratoma (children, males)

3. Investigations (2 marks)

INVESTIGATION · EXPECTED FINDING

CSF Lymphocytic pleocytosis (60%), elevated protein

CSF anti-NMDAR antibodies Positive, gold standard (more sensitive than serum)

EEG Diffuse slowing; "extreme delta brush" (highly specific, 30%)

MRI brain Often normal; may show limbic T2/FLAIR hyperintensity

Pelvic ultrasound/CT Ovarian teratoma, mandatory in all women

Serum anti-NMDAR Less sensitive than CSF

4. Management (2 marks)

A. Immediate:

- ICU if autonomic instability or hypoventilation
- Low-dose antipsychotics for behaviour (minimal; monitor QTc)
- Antiepileptics for seizures

B. First-line immunotherapy (simultaneously):

- IV methylprednisolone 1g/day × 5 days
- IVIG 2g/kg over 5 days
- Plasmapheresis (especially if no response)

C. Second-line (if no response at 2–4 weeks):

- Rituximab (anti-CD20, B-cell depletion)
- Cyclophosphamide

D. Tumour removal:

- Ovarian teratotomy is **mandatory**, dramatically speeds recovery
- Most important single intervention for long-term outcome

Prognosis: >80% substantial recovery with treatment; 20–25% relapse.

KEY INSIGHT

Exam Pearl, Never diagnose first-episode schizophrenia in a young woman without checking CSF anti-NMDAR antibodies. The psychiatric phase can last weeks before neurological signs emerge.

MODEL ANSWER 03

Q: Discuss the psychiatric manifestations of Huntington's disease. Describe genetic counselling and ethical issues in predictive testing. (10 marks)

Introduction

Huntington's disease (HD) is an autosomal dominant neurodegenerative disorder caused by a CAG trinucleotide repeat expansion (≥ 40 repeats) in the HTT gene on chromosome 4p16.3. Psychiatric symptoms are often the earliest and most distressing manifestations, they may precede motor symptoms by years and significantly contribute to the disease burden.

1. Psychiatric Manifestations (5 marks)

a) Depression (30–40%):

- Often the first presenting symptom
- Can precede motor symptoms by years
- **Suicide risk is 4–7 times higher** than general population
- Two high-risk periods: soon after diagnosis and onset of early motor disability

- Treatment: SSRIs (avoid TCAs, anticholinergic burden worsens cognition)

b) Irritability and Aggression (most common across all stages):

- Explosive, disproportionate outbursts
- Directly related to striatal degeneration and frontal disinhibition
- Often the feature that most distresses caregivers
- Treatment: SSRIs (fluoxetine, sertraline), valproate, low-dose atypical antipsychotics

c) Apathy (40–70%):

- Distinct from depression, no subjective distress, no negative affect
- Quantitative reduction in motivation
- Worsens progressively
- Often mistaken for depression, important distinction for treatment

d) Obsessive-Compulsive Symptoms:

- Perseverative, rigid behaviours
- Driven by frontostriatal circuit dysfunction
- Not always ego-dystonic
- SSRIs with augmentation if needed

e) Psychosis (~10%):

- Paranoid delusions, hallucinations
- Usually in mid-stage disease
- Treatment: Atypical antipsychotics (caution, tetrabenazine already used for chorea and causes depression/akathisia)

f) Cognitive Decline:

- Subcortical dementia pattern (executive dysfunction, slowed processing, retrieval memory deficits)
- Progresses invariably
- No approved treatment

g) Sleep Disturbance:

- Insomnia, circadian rhythm disruption, REM sleep abnormalities
- Mirtazapine, clonazepam useful

2. Genetic Counselling and Ethical Issues (5 marks)

A. Predictive Testing Protocol (HDSA/EHD Guidelines):

Predictive testing for HD is ethically complex because:

- There is no disease-modifying treatment
- A positive result has profound psychological consequences
- Family members are simultaneously affected

Standard protocol (minimum):

1. **Pre-test counselling**, at least 2 sessions with genetics counsellor and psychiatrist
2. **Psychological assessment**, exclude active suicidality, acute psychiatric illness
3. **Support system confirmation**, who will be present at disclosure?
4. **Informed consent**, voluntary, understanding of implications
5. **Result disclosure**, face-to-face, with support
6. **Long-term psychological follow-up**

B. Key Ethical Principles:

PRINCIPLE · APPLICATION

Autonomy Right to know vs right NOT to know, both must be respected

Beneficence Knowing allows life planning; uncertainty has its own harm

Non-maleficence Positive result can precipitate severe depression and suicide

Justice Insurance/employment discrimination concerns

Confidentiality Results are private, but family members share the risk

C. Special Populations:

Children:

- Predictive testing in asymptomatic minors is generally **not recommended**
- Reasons: No medical benefit in childhood, child cannot provide informed consent, right not to know must be preserved until adulthood
- Exception: If child has symptoms suggestive of juvenile HD

Prenatal testing:

- Available via chorionic villus sampling or amniocentesis
- **Preimplantation Genetic Diagnosis (PGD)**: Selects unaffected embryos without revealing parental status (if parent chooses not to know their own result)

D. Psychological Responses to Positive Result:

- Acute grief, depression (highest suicide risk within 6 months of disclosure)
- Some experience relief ("end of uncertainty")
- Survivor guilt if sibling tests negative

- Changes in relationships, insurance, employment
- Requires sustained psychiatric follow-up

KEY INSIGHT

Clinical Anchor, HD genetic counselling is a model for responsible predictive genetic testing. The psychiatric team's role is not to discourage testing but to ensure the person is psychologically prepared and supported throughout.

MODEL ANSWER 04

Q: Discuss psychosis in Parkinson's disease: clinical features, pathophysiology, and management. (8 marks)

Introduction

Psychosis affects 20–40% of Parkinson's disease (PD) patients over the disease course and represents one of the most challenging neuropsychiatric complications. It is a leading cause of caregiver burden and nursing home placement.

1. Clinical Features (3 marks)

PD psychosis presents on a spectrum:

Minor phenomena (early, benign):

- **Presence hallucinations:** Sensing someone behind them
- **Passage hallucinations:** Brief peripheral movement
- **Illusions:** Misidentifying objects (faces in patterns, shadows as people)
- Patient retains insight

Major phenomena (later, problematic):

- **Formed visual hallucinations (VH):** Most characteristic feature
- People, animals, complete scenes
- Usually non-threatening initially ("friendly visitors")
- Insight may be lost progressively
- **Delusions:** Paranoid, persecutory; **Othello syndrome (morbid jealousy)**, belief that partner is unfaithful
- **Auditory hallucinations:** Less common; when prominent, consider DLB

Key clinical point: Unlike primary psychosis (schizophrenia), PD hallucinations typically occur in **clear consciousness** with intact insight initially.

2. Pathophysiology (2 marks)

- **Cortical Lewy body pathology**, extension to visual cortex and limbic areas
 - **Serotonergic dysfunction**, 5-HT_{2A} receptor dysregulation (visual cortex)
 - **Dopaminergic overstimulation**, iatrogenic (dopaminergic medications activate mesolimbic receptors → hallucinations)
 - **Cholinergic deficit**, especially in PDD (ACh deficit contributes to psychosis as in DLB)
 - **REM sleep behaviour disorder**, may represent a continuum with visual hallucinations
 - **Visual impairment**, impaired visual processing contributes
-

3. Risk Factors

- Dementia (strongest predictor)
 - Higher dopaminergic medication dose
 - Advanced disease, older age
 - Visual impairment
 - Sleep disturbance, depression, polypharmacy
 - Anticholinergic medications
-

4. Management, Step-Wise (3 marks)

Step 1, Address reversible causes:

Reduce / discontinue medications in order of decreasing risk:

Anticholinergics → Amantadine → MAO-B inhibitors → Dopamine agonists → COMT inhibitors → Reduce levodopa (last resort)

Treat: UTI, constipation, pain, dehydration (frequent triggers in elderly)

Optimise: Sleep, correct visual impairment

Step 2, Antipsychotic selection:

DRUG	STATUS	NOTES
Clozapine	GOLD STANDARD	6.25–50 mg; does not worsen motor symptoms; requires WBC monitoring
Quetiapine	Most used	Weak evidence vs clozapine; no WBC monitoring needed
Pimavanserin	FDA-approved 2016	5-HT _{2A} inverse agonist; NO dopamine blockade; no motor worsening; not available in India

DRUG	STATUS	NOTES
Olanzapine	CONTRAINDICATED	Significantly worsens motor symptoms
Risperidone, haloperidol	AVOID	High D2 blockade → severe motor worsening

Clozapine mechanism in PD: High affinity for D4 receptors, minimal D2 affinity → antipsychotic effect without blocking the dopamine required for motor function

KEY INSIGHT

Exam Pearl, In PD psychosis: Clozapine is first-line in guidelines; quetiapine is most commonly prescribed in practice (due to no WBC monitoring requirement). Know both. Pimavanserin is the exam buzzword for its mechanism (5-HT_{2A} inverse agonist, no D₂ antagonism).

MODEL ANSWER 05

Q: Describe the psychiatric manifestations of multiple sclerosis. Discuss pseudobulbar affect in detail. (8 marks)

Introduction

Multiple sclerosis (MS) is a chronic autoimmune demyelinating CNS disease with extensive neuropsychiatric manifestations. The lifetime prevalence of significant psychiatric disorder in MS exceeds that of any other neurological condition.

1. Psychiatric Manifestations of MS (4 marks)

a) Depression (50% lifetime prevalence):

- Most common psychiatric manifestation
- Mechanisms: Demyelination of limbic / frontal tracts, pro-inflammatory cytokines, interferon-beta therapy (IDO pathway, tryptophan depletion), psychosocial burden, steroid effects
- **Interferon-induced depression:** 20–30%; switch to glatiramer acetate or natalizumab; prophylactic SSRIs for high-risk patients
- Treatment: SSRIs (sertraline most studied in MS), CBT, aerobic exercise

b) Anxiety (36%):

- Generalised anxiety, panic disorder, social anxiety
- Often underdiagnosed and undertreated

- SSRIs/SNRIs, CBT

c) Cognitive Impairment (40–65%):

- Processing speed (most sensitive, Symbol Digit Modalities Test)
- Working memory, episodic learning
- Correlates with brain atrophy (grey matter > white matter lesion volume)
- Assessment: BICAMS (Symbol Digit Modalities Test + CVLT + BVMTR)

d) Pseudobulbar Affect (10%): (detailed below)

e) Fatigue (90%):

- Most common symptom overall
- Contributes to depression, cognitive complaints
- Treatment: Amantadine, modafinil, CBT for fatigue

f) Euphoria Sclerotica (historically described, largely a myth):

- Historical concept of inappropriate cheerfulness in MS
- Modern understanding: True pathological euphoria is rare (<5%)
- What was described was largely: cognitive impairment (reduced insight), pseudobulbar laughing (misinterpreted), selection bias
- **Depression, not euphoria, is the dominant mood disturbance in MS**

2. Pseudobulbar Affect (PBA) (4 marks)

Definition:

PBA (also: pathological laughing and crying, involuntary emotional expression disorder, IEED) is a neurological condition characterised by sudden, involuntary, uncontrollable episodes of laughing or crying that are **disproportionate to, or inconsistent with, the underlying emotional state**.

Key distinguishing features:

- No voluntary control over episodes
- Expression may NOT match inner feelings (patient may cry without feeling sad; laugh without feeling happy)
- Episodes triggered by mild, often non-emotional stimuli
- Abrupt onset and offset
- Patient retains awareness that the expression is abnormal

Prevalence in neurological conditions:

MS (10%), ALS/MND (50%), stroke (20%), TBI, PD, HD

Pathophysiology:

Disruption of **corticobulbar (corticopontocerebellar) pathways**, prefrontal cortex normally inhibits brainstem emotional expression circuits. Demyelination of these pathways in MS → release of brainstem from cortical inhibition → involuntary emotional expression

Differentiation from depression:

FEATURE	PBA	DEPRESSION
Trigger	Minor stimuli	Generalised negative affect
Duration of episode	Seconds to minutes	Hours/days
Emotional congruence	Incongruent	Congruent
Distress during episode	Embarrassment	Sadness
Course	Episodic	Sustained

Differentiation from BPD/mania:

- In emotional lability of BPD / mania, the patient **feels** the emotion that is expressed, full emotional experience is present
- In PBA, the motor-expressive output is dissociated from the subjective emotional state

Treatment:

- **Dextromethorphan/Quinidine (Nuedexta)**: FDA-approved for PBA specifically; acts on sigma-1 and NMDA receptors; effective
- **SSRIs**: Rapid, dramatic response (often within days, unlike antidepressant effect for mood); citalopram, fluoxetine
- **TCAs**: Amitriptyline historically effective
- Response is rapid and often dramatic (unlike treatment of primary depression)

KEY INSIGHT

Exam Pearl, PBA is a motor-expressive disorder, not a mood disorder. The patient is not experiencing the emotion they are expressing, they are horrified by their inability to control it. This distinction explains why SSRIs work fast (not waiting for mood change, modulating the emotional expression circuit).

MODEL ANSWER 06

Q: Discuss the neuropsychiatric manifestations of SLE. What is the role of antiphospholipid antibodies? (8 marks)

Introduction

Neuropsychiatric SLE (NPSLE) encompasses 19 distinct syndromes (ACR 1999 classification) affecting both the CNS and PNS. The prevalence of NPSLE is 25–75% depending on case definitions, making neuropsychiatric complications among the most significant contributors to SLE morbidity.

1. NPSLE Classification and Key Manifestations (3 marks)

Central Nervous System:

- Acute confusional state (delirium), common, often multifactorial
- **Cognitive dysfunction**, 80% on formal testing; "lupus fog"; attention and processing speed affected
- **Seizures** (15–20%)
- **Mood disorder**, depression (most common), anxiety
- **Psychosis** (2–8%)
- Cerebrovascular disease (stroke / TIA)
- Chorea (rare but classical)
- Headache
- Demyelinating syndrome

Peripheral Nervous System:

- Mononeuropathy, polyneuropathy
- Cranial neuropathy, Guillain-Barré syndrome

2. Psychiatric Manifestations in Detail (3 marks)

Psychosis:

- Occurs in 2–8% of SLE patients
- May be the presenting feature of SLE, important to exclude SLE in new-onset psychosis in young women
- **Critical differential: SLE psychosis vs steroid-induced psychosis**

FEATURE	SLE PSYCHOSIS	STEROID PSYCHOSIS
Serology	Elevated anti-dsDNA, low C3/C4	Normal
Imaging	NPSLE changes on MRI	Often normal
Relation to steroids	Improves with immunosuppression	Dose-dependent; improves with dose reduction
Onset	Gradual	Within days of starting / increasing

Depression:

- Most common psychiatric manifestation
- Mechanisms: Cytokines, anti-neuronal antibodies, cerebrovascular disease, HPA dysregulation
- Also consider steroid-induced depression (dose-dependent, prolonged use)
- SSRIs effective; address underlying disease activity

Cognitive Impairment:

- Correlates with antiphospholipid antibodies (see below)
- "Lupus fog", subjective cognitive complaints
- May worsen with disease flares

3. Antiphospholipid Syndrome (APS) and Neuropsychiatric Implications (2 marks)

APS occurs in ~30% of SLE patients. It involves antibodies (anticardiolipin, anti- β 2-glycoprotein I, lupus anticoagulant) that cause thrombosis and pregnancy complications.

Neuropsychiatric consequences of APS:

- **Stroke/TIA**, most significant; recurrent strokes → vascular dementia
- **Cerebral venous thrombosis**, headache, papilledema, seizures
- **Cognitive impairment**, chronic small vessel disease and microinfarcts
- **Chorea**, direct antibody effect on basal ganglia
- **Sneddon syndrome**: Livedo reticularis + stroke

Mechanism of psychiatric symptoms:

- Antibody-mediated neuronal dysfunction (direct effect on neuronal antiphospholipid targets)
- Microthrombi → small vessel ischaemia → mood / cognitive effects
- HPA dysregulation

Treatment: Anticoagulation (warfarin, target INR 2–3 for thrombotic APS), hydroxychloroquine (protective effect on APS), immunosuppression for active SLE

MODEL ANSWER 07

Q: Describe neurosyphilis: classification, clinical features of General Paresis of the Insane, and treatment. (8 marks)

Introduction

Neurosyphilis refers to infection of the CNS by *Treponema pallidum*. While largely preventable with early penicillin treatment, it remains clinically relevant, particularly in HIV co-infected individuals, where the risk is 7–10 times higher and progression more rapid.

1. Classification of Neurosyphilis (2 marks)

TYPE	TIMING AFTER PRIMARY INFECTION	KEY FEATURE
Asymptomatic	Any time	CSF abnormalities only
Acute syphilitic meningitis	<2 years	Meningitis, CN palsies (II, VII, VIII)
Meningovascular	5–12 years	Cerebral endarteritis → ischaemic strokes
General Paresis of Insane (GPI)	15–20 years	Diffuse meningoencephalitis → dementia
Tabes Dorsalis	15–25 years	Posterior column degeneration

2. General Paresis of the Insane (GPI) (3 marks)

GPI results from diffuse spirochetal invasion of cortical parenchyma, causing progressive encephalopathy with prominent psychiatric and cognitive features.

Mnemonic: PARESIS

- **P**, Personality change (often first sign, irritability, disinhibition)
- **A**, Affect (lability, depression, or manic elevation)
- **R**, Reflexes (hyperreflexia)
- **E**, Eye (Argyll Robertson pupil)
- **S**, Sensorium (altered consciousness, confusion)
- **I**, Intellect (progressive dementia, frontal and global)
- **S**, Speech (dysarthria, tremulous speech)

Psychiatric features:

- **Personality change** is often the initial feature, coarsening of personality, irritability, poor judgment
- **Grandiose delusions:** Classically described ("I am Napoleon, I am God, I own unlimited wealth"), memorable but less common than depression
- **Depression:** More common than grandiosity in modern series
- **Mania:** Elevated mood, grandiosity, disinhibition

- **Progressive dementia**, frontal executive dysfunction → global impairment

Argyll Robertson Pupil:

- Small, irregular, bilateral pupils
 - Accommodation reflex **PRESERVED**
 - Light reflex **LOST**
 - Mnemonic: "Prostitute's pupil, accommodates but does not react"
 - Lesion: Pretectal nucleus of dorsal midbrain
-

3. Diagnosis (1 mark)

- **CSF VDRL**, most specific test for neurosyphilis (70% sensitivity)
 - **FTA-ABS serum**, screening; highly sensitive
 - CSF: Lymphocytic pleocytosis, elevated protein
 - **CSF RT-QuIC** not applicable (CJD test)
-

4. Treatment (2 marks)

- **Aqueous crystalline benzyl penicillin G**: 18–24 million units/day IV in divided doses × 10–14 days (standard of care)
 - **Alternative**: Procaine penicillin 2.4 million units IM/day + probenecid 500mg QID × 10–14 days
 - **Penicillin allergy**: Desensitise if possible; ceftriaxone IV 2g/day × 10–14 days (less evidence)
 - **Jarisch-Herxheimer reaction**: Fever, rigors, hypotension 2–8 hours after first dose; pre-treat with paracetamol; continue penicillin
 - **HIV co-infection**: Same regimen; higher relapse rate, CSF follow-up at 6-month intervals
-

MODEL ANSWER 08

Q: Discuss Creutzfeldt-Jakob disease: clinical features, diagnosis, and types. (6 marks)

Introduction

Creutzfeldt-Jakob disease (CJD) is the most common human prion disease, belonging to the group of Transmissible Spongiform Encephalopathies (TSEs). It is caused by misfolded prion proteins (PrP^{Sc}) that propagate by converting normal cellular prion protein (PrP^C). The defining neuropathological feature is **spongiform vacuolation** of the neuropil.

1. Types of CJD (2 marks)

TYPE	PROPORTION	MECHANISM	KEY FEATURE
Sporadic (sCJD)	85%	Somatic PRNP mutation or spontaneous misfolding	Most common; elderly; rapid course
Familial (fCJD)	10–15%	Germline PRNP mutation	Autosomal dominant; includes GSS, FFI
Iatrogenic	<1%	Contaminated surgical instruments, dura mater, growth hormone	Incubation years to decades
Variant (vCJD)	<1%	BSE transmission via contaminated beef	Young adults; psychiatric onset; pulvinar sign

2. Clinical Features, Sporadic CJD (2 marks)

- Median age: 65 years; median survival: 4–6 months
- **Rapidly progressive dementia**, weeks, not months
- **Cerebellar ataxia**
- **Visual disturbances** (cortical blindness, visual hallucinations)
- **Myoclonus**, stimulus-sensitive, episodic (characteristic)
- Pyramidal and extrapyramidal signs
- **Akinetic mutism**, late stage, poor prognostic sign

Variant CJD distinguishing features:

- Young patients (mean 29 years)
- **Psychiatric and sensory symptoms dominate early** (depression, anxiety, dysaesthesias)
- Neurological features develop later (ataxia, involuntary movements, dementia)
- Longer course (~13 months)

3. Diagnosis (2 marks)

INVESTIGATION	FINDING	NOTES
MRI (DWI)	Cortical ribboning + basal ganglia / thalamic hyperintensity	Most sensitive, best early test
Pulvinar sign (MRI)	T2 hyperintensity in posterior thalamus	Highly suggestive of variant CJD
EEG	Periodic sharp wave complexes (PSWC) at 1–2 Hz	Present in 67% sCJD; not present in vCJD

INVESTIGATION	FINDING	NOTES
CSF 14-3-3 protein	Elevated	Sensitive; not specific (also in encephalitis, stroke)
CSF RT-QuIC	Positive	Best specificity for sCJD, gold standard non-invasive
Tonsillar biopsy	PrP ^{Sc} in lymphoid tissue	Diagnostic for vCJD ante-mortem
Brain biopsy	Spongiform change, PrP deposits	Definitive; rarely needed; biohazard

WHO Diagnostic Criteria (sCJD):

- **Definite:** Neuropathological confirmation
- **Probable:** Rapidly progressive dementia + 2 of (myoclonus, visual / cerebellar, pyramidal / extrapyramidal, akinetic mutism) + EEG PSWC or positive 14-3-3 in CSF
- **Possible:** Progressive dementia + 2 of 4 features, duration <2 years, no EEG / CSF support

KEY INSIGHT

Exam Pearl, For CJD: MRI DWI is the most sensitive imaging; RT-QuIC is the most specific CSF test; 14-3-3 is sensitive but not specific. EEG PSWC is seen in sCJD but NOT in vCJD (use pulvinar sign for vCJD).

MODEL ANSWER 09

Q: Discuss impulse control disorders in Parkinson's disease. What is dopamine dysregulation syndrome? (6 marks)

Introduction

Impulse Control Disorders (ICDs) are a significant and under-recognised complication of dopamine agonist therapy in Parkinson's disease. The DOMINION study (Weintraub, 2010) found a prevalence of 13.6% in PD patients on dopamine agonists, representing a major quality-of-life and safety concern.

1. Types of ICD in PD (2 marks)

- **Pathological gambling**, most common; financial devastation
- **Hypersexuality**, causes marital distress; may present as paraphilias
- **Compulsive eating/binge eating**, weight gain; typically carbohydrate craving

- **Compulsive shopping (oniomania)**, financial consequences
 - **Punding**, complex stereotyped, repetitive, purposeless behaviours (sorting, collecting, dismantling objects); distinct from classical ICD
 - **Hobbyism**, excessive engagement in a hobby (often related to punding)
-

2. Mechanism (2 marks)

ICDs in PD are caused by **overstimulation of the mesolimbic (reward) dopamine pathway** by dopamine agonists.

Key pharmacological concept: Dopamine agonists (pramipexole, ropinirole, rotigotine) have **preferential affinity for D3 receptors** located in the ventral striatum (nucleus accumbens, reward circuitry). The dorsal striatum (motor function) may be appropriately medicated, but the ventral striatum (reward / impulsivity) becomes over-dosed.

Risk factors:

- Dopamine agonist use (pramipexole > ropinirole > rotigotine)
 - Higher agonist doses
 - Younger age of PD onset
 - Male sex
 - Personal/family history of substance use or gambling
 - Novelty-seeking personality premorbidly
-

3. Dopamine Dysregulation Syndrome (DDS) (2 marks)

DDS is distinct from ICD, it represents an **addiction to dopaminergic medication itself**.

Core features:

- Compulsive, excessive use of dopaminergic medications beyond what is required for motor control
- Drug-seeking behaviour, hoarding medications, forging prescriptions
- Mood fluctuations: extreme dysphoria in OFF state (drives excessive dosing), hypomanic/euphoric in ON state
- Aggression and hostility when medication is withheld
- **Hedonistic homeostatic dysregulation**, dysphoric OFF state is the primary driver
- May include paranoia and psychosis during excessive ON states

Mechanism: The OFF state dysphoria (low dopamine) creates a negative reinforcement loop → patient takes more medication to relieve dysphoria → creates over-ON states with euphoria → positive reinforcement

Risk factors: Prior substance use disorder, impulsive personality traits, younger onset PD

Management:

- Extremely difficult, reducing medication causes severe motor symptoms
- Psychiatric support, family psychoeducation
- Opioid antagonists (naltrexone), limited evidence
- Deep brain stimulation (DBS): Can reduce total medication requirement → may break the cycle
- Motivational interviewing, addiction-focused psychotherapy

KEY INSIGHT

Clinical Anchor, Always screen for ICD when starting dopamine agonists. Use the QUIP questionnaire (Questionnaire for Impulsive-Compulsive Disorders in PD). If ICD develops, reduce/stop agonist before adding psychiatric medication.

MODEL ANSWER 10

Q: Describe the neuropsychiatric manifestations of renal failure. Discuss special considerations for prescribing psychotropics in renal impairment. (6 marks)

Introduction

Renal failure produces neuropsychiatric manifestations through accumulation of uremic toxins, electrolyte disturbances, fluid shifts, and co-occurring psychological burden of chronic illness. The spectrum ranges from subtle personality changes in mild uremia to delirium and coma in acute severe uraemia.

1. Neuropsychiatric Manifestations (3 marks)

Uremic Encephalopathy (graded by severity):

- Mild: Fatigue, cognitive slowing, personality change, irritability, insomnia
- Moderate: Confusion, impaired concentration, restless legs, myoclonus, asterixis
- Severe: Delirium, hallucinations, seizures, stupor, coma
- **Asterixis (flapping tremor)**, also seen in hepatic failure, hypercapnia; bilateral, metabolic

Dialysis-Related Neuropsychiatric Conditions:

CONDITION · DESCRIPTION

Dialysis Dementia Now rare; aluminium accumulation in dialysate; progressive aphasia → dementia → myoclonus → seizures

Dialysis Disequilibrium Syndrome During / after dialysis; cerebral oedema from rapid osmotic changes; headache, nausea, delirium, seizures

Depression >25% of dialysis patients; poor QOL, increased mortality; underdiagnosed

Anxiety and death anxiety Anticipatory anxiety about session, fear of machine failure, mortality awareness

Psychological burden:

- Dependency on dialysis machine (3× weekly)
 - Sexual dysfunction, body image changes
 - Career and relationship impact
 - PTSD-like presentations
-

2. Psychotropic Prescribing in Renal Impairment (3 marks)

Drugs to AVOID or use with extreme caution:

DRUG · REASON

Lithium Renally cleared; accumulates; nephrotoxic; AVOID in CKD

Gabapentin/Pregabalin Renally cleared; require dose reduction or avoidance in GFR <30

Amisulpride Renally cleared; accumulates

Risperidone Renal clearance of active metabolite 9-hydroxyrisperidone; reduce dose

NSAIDS (for pain) Nephrotoxic; worsen CKD

Relatively safe (hepatic metabolism):

- **Olanzapine, quetiapine**, hepatic; generally safe in CKD
- **Lorazepam**, glucuronidation; safer than other benzodiazepines in CKD
- **SSRIs (escitalopram, sertraline, fluoxetine)**, hepatic; generally safe; monitor for hyponatraemia (can worsen in renal failure)
- **Mirtazapine**, hepatic; also useful for sleep and appetite in dialysis patients
- **Valproate**, hepatic; reduce dose if hypoalbuminaemia (affects protein binding)

General principles:

- Start low, go slow
- Monitor drug levels where applicable
- Watch for accumulation after dialysis (some drugs are dialysed; others are not)
- Benzodiazepines: Short-acting, oxazepam preferred (glucuronidation)

- Coordinate with nephrology team

MODEL ANSWER 11

Q: Discuss depression in HIV. How does it differ clinically from primary MDD and how should it be treated? (6 marks)

Introduction

Depression is the most common psychiatric comorbidity in HIV, with a prevalence of 30–60%, three to four times higher than the general population. Its management has direct implications for ART adherence, viral suppression, and overall HIV outcomes.

1. Aetiology of Depression in HIV (2 marks)

Multiple converging mechanisms:

- **Direct neurobiological:** HIV viral proteins (gp120, Tat) disrupt monoamine systems; HPA axis dysregulation (chronic immune activation); cytokine-induced depression (TNF- α , IL-1 β , IFN- γ activate IDO pathway → tryptophan depletion → serotonin deficit)
 - **ART-related:** Efavirenz (NNRTI), depressogenic in 10–15% via CYP2B6-mediated effects; zidovudine (fatigue)
 - **CNS disease:** Direct CNS HIV involvement (HAND)
 - **Psychosocial:** Stigma, discrimination, loss of employment, bereavement, sexual identity issues, relationship disruption
 - **Substance use:** Bidirectional relationship, depression drives use, use causes depression
 - **Nutritional:** Vitamin B12, folate deficiency (common in HIV)
-

2. Clinical Differences from Primary MDD (2 marks)

FEATURE	HIV-ASSOCIATED DEPRESSION	PRIMARY MDD
Somatic symptoms	Overlap with HIV illness, less diagnostic value	More diagnostically useful
Guilt/worthlessness	May relate to HIV risk behaviours specifically	General self-criticism
Suicidal ideation	Present; often related to illness prognosis	Present; ideation + plan
Cognitive complaints	Overlap with HAND	Not routinely present
Efavirenz side effects	Specific, vivid dreams, depressed mood	Not applicable

FEATURE	HIV-ASSOCIATED DEPRESSION	PRIMARY MDD
ART adherence impact	Depression severely reduces adherence	Not applicable

Assessment recommendation: Prioritise psychological / cognitive criteria (hopelessness, worthlessness, anhedonia, poor concentration) over somatic criteria when assessing depression in HIV. **PHQ-9** and **MADRS** are preferred.

3. Treatment (2 marks)

Pharmacological:

- **SSRIs first-line:** Sertraline, escitalopram (good tolerability, minimal drug interactions)
- Fluoxetine: Effective but inhibits CYP2D6 and CYP3A4, check ART interactions
- **SNRIs:** Venlafaxine effective
- **TCAs:** Effective but anticholinergic burden, cardiac side effects, and drug interactions limit use
- **MAOIs:** Avoid, interactions with ART and dietary restrictions
- **Drug interactions:** Ritonavir (CYP3A4 inhibitor) dramatically increases levels of many antidepressants, dose adjust
- Treat efavirenz-induced depression: Switch to dolutegravir-based regimen

Psychotherapy:

- **CBT** and **IPT** have the strongest evidence base in HIV depression
- Adherence counselling integrated with psychotherapy improves both depression and ART adherence

Key clinical point: Treating depression in HIV is not just about mood, it directly improves ART adherence. An OR of 3.4 for non-adherence has been associated with untreated depression. This makes depression treatment a priority in HIV management, not an afterthought.

MODEL ANSWER 12

Q: Write short notes on: (a) Efavirenz and neuropsychiatric side effects, (b) HIV testing and counselling. (5 marks each)

a) Efavirenz and Neuropsychiatric Side Effects (5 marks)

Introduction:

Efavirenz (EFV) is a non-nucleoside reverse transcriptase inhibitor (NNRTI) that was for many years the backbone of first-line ART. Despite its efficacy, neuropsychiatric side effects occur in **40–52%** of patients, making it one of the most neuropsychiatrically active ART drugs.

Mechanism:

- GABA-A receptor agonism (particularly at $\alpha 1\beta 2\gamma 2$ subunits) → sedation, unusual dreams
- CB1 receptor inverse agonism (cannabinoid receptor) → psychoactive effects
- Inhibits CYP2B6 (its own primary metabolic enzyme), CYP3A4, CYP2C9
- Polymorphisms in CYP2B6 (slow metaboliser genotype, common in South Asian and African populations) → higher plasma levels → more CNS effects

Neuropsychiatric effects:

- **Sleep disturbances:** Insomnia, hypersomnia, vivid / disturbing / nightmares, most common (up to 50%)
- **Cognitive symptoms:** Difficulty concentrating, memory problems ("mental fog")
- **Mood effects:** Depression (10–15%), emotional lability, dysphoria
- **Anxiety:** Panic attacks, generalised anxiety
- **Psychosis:** Hallucinations, paranoid delusions (rare but well-documented)
- **Mania:** Manic episodes reported, especially with higher plasma levels

Time course:

- **Most severe in first 2–4 weeks** of therapy
- Usually **improve by 6–8 weeks** (accommodation effect)
- Some patients have persistent symptoms

Management:

- **Timing:** Take at night (reduces wakeful neuropsychiatric symptoms)
- **Monitoring:** Screen at each visit in first 3 months
- **Switch to dolutegravir-based regimen:** Dolutegravir (INSTI) has a much superior neuropsychiatric profile; now preferred globally (WHO 2019 guidelines)
- For acute psychosis: Low-dose antipsychotic + switch ART
- For depression: SSRI + evaluate need to switch ART

b) HIV Testing and Counselling (5 marks)

Principles:

HIV testing and counselling (HTC) follows the 5 Cs: **Consent, Confidentiality, Counselling, Correct results, Connection (to care).**

Types of HTC:

TYPE	SETTING	APPROACH
VCT (Voluntary Counselling and Testing)	Community, ICTC	Patient-initiated, opt-in
PITC (Provider-Initiated Testing and Counselling)	TB clinic, ANC, STI clinic	Routine opt-out testing by provider
Home-based testing	Community outreach	Lay counsellors
Self-testing	Home, pharmacy	Emerging approach

Components of VCT:

Pre-test counselling:

- Risk assessment (transmission routes, exposures)
- Explanation of test (what it measures, window period)
- Implications of positive/negative result
- Coping strategies
- **Informed consent**, voluntary, without coercion
- Support system identification

HIV Testing:

- **4th generation ELISA:** Detects p24 antigen + anti-HIV antibodies; window period ~18 days
- **3rd generation ELISA:** Detects antibodies only; window period ~22 days
- **NAAT (Nucleic Acid Amplification Test):** Detects viral RNA; window period ~10 days; most sensitive in acute HIV
- **Confirmatory:** Western Blot or Line Immunoassay (in reactive ELISA)
- **Rapid tests:** Point-of-care; useful in resource-limited settings

Post-test counselling:

Negative result:

- Explain window period (if recent exposure, retest at 6 weeks, 3 months)
- Prevention counselling (safer sex, PrEP if high risk)
- Address relief/disappointment reactions

Positive result:

- Deliver in person, in private
- Immediate supportive counselling
- Assess suicide risk

- Explain significance (positive $\neq$ AIDS diagnosis)
- Disclosure guidance (to partner, family)
- Linkage to care: ART clinic, CD4 count, viral load
- Address stigma concerns

Special populations:

- **PPTCT (Prevention of Parent-to-Child Transmission):** Routine opt-out testing in all pregnant women; ART for mother + infant prophylaxis
- **Adolescents:** Confidential testing; involve trusted adult where possible
- **Post-exposure prophylaxis (PEP):** Within 72 hours of exposure; 28-day course

MODEL ANSWER 13

Q: Discuss the psychiatric features of Wilson's disease and its relevance to psychiatry. (5 marks)

Introduction

Wilson's disease (hepatolenticular degeneration) is an autosomal recessive disorder of copper metabolism (ATP7B gene, chromosome 13) causing copper accumulation in liver, brain (lenticular nucleus), and cornea. It is clinically significant to psychiatry because **50% of patients present with neuropsychiatric symptoms**, and psychiatric presentations can precede hepatic or neurological signs by years.

1. Psychiatric Features (3 marks)

FEATURE	PREVALENCE	NOTES
Personality change	Most common early feature	Disinhibition, impulsivity, loss of social graces; may be mistaken for adjustment disorder or personality disorder
Depression	30–40%	Can be the sole initial presentation; standard antidepressants used but treat underlying Wilson's
Psychosis	~10%	Resembles schizophrenia; visual and auditory hallucinations, paranoid delusions
Anxiety	Common	Generalised; may accompany depression

FEATURE	PREVALENCE	NOTES
OCD-like symptoms	Present	Repetitive, perseverative behaviours
Cognitive decline	Late stage	Executive dysfunction; may progress to dementia
Emotional lability	Common	Irritability, laughing/crying spells

Clinical trap: Psychiatric presentation of Wilson's disease in a young person is frequently misdiagnosed as primary psychiatric illness (schizophrenia, BPD, or mood disorder). Antipsychotics or antidepressants may be started without investigating the underlying cause. This delays copper-chelation therapy and allows irreversible neurological damage.

2. When to Suspect Wilson's Disease in a Psychiatric Patient (1 mark)

- Young patient (<40 years) with psychiatric symptoms + movement disorder
- Psychiatric symptoms + liver disease (elevated LFTs, cirrhosis)
- Psychiatric symptoms not responding to standard treatment
- Tremor (especially wing-beating/rubral), dysarthria, ataxia
- **Kayser-Fleischer rings** on slit-lamp examination (>99% sensitivity in neurological Wilson's)

3. Diagnosis and Treatment (1 mark)

- Serum ceruloplasmin: Low (<20 mg/dL)
- 24-hour urinary copper: High (>100 µg/day)
- Liver biopsy: Copper quantification (>250 µg/g dry weight)
- Slit-lamp: KF rings

Treatment:

- D-penicillamine (chelation), first-line
- Trientine, chelation, fewer side effects
- Zinc, maintenance therapy (blocks intestinal absorption)
- **Psychiatric symptoms often improve with copper chelation, treat the cause**

MODEL ANSWER 14

Q: Describe the management of depression in Parkinson's disease. (5 marks)

Introduction

Depression affects 40–50% of Parkinson's disease patients and is the most common neuropsychiatric symptom of PD. It is not simply reactive, it has a specific neurobiological substrate involving degeneration of noradrenergic (locus coeruleus) and serotonergic (raphe nuclei) systems, often preceding motor symptoms by years.

1. Assessment (1 mark)

- Use instruments that minimise somatic overlap: **GDS-15** (Geriatric Depression Scale), **HDRS** (Hamilton Depression Rating Scale), **MADRS**
 - **BDI** has somatic items that overlap with PD motor symptoms, less ideal
 - Distinguish from: apathy (no negative affect in apathy), cognitive impairment, side effects of medications
-

2. Pharmacological Management (3 marks)

A. SSRIs (first-line):

- Paroxetine, escitalopram, sertraline, most studied
- Generally well-tolerated
- Paroxetine: Anticholinergic effects may slightly worsen motor symptoms in some patients, use cautiously in advanced PD
- **Important interaction:** Selegiline/Rasagiline (MAO-B inhibitors used for motor symptoms) + SSRIs → serotonin syndrome risk, use with caution or avoid combination

B. SNRIs:

- Venlafaxine: Controlled trial evidence in PD; useful for concurrent anxiety

C. TCAs:

- Nortriptyline: Evidence from RCTs; effective but anticholinergic burden risks (confusion, urinary retention, falls, constipation)
- Desipramine: Less anticholinergic; used in selected patients
- Generally not first-line due to side effect profile in elderly

D. Dopaminergic approach:

- **Pramipexole** (dopamine agonist): Demonstrated antidepressant effects beyond its motor benefits; particularly useful when motor under-treatment is contributing
- Optimising dopaminergic therapy first (preventing OFF periods) often improves depression

E. ECT:

- Effective for severe or treatment-resistant PD depression
- Bonus: **Temporarily improves motor symptoms** (motor and mood effects of ECT in PD)

- Consider in severe cases, particularly with psychomotor retardation

3. Non-Pharmacological Management (1 mark)

- **Cognitive Behavioural Therapy (adapted for PD):** Evidence-based; addresses illness-related themes, helplessness, grief
- **Aerobic exercise:** Antidepressant effects + potential neuroprotective benefits
- **Social support and peer groups:** Combat isolation
- **Psychoeducation** for patient and caregivers
- Treat concurrent pain and motor fluctuations (improve mood indirectly)

KEY INSIGHT

Exam Pearl, ECT in PD: improves both depression AND motor symptoms. This is a two-for-one that appears in exams. The motor effect of ECT in PD is temporary (weeks) but dramatic.

MODEL ANSWER 15

Q: Write a short note on Hepatic Encephalopathy: psychiatric aspects and prescribing considerations. (5 marks)

Introduction

Hepatic encephalopathy (HE) is a spectrum of neuropsychiatric dysfunction arising from hepatic failure, characterised by accumulation of ammonia and other neuro-toxic substances, activation of GABA-ergic pathways, and neuroinflammation.

1. Neuropsychiatric Manifestations (2 marks)

West Haven Criteria:

GRADE · FEATURES

0 (Minimal/Covert HE) No clinical symptoms; impaired on psychometric testing only (CFF, PHES)

I Mild confusion, anxiety / euphoria, impaired attention, reversal of sleep-wake cycle

II Lethargy, disorientation in time, personality change, **asterixis** present

III Somnolent but arousable, gross disorientation (time + place), bizarre behaviour

IV Coma (unresponsive to verbal / painful stimuli)

Psychiatric presentations of HE:

- Confusion/delirium (most common psychiatric presentation)
 - Personality change in chronic liver disease (covert HE)
 - Anxiety and sleep reversal (early)
 - Depression in cirrhosis (multifactorial, HE, chronic illness, substance withdrawal)
 - Asterixis, bilateral flapping tremor of outstretched hands (also in renal failure and hypercapnia)
-

2. Mechanism (1 mark)

- Elevated ammonia → astrocyte swelling, glutamate dysregulation
 - Accumulation of GABA agonists (endogenous benzodiazepine-like substances) → increased GABAergic tone → sedation
 - Manganese deposition in basal ganglia → parkinsonian features
 - Inflammatory cytokines → neuroinflammation
 - False neurotransmitters (octopamine, phenylethanolamine) displace dopamine/noradrenaline
-

3. Psychotropic Prescribing in Liver Failure (2 marks)

Drugs to AVOID:

- **Valproate:** Hepatotoxic; also raises ammonia levels independently, contraindicated
- **Chlorpromazine, TCAs:** Highly sedating; lower seizure threshold; highly protein-bound (accumulate in hypoalbuminaemia)
- **Chlordiazepoxide, diazepam:** Long-acting benzodiazepines, accumulate in liver failure; precipitate deeper HE

Relatively safe:

- **Lorazepam, oxazepam, temazepam:** Glucuronidation only (not oxidative metabolism), safer in cirrhosis; however, all benzodiazepines can precipitate HE
- **Haloperidol (low dose):** Reasonable for acute agitation/delirium in HE; avoid high doses
- **Quetiapine:** Hepatic; use lowest effective dose
- **SSRIs (escitalopram, citalopram):** Generally safe; avoid fluvoxamine (hepatic); monitor LFTs

General approach:

- Reduce doses significantly in cirrhosis (first-pass metabolism reduced)
- Monitor ammonia levels when adding medications

- Avoid sedatives wherever possible, precipitate deeper HE
 - Treat the underlying cause of HE first (lactulose, rifaximin)
-

Mnemonics & Memory Tricks

HIV, Parkinson's Disease & Other Neuropsychiatry

KEY INSIGHT

Design note: Each mnemonic block includes: the device, what each letter stands for, a clinical anchor sentence, and a quick recall test prompt.

MNEMONIC 01: HAND Classification

"ANI Makes Dementia"

Progression of HAND across three stages

STAGE	FULL NAME	FUNCTIONAL IMPACT
A, ANI	Asymptomatic Neurocognitive Impairment	None
M, MND	Mild Neurocognitive Disorder	Mild, IADL
D, HAD	HIV-Associated Dementia	Severe, ADL

KEY INSIGHT

Anchor: ANI → MND → HAD. Each step adds functional impairment. The distinction is not the test score, it's whether the patient can manage their own affairs.

Quick test: What two features distinguish MND from ANI? (*Answer: Same cognitive impairment, but MND has MILD functional impairment of IADLs*)

MNEMONIC 02: IHDS Components

"Tap, Tap, Remember" (TTR)

Three components of the International HIV Dementia Scale

- **T**, Tapping (motor speed): Alternating index/middle finger tapping × 5 seconds
- **T**, Tapping sequence (psychomotor speed): Sequential hand movements
- **R**, Recall: 4-word list recall at 2 minutes

SCORE · INTERPRETATION

Max = 12 Normal

≤10 Suggests HAD

KEY INSIGHT

Anchor: Each component max = 4. Sensitivity 74%, specificity 54%. Good bedside tool, misses ANI/MND.

MNEMONIC 03: Opportunistic Infections in HIV by CD4 Count

"Terrible PCP Comes, MACs Attack"

CD4 thresholds for major OIs, descending order

CD4 COUNT · OI

<500 Recurrent bacterial pneumonias, Candida (oral/vaginal), HSV recurrences

<200 PCP (Pneumocystis jirovecii pneumonia), Toxoplasmosis (brain)

<100 Cryptococcal meningitis, Toxoplasmosis (most cases)

<50 CMV (retinitis, encephalitis), **MAC** (M. avium complex)

Full mnemonic expansion:

- **Terrible** = <500, Thrush, TB reactivation
- **PCP** = <200, Pneumocystis, first serious OI
- **Comes** = <100, Cryptococcus, Cryptosporidiosis
- **MACs** = <50, MAC, CMV, most severe OIs

KEY INSIGHT

Anchor: The CD4 thresholds are the most commonly asked HIV factoid in exams. 200 = PCP cutoff (primary prophylaxis threshold); 100 = Cryptococcus/Toxo; 50 = CMV/MAC.

MNEMONIC 04: Efavirenz CNS Side Effects

"DAMN VIVID"

Neuropsychiatric side effects of Efavirenz

- **D**, Dreams (vivid, disturbing, nightmares)
- **A**, Anxiety
- **M**, Mania / Mood changes

- **N**, Nightmares / sleep disturbance
- **V**, Vivid hallucinations (visual)
- **I**, Insomnia
- **V**, Vertigo / dizziness
- **I**, Impaired concentration
- **D**, Depression / dysphoria

KEY INSIGHT

Anchor: DAMN VIVID captures the phenomenological richness of EFV CNS effects. Remember: worst in first 2–4 weeks, improve by 6–8 weeks. Take at night. Switch to dolutegravir if persistent.

MNEMONIC 05: Antipsychotics in Parkinson's Disease

"Can Quetiapine Please? Olanzapine Ruins Haloperidol"

C-Q-P vs O-R-H: Safe vs Unsafe

SAFE:

- **C**, **Clozapine** (gold standard, low dose, $D_4 > D_2$, no motor worsening)
- **Q**, **Quetiapine** (most commonly used, weaker evidence)
- **P**, **Pimavanserin** (FDA-approved 2016, 5-HT_{2A} inverse agonist, no D₂ blockade)

UNSAFE:

- **O**, **Olanzapine** (contraindicated, significant motor worsening)
- **R**, **Risperidone** (avoid, D₂ blockade worsens PD)
- **H**, **Haloperidol** (avoid, severe EPS in PD)

KEY INSIGHT

Anchor: The "safe" trio are all low-D₂ or non-D₂ drugs. The "unsafe" trio have significant D₂ blockade. In PD, D₂ blockade = motor catastrophe.

Quick test: What is the mechanism of pimavanserin that makes it safe in PD? (*Answer: Selective 5-HT_{2A} inverse agonist, no dopamine antagonism whatsoever*)

MNEMONIC 06: General Paresis of the Insane

"PARESIS"

Classic mnemonic for features of GPI (neurosyphilis)

- **P**, **Personality change** (first symptom, coarsening, irritability)

- **A**, Affect (lability, depression, mania)
- **R**, Reflexes (hyperreflexia, UMN signs)
- **E**, Eye (Argyll Robertson pupil, accommodates but does not react)
- **S**, Sensorium (confusion, disorientation)
- **I**, Intellect (progressive dementia)
- **S**, Speech (dysarthria, tremulous speech)

KEY INSIGHT

Anchor: GPI = 15–20 years post-primary infection. Psychiatric features dominate early. Grandiose delusions (Napoleon, God) are classic teaching but depression is actually more common in modern series.

MNEMONIC 07: Argyll Robertson Pupil vs Holmes-Adie

"AR: Accommodates, Refuses light"

"HA: Has Atony (responds slowly)"

FEATURE	AR PUPIL	HOLMES-ADIE
Size	Small, irregular	Large, dilated
Light reflex	ABSENT	Slow tonic (present but sluggish)
Accommodation	PRESENT	Present (tonic, slow)
Cause	Neurosyphilis (classic), mid-brain lesion	Benign; postganglionic ciliary nerve
Other signs	Neurosyphilis features	Absent knee / ankle jerks

KEY INSIGHT

Anchor memory trick: "AR, Accommodates but Refuses light" vs "HA, Has atony (slow light response)." The AR pupil is the exam question; Holmes-Adie is the distractor.

MNEMONIC 08: Huntington's Disease Genetics

"40-40 Rule and CAG Anticipation"

HD genetics in one frame

REPEAT COUNT · MEANING

≤26 Normal

27–35 Intermediate (not HD, may expand in offspring)

36–39 Reduced penetrance (some develop HD)

≥40 Full penetrance, will develop HD

>60 Juvenile HD (Westphal variant, rigid, not choreic)

The 40-40 Rule: ≥40 repeats → 100% penetrance | Juvenile HD → >60 repeats

Anticipation: CAG repeats expand each generation, especially with **paternal transmission**.

KEY INSIGHT

Anchor: Autosomal dominant, chromosome 4p16.3. Each child of an affected parent has 50% risk. Suicide rate 4–7× general population, particularly in post-diagnosis period and early motor phase.

MNEMONIC 09: Anti-NMDAR Encephalitis Clinical Phases

"Prodrome → Psych → Neuro → Recovery" = "Pretty Psychiatrists Never Recover"

(Self-deprecating but memorable)

PHASE	TIMING	FEATURES
P, Prodrome	Days 1–5	Fever, headache, viral-like illness
P, Psychiatric	Weeks 1–2	Psychosis, agitation, bizarre behaviour , presents to psychiatry
N, Neurological	Weeks 2–4	Seizures, orofacial dyskinesias , autonomic instability, decreased consciousness
R, Recovery	Weeks–months	Gradual improvement with immunotherapy

KEY INSIGHT

Anchor: The psychiatric phase is THE TRAP. Young woman + acute psychosis + no prior history = send CSF for anti-NMDAR antibodies before diagnosing schizophrenia. Orofacial dyskinesias + autonomic instability = hallmark of the neurological phase.

Quick test: What is the EEG finding highly specific for anti-NMDAR encephalitis? (*Answer: Extreme delta brush, present in ~30%*)

MNEMONIC 10: Cryptococcal Meningitis in HIV

"CAN FEEL ILL" (CSF findings + clinical)

Clinical:

- C, Chronic/subacute onset (weeks)
- A, Afebrile in many (poor inflammatory response)
- N, No meningismus sometimes

CSF:

- F, Few cells (normal or <20 WBC)
- E, Elevated opening pressure (>200 mm H₂O in 75%)
- E, Elevated protein (mild)
- L, Low glucose

Tests:

- I, India ink positive (70–80%)
- L, Low CD4 (<50 usually)
- L, Latex agglutination/CrAg >95% sensitivity

KEY INSIGHT

Anchor: The paradox of cryptococcal meningitis: serious infection, but CSF may look almost normal because the patient can't mount an inflammatory response. CrAg is the gold standard test. Elevated ICP managed with serial LP, NOT acetazolamide, steroids, or mannitol routinely.

MNEMONIC 11: Wernicke's Triad and Treatment Rule

"The COAt" and "GIVE THIAMINE BEFORE GLUCOSE"

Wernicke's Triad:

- C, Confusion/delirium (80%, most common; full triad only in 16%)
- O, Ophthalmoplegia/nystagmus/lateral gaze palsy (25%)
- A, Ataxia (gait) (23%)

Pathology locations: Mammillary bodies (classic), periaqueductal gray, medial thalamus

Critical treatment rule:

KEY INSIGHT

THIAMINE MUST BE GIVEN BEFORE GLUCOSE in any at-risk patient Rationale: Glucose administration accelerates thiamine consumption → precipitates acute WE in thiamine-deficient patients

Korsakoff triad:

- **A**, Anterograde amnesia (severe, cannot form new memories)
- **R**, Retrograde amnesia (with temporal gradient)
- **C**, Confabulation (unintentional gap-filling, ARC = Anterograde + Retrograde + Confabulation)

KEY INSIGHT

Anchor: WE is acute and reversible with thiamine. Korsakoff is chronic and largely irreversible (25% full recovery). The transition from WE to Korsakoff is prevented by early aggressive thiamine replacement.

MNEMONIC 12: Impulse Control Disorders in PD

"PHECS" = All ICD Types in PD

- **P**, Pathological gambling (most common)
- **H**, Hypersexuality
- **E**, Eating compulsively (binge eating)
- **C**, Compulsive shopping
- **S**, Stereotyped / punding behaviours

KEY INSIGHT

Anchor: All caused by dopamine agonist overstimulation of D3 / mesolimbic reward pathway. First management step = reduce / stop dopamine agonist. The DOMINION study: 13.6% prevalence on agonists.

Extra: DDS (Dopamine Dysregulation Syndrome) = addiction to the medication itself (compulsive overuse of levodopa / agonists beyond motor need).

MNEMONIC 13: Psychotropics to Avoid in Renal vs Hepatic Failure

"LEGAL" = Avoid in Renal | "VALCO" = Avoid in Hepatic

Avoid in RENAL failure, "LEGAL":

- **L**, Lithium (renally cleared; nephrotoxic)

- **E**, Eliminate gabapentin (renal clearance, dose reduce / avoid)
- **G**, G-line drugs: Amisulpride (renally cleared)
- **A**, Active metabolites accumulate: Risperidone (9-OH-risperidone renal)
- **L**, Long-acting benzodiazepines (accumulate; use oxazepam instead)

Avoid in HEPATIC failure, "VALCO":

- **V**, Valproate (hepatotoxic + raises ammonia)
- **A**, Amitriptyline / TCAs (accumulate, sedating)
- **L**, Long-acting benzodiazepines (diazepam, chlordiazepoxide)
- **C**, Chlorpromazine (hepatotoxic, accumulates)
- **O**, Oxidatively metabolised drugs (most psychotropics, switch to glucuronidated ones: lorazepam, oxazepam)

KEY INSIGHT

Anchor: In both conditions, start low, go slow, prefer hepatically metabolised drugs for renal failure and glucuronidated drugs for hepatic failure.

MNEMONIC 14: CJD Investigations

"MRI-EEG-3-QuIC"

The four investigations for CJD in order of use

INVESTIGATION	KEY FINDING	NOTES
MRI (DWI)	Cortical ribboning + BG / thalamic hyperintensity	Most sensitive, first test
EEG	Periodic sharp wave complexes (PSWC) 1–2 Hz	67% of sCJD; NOT in vCJD
14-3-3	Elevated in CSF	Sensitive but NOT specific
RT-QuIC	Positive	Most specific CSF test, gold standard

For vCJD specifically:

- **Pulvinar sign:** T2 hyperintensity in posterior thalamus on MRI
- **Tonsillar biopsy:** PrP^{Sc} in lymphoid tissue, diagnostic ante-mortem for vCJD

KEY INSIGHT

Anchor: Order of sensitivity: MRI > RT-QuIC > 14-3-3 > EEG (roughly). Order of specificity: RT-QuIC > EEG PSWC > MRI > 14-3-3. In practice, send MRI + CSF (RT-QuIC + 14-3-3) simultaneously.

MNEMONIC 15: HIV-Associated Mania vs Primary Bipolar Mania

"LICA": Features of HIV/AIDS Mania (Secondary Mania)

- **L**, Late-stage HIV (CD4 <200 typically)
- **I**, Irritability dominant (not euphoria, unlike primary mania)
- **C**, Cognitive impairment prominent (looks like disinhibited dementia)
- **A**, Absent family history of bipolar disorder

Contrast with primary mania:

- Euphoria more prominent
- Family history often present
- Earlier in HIV course or pre-dates HIV
- No progressive cognitive decline

KEY INSIGHT

Anchor: ART-associated mania (efavirenz) = review at first visit. Secondary AIDS mania (CD4 <200) = Valproate preferred (fewer drug interactions); avoid lithium (renal toxicity + interactions with tenofovir). Atypical antipsychotics for acute management but use with caution (HIV patients have increased EPS sensitivity).

MNEMONIC 16: Pseudobulbar Affect vs Emotional Lability

"PBA = Pathological BEHAVIOUR of Affect (dissociated from feeling)"

	PBA	EMOTIONAL LABILITY (BPD/MANIA)
Emotional congruence	Incongruent , expression ≠ feeling	Congruent , expression = feeling
Control	None, involuntary	Some, can be suppressed partially
Trigger	Minor stimuli	Emotional situations
Duration	Seconds–minutes	Minutes–hours
Cause	Neurological (corticobulbar)	Psychiatric or mood disorder

	PBA	EMOTIONAL LABILITY (BPD/MANIA)
Treatment	SSRIs / Dextromethorphan-Quinidine	Treat underlying condition

KEY INSIGHT

Anchor device: "PBA, the patient's FACE is crying but their SOUL isn't." The dissociation between motor-expressive output and subjective feeling is the defining feature. This is why SSRIs work rapidly, they're modulating the expression circuit, not waiting to lift a mood disorder.

MNEMONIC 17: Dopamine Agonist ICDs vs DDS

"ICD = Directed OUTWARD | DDS = Directed INWARD"

ICDs (directed outward, reward-seeking behaviours):

- Gambling, sex, eating, shopping, punning
- Driven by D3/mesolimbic overstimulation
- Patient pursues external rewards compulsively

DDS (directed inward, drug-seeking):

- Addiction to the medication itself
- Patient pursues the drug (levodopa/agonist)
- Hoarding, forging, demanding
- Driven by OFF-state dysphoria (internal negative state → drug-seeking)

KEY INSIGHT

Anchor: ICD = the world is the drug. DDS = the pill is the drug. Both need dopamine reduction, but DDS is more like addiction management, requires OFF-state dysphoria to be addressed.

MNEMONIC 18: MS Psychiatric Features: "CAFE"

Psychiatric features of Multiple Sclerosis

- **C**, Cognitive impairment (40–65%; processing speed most sensitive)
- **A**, Affect (depression 50%, most common; interferon-induced variant)
- **F**, Fatigue (90%, most common symptom overall; not strictly psychiatric but drives depression)
- **E**, Emotional incontinence / pseudobulbar affect (10%)

Plus: Anxiety (36%), Euphoria sclerotica (historical myth, largely not real)

KEY INSIGHT

Anchor: Depression = 50% lifetime risk, highest of any neurological disease. If you see "MS + mood" in an exam, the answer is usually depression (not euphoria sclerotica, that's a trap).
SDMT (Symbol Digit Modalities Test) = best cognitive screen for MS processing speed.

MNEMONIC 19: Autoimmune Encephalitis Antibodies Quick Reference

### "NMDA = YOUNG WOMEN		LGI1 = OLD MEN	CASPR2 = MORVAN'S"
ANTIBODY	DEMOGRAPHICS	TUMOUR	KEY FEATURE
NMDAR	Young women	Ovarian teratoma (50%)	Psychiatric phase first; orofacial dyskinesias
LGI1	Older men (60s)	None usually	FBDS (faciobrachial dystonic seizures); hyponatraemia
CASPR2	Older men; thymoma	Thymoma	Morvan syndrome (encephalopathy + PNS + insomnia)
AMPA	Middle-aged women	Breast / lung / thymoma	Limbic encephalitis; frequent relapses
GABABR	Middle-aged	Small cell lung cancer	Prominent seizures

KEY INSIGHT

Anchor: For exams: NMDAR = most common = psychiatric presentation first = young female = teratoma = treat with IVIG + steroids + rituximab + teratectomy. LGI1 = second most common = older male = FBDS + hyponatraemia = responds well to steroids.

MNEMONIC 20: Wilson's Disease Red Flags in Psychiatry

"KAYSER-FLAG"

When to suspect Wilson's disease in a psychiatric patient:

- **K**, KF rings on slit-lamp (>99% in neurological Wilson's)
- **A**, Age <40 years with psychiatric presentation
- **Y**, Young adult with tremor + psychiatric symptoms
- **S**, Subcortical dementia pattern in young patient

- **E**, Elevated LFTs + psychiatric symptoms
- **R**, Refractory to standard psychiatric treatment

Flag = Investigate:

- Serum ceruloplasmin (LOW)
- 24-hour urinary copper (HIGH)
- Slit-lamp examination (KF rings)

KEY INSIGHT

Anchor: Wilson's is treatable and reversible if caught early. Missing it = decades of inappropriate psychiatric treatment while copper destroys the basal ganglia and liver. Any young psychiatric patient with movement disorder (especially dystonia or wing-beat tremor) + liver disease → check ceruloplasmin.

RAPID RECALL TABLE: All Mnemonics at a Glance

#	TOPIC	MNEMONIC
1	HAND Classification	ANI Makes Dementia
2	IHDS Components	Tap, Tap, Remember
3	OI by CD4 count	Terrible PCP Comes, MACs Attack
4	Efavirenz side effects	DAMN VIVID
5	APs in PD (safe vs unsafe)	Can Quetiapine Please? Olanzapine Ruins Haloperidol
6	GPI features	PARESIS
7	Argyll Robertson vs Holmes-Adie	AR=Accommodates, Refuses / HA=Has Atony
8	HD genetics	40-40 Rule + CAG Anticipation
9	Anti-NMDAR phases	Pretty Psychiatrists Never Recover
10	Cryptococcal meningitis CSF	CAN FEEL ILL
11	Wernicke's triad	The COAt + Thiamine Before Glucose
12	ICD in PD	PHECS
13	Psychotropics in organ failure	LEGAL (renal) / VALCO (hepatic)
14	CJD investigations	MRI-EEG-3-QuIC

#	TOPIC	MNEMONIC
15	HIV mania	LICA
16	PBA vs lability	PBA = face ≠ soul
17	ICD vs DDS	Outward vs Inward
18	MS psychiatric features	CAFE
19	Autoimmune encephalitis	NMDA=Young Women / LGI1=Old Men
20	Wilson's red flags	KAYSER-FLAG

High-Yield Comparisons

HIV, Parkinson's Disease & Other Neuropsychiatry

KEY INSIGHT

Design note: All tables follow the spec, --earth header background, --sage-tint alternating rows, 8pt header / 8.5pt body, overflow-wrap: break-word . Tables are the highest-yield format for exam revision.

TABLE 01: HAND Staging: ANI vs MND vs HAD

FEATURE	ANI	MND	HAD
Full name	Asymptomatic Neurocognitive Impairment	Mild Neurocognitive Disorder	HIV-Associated Dementia
Neuropsychological impairment	≥2 domains, ≥1 SD below norm	≥2 domains impaired	Marked, multiple domains
Functional impairment	None	Mild, IADL affected	Severe, ADL affected
Prevalence (cART era)	~33%	~12%	2–8%
Pre-cART HAD prevalence			25–30%
Cognitive pattern	Subtle; only on formal testing	Affects complex daily tasks	Cannot manage self-care
Memory type affected	Retrieval deficit	Retrieval + learning	Global
Psychomotor slowing	Present	Present	Prominent
Depression comorbidity	Common	Common	Very common
Dementia type	Subcortical	Subcortical	Subcortical
ART response	Good	Moderate	Partial

KEY INSIGHT

Exam Pearl, The distinction between ANI and MND is FUNCTIONAL, not cognitive test scores alone. If the patient functions normally at work and home, it's ANI despite test impairment.

TABLE 02: PD Depression vs Primary MDD

FEATURE	PD-ASSOCIATED DEPRESSION	PRIMARY MDD
Neurobiological basis	LC noradrenergic + raphe serotonergic degeneration + mesolimbic dopamine loss	Monoamine dysregulation without structural degeneration
Guilt / worthlessness	Less prominent	Prominent (core DSM criterion)
Suicidal ideation	Present but less lethal plans; less common	More common; higher lethality
Anxiety	Very prominent; panic attacks common	Variable
Mood reactivity	Present, responds to positive events	Absent in melancholic subtype
Anhedonia	Prominent	Prominent
Irritability	Very prominent	Variable
Onset relative to motor	May PRECEDE motor symptoms by years	After psychosocial stressor typically
Diurnal variation	Less classic	Classic (worse in morning)
Somatic overlap	Heavy, fatigue, sleep, psychomotor changes overlap with PD	Less confounded
ECT response	Yes, AND improves motor symptoms	Yes, motor not affected
Dopaminergic treatment	Pramipexole has antidepressant properties	No dopaminergic effect
MAO-B inhibitor interaction	Selegiline / rasagiline + SSRI = serotonin syndrome risk	Less of a concern
Preferred assessment tool	GDS-15, HDRS	PHQ-9, BDI-II, MADRS

TABLE 03: DLB vs PDD (Lewy Body Spectrum)

FEATURE	DEMENTIA WITH LEWY BODIES (DLB)	PARKINSON'S DISEASE DEMENTIA (PDD)
Temporal relationship	Dementia first (or within 1 year of motor symptoms)	Motor symptoms ≥ 1 year BEFORE dementia
"One-year rule"	Defines DLB (dementia ≤ 1 year of parkinsonism)	Defines PDD (dementia > 1 year after motor onset)

FEATURE	DEMENTIA WITH LEWY BODIES (DLB)	PARKINSON'S DISEASE DEMENTIA (PDD)
Core motor features	Parkinsonism (usually less severe)	Full PD motor syndrome (tremor, rigidity, bradykinesia)
Fluctuating cognition	Prominent, hallmark core feature	Present but less pronounced
Visual hallucinations	Core feature; early and prominent	Common but later in course
REM Sleep Behaviour Disorder	Supportive feature, present early	Present
Autonomic dysfunction	Present	Present
Neuroleptic sensitivity	SEVERE, can cause irreversible parkinsonism or death	Present, avoid typical APs
DaTSCAN	Abnormal (reduced dopamine uptake)	Abnormal
Cholinergic deficit	More pronounced (contributes to psychosis)	Present
AChEI response	Good (rivastigmine approved)	Rivastigmine approved (EX-PRESS trial)
Neuropathology	Widespread cortical + subcortical Lewy bodies	Predominantly subcortical early; cortical late
Genetic relationship	Same disease spectrum as PDD	Same disease spectrum as DLB

KEY INSIGHT

Exam Pearl, DLB and PDD are almost certainly the same disease at different points on a spectrum. The one-year rule is an arbitrary clinical convention. Both require the same caution with antipsychotics and both respond to rivastigmine.

TABLE 04: Anti-NMDAR Encephalitis vs First-Episode Schizophrenia

FEATURE	ANTI-NMDAR ENCEPHALITIS	FIRST-EPIISODE SCHIZOPHRENIA
Onset	Acute, days to weeks	Insidious, months to years
Age	Any; most common 12–45 years, female	18–25 years (M), 25–35 years (F)
Sex predominance	Female (young women, ovarian teratoma)	Male earlier onset; roughly equal overall
Prodrome	Viral, fever, headache, malaise	Social withdrawal, academic decline

FEATURE	ANTI-NMDAR ENCEPHALITIS	FIRST-EPISODE SCHIZOPHRENIA
Psychiatric phase	Psychosis, agitation, bizarre behaviour	Positive symptoms, negative symptoms
Seizures	Yes, common; early	Rare (unless antipsychotic effect)
Movement disorders	Orofacial dyskinesias, choreoathetosis, characteristic	None (unless tardive dyskinesia from AP)
Autonomic instability	Yes, tachycardia, hyperthermia, BP changes	No
Consciousness	Decreased in neurological phase	Intact
Fever	Yes (prodrome)	No
CSF	Pleocytosis (60%), elevated protein	Normal
EEG	Abnormal, diffuse slowing; extreme delta brush	Usually normal
MRI	May show limbic T2/FLAIR changes	Subtle structural changes
Anti-NMDAR antibodies	Positive (CSF > serum)	Absent
Ovarian teratoma	50–60% of female cases	Not applicable
Response to antipsychotics	Partial at best; definitive treatment is immunotherapy	Responds to antipsychotics
Treatment	IVIG + steroids + plasmapheresis → rituximab; teratectomy	Antipsychotics + psychosocial
Prognosis	>80% recovery with treatment	Variable; often chronic relapsing

KEY INSIGHT

Clinical Anchor, Any "first-episode psychosis" in a young woman with ANY of: fever, seizures, movement disorder, autonomic symptoms, decreased consciousness, rapid onset → send CSF for anti-NMDAR antibodies before diagnosing schizophrenia.

TABLE 05: Huntington's Disease vs Other Causes of Choreiform Dementia

FEATURE	HUNTINGTON'S DISEASE	NEUROACANTHOCYTOSIS	WILSON'S DISEASE	NPSLE (SLE CHOREA)	SYDENHAM'S CHOREA
Genetics	CAG repeat, AD, chr 4	VPS13A mutation, AR	ATP7B mutation, AR	Acquired (autoimmune)	Acquired (post-strep)
Age of onset	30–50 (full penetrance)	Young adults	<40 years	Young adults	5–15 years
Type of chorea	Generalised, flowing	Oro-facio-lin-gual + limb	Coarse tremor + dystonia	Generalised, unilateral	Generalised; self-limiting
Dementia	Prominent, progressive, subcortical	Late	Yes	Mild, fluctuating	Rare
Psychiatric features	Depression, irritability, apathy, OCD, psychosis	Personality change, depression	Personality change, psychosis, depression	Psychosis, depression, cognitive	Emotional lability, OCD
Motor features besides chorea	Rigidity (late / juvenile), oculomotor	Tongue + lip biting, tics	Wing-beat tremor, dysarthria, dysphagia		Ballismus
Specific biomarker	CAG repeat >40	Acanthocytes on blood film	Low ceruloplasmin, KF rings	Anti-dsDNA, APS antibodies	Anti-streptolysin O
Liver involvement	None	None	Yes, hepatic	Rare (lupus hepatitis)	None
Treatment of chorea	Tetrabenazine, deutetabenazine	Symptomatic	D-penicillamine, trientine	Immunosuppression	Penicillin prophylaxis + haloperidol

TABLE 06: NPSLE Classification, CNS vs PNS Manifestations

SYSTEM	MANIFESTATION	KEY PSYCHIATRIC/NEUROLOGICAL POINT
CNS	Acute confusional state (delirium)	Most common CNS-NPSLE; multifactorial
CNS	Cognitive dysfunction	80% on formal testing; "lupus fog"

SYSTEM	MANIFESTATION	KEY PSYCHIATRIC/NEUROLOGICAL POINT
CNS	Mood disorder (depression)	Most common psychiatric NPSLE; SSRIs
CNS	Anxiety disorder	Underdiagnosed
CNS	Psychosis	2–8%; exclude steroid-induced
CNS	Seizures	15–20%; may require chronic AED
CNS	Cerebrovascular disease	Stroke / TIA, often APS-mediated
CNS	Chorea	Rare; APS-associated; basal ganglia
CNS	Demyelinating syndrome	MS-like; optic neuritis, myelitis
CNS	Headache	Not explained otherwise
CNS	Myelopathy	Longitudinally extensive; APS or inflammation
PNS	Polyneuropathy	Sensorimotor; vasculitis of vasa nervorum
PNS	Mononeuropathy / multiplex	Vasculitis
PNS	Autonomic disorder	Dysautonomia
PNS	Guillain-Barré syndrome	Rare
PNS	Myasthenia gravis	Rare; overlap syndrome
PNS	Cranial neuropathy	CN V (trigeminal) most common

KEY INSIGHT

Exam Pearl, ACR 1999 defined 19 NPSLE syndromes (12 CNS + 7 PNS). The 3 most common = cognitive dysfunction, headache, mood disorder. The most dramatic = psychosis. The most dangerous long-term = cerebrovascular disease (via APS).

TABLE 07: Antipsychotic Safety in Special Neurological Populations

DRUG	PD/DLB	HD	HIV	HEPATIC FAILURE	RENAL FAILURE
Clozapine	PREFERRED (low D2)	Use cautiously	Caution (agranulocytosis + HIV neutropenia)	Reduce dose	Reduce dose
Quetiapine	Acceptable (low D2)	Acceptable	Acceptable	Reduce dose	Generally safe
Pimavanserin	FDA-approved	Not indicated	Not indicated	Use caution	Generally safe
Olanzapine	CONTRAINDICATED (motor worsening)	Acceptable	Acceptable; metabolic effects	Reduce dose	Generally safe
Risperidone	AVOID (motor worsening)	Acceptable	Use caution (EPS sensitivity in HIV)	Reduce dose	Reduce dose (renal clearance of 9-OH)
Haloperidol	AVOID (severe EPS)	Use cautiously	AVOID in advanced HIV (severe EPS)	Reduce dose	Generally safe
Aripiprazole	Caution (partial D2 agonism, theoretical worsening of psychosis in PD)	Acceptable	Acceptable	Reduce dose	Generally safe
Amisulpride	AVOID (D2 blockade)	Acceptable	Use caution	Generally safe	AVOID (renal clearance)

TABLE 08: Dementia Profiles: Subcortical vs Cortical

FEATURE	SUBCORTICAL DEMENTIA (HD, PD, HAND, WILSON'S)	CORTICAL DEMENTIA (ALZHEIMER'S, FRONTOTEMPORAL)
Primary deficit	Processing speed, executive function, retrieval memory	Encoding memory (Alzheimer's), language/personality (FTD)
Memory type	Retrieval deficit, cues HELP	Encoding deficit, cues do NOT help
Language	Relatively spared (dysarthria in motor disease)	Aphasia (Alzheimer's, FTD semantic)

FEATURE	SUBCORTICAL DEMENTIA (HD, PD, HAND, WILSON'S)	CORTICAL DEMENTIA (ALZHEIMER'S, FRONTOTEMPORAL)
Praxis	Relatively spared	Apraxia (Alzheimer's)
Agnosia	Rare	Common (Alzheimer's)
Personality	Apathy, slowing	FTD: disinhibition/apathy; AD: late change
Mood	Depression very common	Depression early in AD; less prominent in FTD
Psychomotor speed	Slowed (prominent)	Not primarily affected early
Movement disorder	Present (parkinsonism, chorea, tremor)	Absent early in most cortical dementias
Prototype	Huntington's disease	Alzheimer's disease

KEY INSIGHT

Exam Pearl, The cue-and-recall test differentiates: Give a category cue after failed free recall. If patient now remembers (cue helps) → retrieval deficit → subcortical. If patient still cannot recall even with cue → encoding failure → cortical (Alzheimer's pattern).

TABLE 09: Neurosyphilis Types Comparison

TYPE	TIMING	PATHOLOGY	MOTOR	COGNITIVE/P SYCHIATRIC	KEY SIGN
Asymptomatic	Any	CSF changes only	None	None	CSF VDRL positive
Acute meningitis	<2 years	Leptomeningitis	CN palsies (II, VII, VIII)	Headache, meningismus	Fever + meningism
Meningovascular	5–12 years	Endarteritis → infarction	Hemiplegia, CN palsies	Personality prodrome → stroke	Hübner's endarteritis stroke
General Paresis (GPI)	15–20 years	Diffuse cortical meningoencephalitis	Hyperreflexia, tremor	Depression, grandiose delusions, progressive dementia	Argyll Robertson pupil
Tabes Dorsalis	15–25 years	Posterior column + dorsal root degeneration	Ataxia, absent reflexes	Primarily motor/sensory	Lightning pains, Romberg+

TYPE	TIMING	PATHOLOGY	MOTOR	COGNITIVE/P SYCHIATRIC	KEY SIGN
Gumma	Years	Granulomatous mass	Focal deficits (mass effect)	Depends on location	Mass lesion on MRI

KEY INSIGHT

Anchor, The mnemonic PARESIS covers GPI. Tabes Dorsalis is the posterior column disease, remember: posterior column = proprioception + vibration → sensory ataxia + Romberg positive + absent knee jerks. Argyll Robertson pupil occurs in BOTH GPI and tabes.

TABLE 10: Prion Disease Comparison: sCJD vs vCJD vs FFI vs Kuru

FEATURE	SPORADIC CJD	VARIANT CJD	FATAL FAMILIAL INSOMNIA	KURU
Cause	Somatic PRNP mutation / spontaneous misfolding	BSE transmission via beef	Germline PRNP D178N mutation (Met129)	Ritual cannibalism
Epidemiology	85% of CJD; 1–2/million/year	Rare; young adults; UK outbreak	Very rare; AD	Fore people of PNG; virtually extinct
Age of onset	Elderly (median 65 years)	Young adults (mean 29 years)	Adult; AD inheritance	Adults; epidemic in women/children
Duration	4–6 months (median 4 months)	~13 months	7–25 months	3–24 months
Dominant feature	Rapidly progressive dementia + myoclonus	Psychiatric/sensory symptoms first; dementia later	Intractable insomnia + dysautonomia	Cerebellar ataxia + tremor ("laughing disease")
Psychiatric features	Late, anxiety, depression as cortex involved	Early and prominent , depression, anxiety, dysaesthesias	Hallucinations, acting out dreams	Emotional lability, inappropriate laughing
Myoclonus	Prominent, stimulus-sensitive	Less prominent	Absent early	Absent
Ataxia	Present	Prominent	Mild	Prominent, dominant feature
EEG	PSWC (1–2 Hz) in 67%	No PSWC	Abnormal sleep studies	Non-specific

FEATURE	SPORADIC CJD	VARIANT CJD	FATAL FAMILIAL INSOMNIA	KURU
MRI	Cortical ribboning + BG/thalamic DWI hyperintensity	Pulvinar sign (posterior thalamus T2)	Thalamic signal changes	Non-specific
CSF 14-3-3	Positive (sensitive)	Less sensitive	Often negative	Rarely tested
RT-QuIC	Positive (highly specific)	May be positive	May be negative	Rarely tested
Ante-mortem diagnosis	RT-QuIC + MRI + EEG	Tonsillar biopsy (PrP ^{Sc} in lymphoid tissue)	Genetic testing	Clinical + exposure history
Thalamic pathology	Diffuse	Posterior thalamus (pulvinar)	Selective , anterior + mediodorsal thalamic nuclei	Not predominant
Transmission risk	Surgical instruments, dura grafts	Infected beef	None (genetic)	Cannibalism only

KEY INSIGHT

Exam Pearl, vCJD is the exam favourite for its unique features: young patients, psychiatric onset, pulvinar sign on MRI, tonsillar biopsy, NO PSWC on EEG. FFI is tested for its pure insomnia phenotype and selective thalamic degeneration. Kuru = historical significance, Nobel Prize (Gajdusek 1976), cerebellar dominant.

SUMMARY COMPARISON TABLE: Autoimmune Encephalitides

WIDE COMPARISON · LANDSCAPE

ANTIBODY	TARGET	DEMOGRAPHICS	TUMOUR	PSYCHIATRIC	NEUROLOGICAL	KEY UNIQUE FEATURE
NMDAR	GluN1 subunit	Young F	Ovarian teratoma (50%)	Psychosis, agitation (FIRST)	Seizures, orofacial dyskinesias, autonomic instability	Psychiatric phase before neuro; extreme delta brush on EEG
LGI1	Leucine-rich glioma-inactivated 1	Older M (60s)	None	Anxiety, depression, psychosis	FBDS, limbic encephalitis, amnesia	Hyponatraemia (SIADH); FBDS pathognomonic
CASPR2	Contactin-associated protein-like 2	Older M; thymoma	Thymoma	Sleep disorder, cognitive decline	Morvan syndrome (encephalopathy + PNS), neuromyotonia	Combined CNS + PNS involvement (Morvan)
AMPA	AMPA receptor	Middle-aged F	Breast, lung, thymoma	Psychosis, mood	Limbic encephalitis, memory	High relapse rate
GABABR	GABA-B receptor	Middle-aged	Small cell lung ca	Depression	Prominent seizures, limbic	Seizures most prominent feature
DPPX	DPP-like protein 6	Middle-aged	None	Agitation, confusion	Hyperekplexia, diarrhoea, weight loss	GI symptoms preceding encephalopathy

PYQ Frequency Analysis

HIV, Parkinson's Disease & Other Neuropsychiatry

KEY INSIGHT

Methodology: Questions reconstructed from recalled exams across PG exams, TN MGR, PG exams, and PG exams PG Psychiatry papers (2010–2025). Frequency, marks allocation, and examiner focus pattern identified. All question themes mapped to D1 Study Notes sections.

SECTION 1: QUESTION FREQUENCY HEATMAP

By Topic Area

TOPIC	ESTIMATED FREQUENCY	MARKS RANGE	TREND
HAND classification + pathophysiology	High	8–10	Stable
Anti-NMDAR encephalitis	High	8–10	Rising (post-2018)
HIV psychiatric co-morbidities (depression, mania, psychosis)	High	6–10	Stable
PD psychosis + antipsychotics	High	6–8	Stable
Neurosyphilis / GPI	Medium-High	5–8	Stable
Huntington's disease (genetics + psychiatric features)	Medium-High	6–10	Rising
ART side effects (efavirenz)	Medium	5–6	Stable
HIV testing and counselling	Medium	5	Stable
CJD / prion diseases	Medium	5–8	Stable
Impulse control disorders in PD	Medium	5–6	Rising

TOPIC	ESTIMATED FREQUENCY	MARKS RANGE	TREND
MS and psychiatry / pseudobulbar affect	Medium	5–8	Stable
Wilson's disease	Medium	5	Stable
Hepatic / renal encephalopathy + psychotropic prescribing	Medium	5–6	Stable
DBS psychiatric effects	Lower	3–5	New
Dopamine dysregulation syndrome	Lower	3–5	New
Fatal familial insomnia	Lower	3–5	Rare

SECTION 2: RECONSTRUCTED PREVIOUS YEAR QUESTIONS

2.1 LONG ANSWER QUESTIONS (10 marks)

PYQ-LA-01

Describe HIV-associated neurocognitive disorders (HAND). Discuss the staging, pathophysiology, assessment tools, and principles of management.

(10 marks, PG Paper IV pattern, 2019, 2022)

Examiner focus: Complete Antinori classification mandatory. IHDS scoring must be correct. Pathophysiology should cover both direct viral protein neurotoxicity AND macrophage-mediated injury. Management = ART optimisation first, then symptomatic.

Marks breakdown (suggested):

- Classification/staging: 3 marks
- Pathophysiology: 3 marks
- Assessment (IHDS + neuropsychological domains): 2 marks
- Management: 2 marks

Common mistakes:

- Stating HIV directly infects neurons (incorrect, no CD4 on neurons)
- Missing the functional impairment criterion that separates ANI from MND
- Omitting CPE score concept in management
- Confusing IHDS total (12) with cutoff (≤ 10)

PYQ-LA-02

A 28-year-old woman presents with acute onset psychosis, agitation, and bizarre behaviour over 2 weeks with no prior psychiatric history. Discuss the differential diagnosis, with emphasis on autoimmune encephalitis. How would you investigate and manage this case?

(10 marks, Exam pattern, 2021; PG exams 2023)

Examiner focus: Red flags for organic psychosis must be listed. Anti-NMDAR encephalitis clinical phases, psychiatric phase presenting first is THE teaching point. Investigation sequence and treatment protocol (first-line vs second-line immunotherapy) must be complete.

Marks breakdown:

- Differential diagnosis with organic vs primary: 2 marks
- Anti-NMDAR clinical profile (phases): 3 marks
- Investigations (CSF, EEG, MRI, antibodies, pelvic imaging): 2 marks
- Management (immunotherapy + teratectomy): 3 marks

Common mistakes:

- Not mentioning ovarian teratoma workup
 - Confusing anti-NMDAR (young women, teratoma) with LGI1 (older men, hyponatraemia)
 - Omitting the "extreme delta brush" EEG finding
 - Not mentioning rituximab as second-line
-

PYQ-LA-03

Discuss the psychiatric manifestations of Huntington's disease. Describe the genetics, genetic counselling protocol, and ethical issues in predictive testing.

(10 marks, PG exams 2020; Exam pattern)

Examiner focus: CAG repeat numbers must be precise. Anticipation with paternal transmission. Psychiatric symptoms may precede motor, suicide risk in two specific periods. Genetic counselling must cover protocol AND ethical principles (autonomy, right not to know, children, PGD).

Marks breakdown:

- Genetics (CAG repeats, anticipation, inheritance): 2 marks
- Psychiatric manifestations (all types with prevalence): 4 marks
- Genetic counselling protocol: 2 marks
- Ethical issues: 2 marks

Common mistakes:

- Stating "dominant" without specifying full penetrance threshold (≥ 40 repeats)
 - Missing anticipation via paternal transmission
 - Not mentioning both high-risk periods for suicide
 - Treating genetic counselling as just "pre-test and post-test" without the ethical substance
-

2.2 MEDIUM ANSWER QUESTIONS (8 marks)

PYQ-MA-01

Discuss psychosis in Parkinson's disease, clinical features, pathophysiology, and management. Which antipsychotic is contraindicated and why?

(8 marks, PG exams 2018, 2021; PG exams 2022)

Examiner focus: Spectrum from minor hallucinations to formed VH to delusions. Step-wise management. Antipsychotic table, clozapine vs quetiapine vs pimavanserin vs AVOID (olanzapine, risperidone, haloperidol). Mechanism of olanzapine contraindication (D2 blockade worsens PD motor).

High-yield points:

- Pimavanserin = 5-HT_{2A} inverse agonist = no D₂ blockade = no motor worsening = FDA 2016
 - Clozapine = gold standard but requires WBC monitoring
 - Olanzapine = contraindicated (not just "use caution")
-

PYQ-MA-02

Describe the neuropsychiatric manifestations of multiple sclerosis. Discuss pseudobulbar affect in detail.

(8 marks, PG exams 2020; PG exams 2022)

Examiner focus: Depression prevalence (50%) must be stated. Interferon-induced depression mechanism. Euphoria sclerotica = largely a myth, examiner expects you to say this, not accept the historical description. PBA: definition, pathophysiology (corticobulbar tract disruption), distinction from depression/BPD, treatment (SSRIs fast-acting; Nuedexta FDA-approved).

PYQ-MA-03

Discuss the classification and clinical features of neurosyphilis. Describe General Paresis of the Insane in detail.

(8 marks, PG exams 2017, 2019; TN MGR 2021)

Examiner focus: Classification table with timing (meningovascular 5–12y, GPI 15–20y, tabes 15–25y). PARETIS mnemonic for GPI. Argyll Robertson pupil, accommodates but does not react. Treatment = benzyl penicillin IV (not IM procaine for CNS disease as first-line). Jarisch-Herxheimer reaction.

PYQ-MA-04

Discuss depression in HIV infection, prevalence, aetiology, clinical features, and management.

(8 marks, PG exams 2016, 2023; PG exams 2020)

Examiner focus: Prevalence (30–60%). Multiple aetiologies (viral, ART, psychosocial, cytokine). Drug interactions with ART, ritonavir + SSRI. Efavirenz as cause of depression. Treat depression = improves ART adherence (this causal link is high-yield).

2.3 SHORT ANSWER QUESTIONS (5–6 marks)

PYQ-SA-01

Write a note on efavirenz and its neuropsychiatric side effects.

(5 marks, PG exams 2015, 2018, 2021; PG exams 2022)

Must include: Prevalence (40–52%), mechanism (GABA-A agonist + CB1 inverse agonist), list of effects (vivid dreams, depression, psychosis, mania, cognitive), time course (worst weeks 1–4, improves by 6–8 weeks), management (night dosing, switch to dolutegravir).

PYQ-SA-02

Describe HIV testing and counselling.

(5 marks, PG exams 2014, 2017, 2020)

Must include: 5 Cs (consent, confidentiality, counselling, correct results, connection to care). Types of HTC (VCT, PITC). Pre-test and post-test components. Window period. PPTCT. Linkage to care.

PYQ-SA-03

Write short notes on impulse control disorders in Parkinson's disease.

(5 marks, PG exams 2019; PG exams 2021; PG exams 2023)

Must include: Types (PHECS), prevalence (13.6% DOMINION study), mechanism (D3/mesolimbic, dopamine agonist preferential effect), risk factors, management

(reduce/stop agonist first, then CBT/naltrexone). DDS as separate entity.

PYQ-SA-04

Write a note on Creutzfeldt-Jakob disease.

(5 marks, PG exams 2016, 2022)

Must include: Types (sCJD 85%, vCJD, fCJD, iatrogenic). sCJD clinical (rapidly progressive dementia, myoclonus, cerebellar, visual). Investigations (MRI DWI, EEG PSWC, 14-3-3, RT-QuIC). vCJD differences (young, psychiatric onset, pulvinar sign, tonsillar biopsy, no PSWC).

PYQ-SA-05

Write a note on Wilson's disease, psychiatric manifestations.

(5 marks, PG exams 2015, 2020)

Must include: ATP7B gene, AR inheritance, psychiatric features (personality change first, depression, psychosis, OCD), KF rings, diagnosis (ceruloplasmin, 24h copper, biopsy), treatment (D-penicillamine, trientine, zinc), clinical trap (misdiagnosed as primary psychiatric illness in young patients).

PYQ-SA-06

Describe the neuropsychiatric manifestations of SLE.

(5 marks, PG exams 2018; PG exams 2022)

Must include: ACR 1999, 19 NPSLE syndromes (12 CNS, 7 PNS). Key manifestations, cognitive dysfunction (most common), depression, psychosis (2–8%), seizures. APS and its neuropsychiatric role. Steroid-induced psychiatric effects vs SLE psychosis differential.

PYQ-SA-07

Short note on apathy in Parkinson's disease, distinguish from depression.

(5 marks, PG exams 2021; PG exams 2023)

Must include: Definition (quantitative reduction in motivated behaviour without mood disturbance). Prevalence (40–70%). Depression vs apathy distinction (negative affect present vs absent). Assessment (Starkstein Apathy Scale). Treatment (dopaminergic optimisation, rivastigmine, methylphenidate).

PYQ-SA-08

Write a note on REM Sleep Behaviour Disorder in Parkinson's disease.

(5 marks, PG exams 2022)

Must include: Definition (loss of normal REM atonia → dream enactment). Prodromal marker of PD (precedes motor symptoms by >10 years). Braak stage 1–2. Risk of injury. Polysomnography for diagnosis. Treatment (clonazepam 0.25–0.5 mg, melatonin high-dose).

2.4 VERY SHORT / SPOT QUESTIONS (2–3 marks)

QUESTION · KEY ANSWER POINTS

What is the IHDS? What is its cutoff? 3-component scale (motor speed, psychomotor speed, 4-word recall); total 12; ≤10 suggests HAD

Name the antipsychotic FDA-approved for PD psychosis. What is its mechanism?

Pimavanserin; 5-HT_{2A} inverse agonist; no D₂ blockade

What is the "one-year rule" in DLB vs PDD? If dementia appears within 1 year of parkinsonism → DLB; if >1 year after motor onset → PDD

Name the EEG finding in CJD. Periodic sharp wave complexes (PSWC) at 1–2 Hz; present in 67% of sCJD; absent in vCJD

What is extreme delta brush? EEG pattern in anti-NMDAR encephalitis; high specificity; present in ~30%

What is the 40-40 rule in Huntington's disease? CAG ≥40 repeats = full penetrance (all will develop HD)

Name the CSF test most specific for sporadic CJD. RT-QuIC (real-time quaking-induced conversion)

What is Argyll Robertson pupil? Small, irregular; accommodates but does not react to light; lesion in pretectal nucleus

What is punding in PD? Complex, stereotyped, repetitive purposeless behaviour (sorting, tinkering, collecting); form of ICD

What is the treatment of cryptococcal meningitis? Amphotericin B + flucytosine (2 weeks) → fluconazole (consolidation + maintenance); serial LP for raised ICP

What is the most common psychiatric symptom in HD? Irritability (across most studies); depression is most clinically significant

Name the VMAT2 inhibitor approved for HD chorea. Tetrabenazine (TBZ); deutetabenazine (newer, fewer side effects)

What is DDS in PD? Dopamine Dysregulation Syndrome, compulsive overuse of dopaminergic medication beyond motor need

What is euphoria sclerotica? Is it real? Historical concept of inappropriate cheerfulness in MS; largely a myth; depression is dominant

What is West Haven grade II hepatic encephalopathy? Lethargy, disorientation in time, personality change, asterixis present

SECTION 3: EXAMINER PATTERN ANALYSIS

3.1 Topics That Appear EVERY Exam Cycle

These topics have appeared at least once in nearly every examination sitting analysed:

1. **HAND**, classification, pathophysiology, IHDS
2. **Psychiatric comorbidities in HIV**, depression, mania (ART-associated), psychosis
3. **PD psychosis and antipsychotic management**, clozapine vs quetiapine vs pimavanserin vs avoid
4. **Neurosyphilis/GPI**, PARESIS mnemonic, Argyll Robertson pupil, treatment

3.2 Rising Frequency Topics (post-2018)

Topics showing increased exam frequency in recent cycles:

1. **Anti-NMDAR encephalitis**, now a standard 10-mark question
2. **Impulse control disorders in PD + DDS**, was rare pre-2018, now medium frequency
3. **HD genetics + psychiatric features**, increasing
4. **Autoimmune encephalitis broadly**, LGI1, CASPR2 appearing as short notes

3.3 Topics Likely Tested as Short Notes Only

These are tested but rarely as long-answer questions, prepare as 5-mark short notes:

- Fatal familial insomnia
- Kuru
- NPSLE classification
- REM sleep behaviour disorder
- Dopamine dysregulation syndrome
- Wilson's disease psychiatric features
- Dialysis dementia

3.4 Topics Never Asked as Standalone But Appear in Differentials

Prepare to mention these when relevant, not as primary answers:

- CNS lymphoma vs toxoplasmosis (PML distinction)
 - Hashimoto's encephalopathy
 - Wernicke-Korsakoff (usually in alcohol paper but may appear in context of nutritional/metabolic)
-

SECTION 4: STRATEGY NOTES BY QUESTION TYPE

For 10-mark HAND questions:

- Open with epidemiology sentence (50–70% lifetime neuropsychiatric burden)
- State cART era shift (HAD declined, milder forms predominant)
- Draw classification table, examiners award marks for visual organisation
- For pathophysiology: TWO mechanisms (direct viral proteins + macrophage bystander)
- For IHDS: state all 3 components, max score, cutoff, sensitivity/specificity
- Close with management hierarchy: ART first → CPE optimisation → symptomatic

For anti-NMDAR encephalitis:

- Lead with epidemiology (most common autoimmune encephalitis, Dalmau 2007)
- Clinical phases table is mandatory, use it
- State the trap: psychiatric phase presents to psychiatry ward FIRST
- Investigations: always mention pelvic ultrasound/CT for ovarian teratoma
- Treatment: name all steps, steroids + IVIG + plasmapheresis → rituximab + cyclophosphamide; teratectomy
- Prognosis: >80% improvement, 20–25% relapse

For PD psychosis antipsychotic questions:

- Present as a table, safe vs avoid
- Name pimavanserin with its mechanism (5-HT_{2A} inverse agonist, 2016 FDA approval)
- Explain WHY olanzapine is contraindicated (D₂ blockade, not just "avoid")
- Clozapine: mention WBC monitoring requirement (limits use despite being gold standard)

For HD genetic counselling:

- Follow the ethical principle structure: Autonomy → Beneficence → Non-maleficence → Justice
 - Specifically address children (not tested, no benefit in childhood, cannot consent)
 - Mention PGD as the option that avoids parental disclosure
 - Two high-risk suicide periods: post-diagnosis + early motor phase
-

SECTION 5: INTEGRATED TOPIC MAP

Topics that commonly appear **TOGETHER** in one question:

COMBINATION	FREQUENCY	EXAMPLE FORMAT
HAND classification + pathophysiology + IHDS	Very High	Single 10-mark LA
Anti-NMDAR phases + investigations + management	Very High	Clinical vignette 10-mark
PD psychosis + antipsychotic choice	High	8-mark standalone
HD genetics + psychiatric features + counselling	High	10-mark standalone
Neurosyphilis classification + GPI + treatment	High	8-mark standalone
Depression in PD + depression in HIV (compare)	Medium	5-mark each in combined
CJD types + investigations	Medium	6–8 mark standalone
ICD in PD + DDS	Medium	5–6 mark standalone
MS depression + PBA	Medium	8-mark combined
Efavirenz + ART neuropsychiatric effects	Medium	5-mark short note

SECTION 6: MARKS ALLOCATION CHEAT SHEET

When marks are not specified, use this allocation guide:

CONTENT ELEMENT · TYPICAL MARKS

Introduction (1–2 lines, epidemiology) 0.5 mark

Classification / staging table 2–3 marks

Pathophysiology (mechanism) 2–3 marks

Clinical features (list or table) 2–3 marks

Investigations 1–2 marks

Management / treatment 2–3 marks

Conclusion / prognosis sentence 0.5 mark

Rule: Never skip investigations and management, they are the most predictable marking zones.

Format tip: One table is worth 3 prose paragraphs in examiner perception. Use them.

SECTION 7: YEAR-WISE QUESTION TRACKING (Reconstructed)

APPROX. YEAR	QUESTION THEME	PAPER	MARKS
2014	HIV testing and counselling	Paper IV	5
2015	Efavirenz neuropsychiatric effects	Paper IV	5
2015	Wilson's disease psychiatric features	Paper IV	5
2016	CJD, types and diagnosis	Paper IV	8
2016	HAND, staging and management	Paper IV	10
2017	Neurosyphilis, classification and GPI	Paper IV	8
2017	HIV testing and counselling	Paper IV	5
2018	PD psychosis, features and management	Paper IV	8
2018	NPSLE neuropsychiatric manifestations	Paper IV	5
2018	Efavirenz CNS side effects	Paper IV	5
2019	HAND, full question	Paper IV	10
2019	ICD in Parkinson's disease	Paper IV	5
2019	Neurosyphilis / GPI	Paper IV	8
2020	Depression in HIV	Paper IV	8
2020	Huntington's disease, psychiatric + genetics	Paper IV	10
2020	MS and psychiatry / PBA	Paper IV	8
2020	Wilson's disease	Paper IV	5

APPROX. YEAR	QUESTION THEME	PAPER	MARKS
2021	Anti-NMDAR encephalitis (vignette)	Paper IV	10
2021	PD psychosis, antipsychotics	Paper IV	8
2021	Apathy in PD (distinguish from depression)	Paper IV	5
2021	ICD in PD + DDS	Paper IV	5
2022	HAND	Paper IV	10
2022	CJD	Paper IV	5
2022	Efavirenz	Paper IV	5
2022	Autoimmune encephalitis (LGI1 short note)	Paper IV	5
2022	REM sleep behaviour disorder in PD	Paper IV	5
2023	Anti-NMDAR encephalitis	Paper IV	10
2023	HD, genetics, psychiatric, counselling	Paper IV	10
2023	Depression in HIV	Paper IV	6
2023	ICD in PD	Paper IV	5

KEY INSIGHT

Ra note: This PYQ analysis is reconstructed from recalled questions, treat frequency data as indicative, not definitive. The most reliable signal is the repeat appearance of HAND, anti-NMDAR, and PD psychosis in virtually every cycle. Prioritise those three for maximum return on study time.

Quick Review

HIV, Parkinson's Disease & Other Neuropsychiatry

KEY INSIGHT

Format: Each vignette contains: presentation, investigation findings, questions, diagnosis with reasoning, key teaching points, and examiner notes. All names are fictitious. Patient identifiers are randomised codes.

VIGNETTE 01: The Psychiatric Ward Trap

****PT-N19-01****FEMALE, 24 YEARS****REFERRED FROM GENERAL
MEDICINE****

Presentation:

Priya, a 24-year-old postgraduate student with no prior psychiatric history, is brought by her parents after 12 days of increasingly bizarre behaviour. She had been well until 2 weeks ago when she developed a low-grade fever, headache, and malaise for 4 days, which her family attributed to examination stress.

Over the next week, she became agitated and suspicious, heard voices commenting on her actions, and developed the belief that her hostel warden was poisoning her food. She was initially seen by a psychiatrist at a private clinic who diagnosed first-episode schizophrenia and started risperidone 2 mg/day. She improved marginally but 3 days later began making repetitive chewing and tongue-thrusting movements and had a generalised tonic-clonic seizure.

On examination: GCS 13/15, oriented to person only, blood pressure 148/96 mmHg, heart rate 114 bpm, temperature 38.1°C. Repetitive orofacial movements noted. No focal neurological deficits.

Investigations:

- Blood: CBC normal, metabolic panel normal, LFTs normal
- MRI brain: Subtle T2/FLAIR hyperintensity in left hippocampus
- EEG: Diffuse delta slowing; brief runs of beta superimposed on delta ("extreme delta brush")
- CSF: 18 lymphocytes/mm³, protein 52 mg/dL, glucose normal, no organisms, Gram stain negative

- CSF anti-NMDAR IgG antibodies: **Positive**
 - Pelvic ultrasound: **Right ovarian cystic lesion 3.2 cm**
-

Questions:

1. What is the diagnosis? What clues in the history point to it?
 2. Why was risperidone an inadequate treatment? What are the risks of continuing it?
 3. Outline the complete management plan.
 4. What is the significance of the pelvic ultrasound finding?
 5. What is "extreme delta brush" on EEG and what is its clinical significance?
-

Diagnosis: Anti-NMDA Receptor Encephalitis

Reasoning:

- Young woman, classic demographic
- Viral prodrome → psychiatric phase (psychosis, paranoia, agitation) → neurological phase (seizure, orofacial dyskinesias)
- CSF pleocytosis (lymphocytic) with normal glucose
- Extreme delta brush on EEG, highly specific (~30% of cases)
- MRI limbic involvement
- Confirmatory: CSF anti-NMDAR IgG positive
- Ovarian cystic lesion = likely teratoma (occurs in 50–60% of female cases)

Why risperidone was inadequate:

- Anti-NMDAR antibodies REDUCE NMDAR surface expression → dopamine disinhibition → psychosis
- Antipsychotics treat the symptom, not the cause
- Risperidone (D2 blocker) may exacerbate sedation and mask neurological deterioration
- No antipsychotic will reverse the antibody-mediated process

Management:

1. **ICU monitoring**, autonomic instability risk (BP, HR, temperature fluctuations); respiratory monitoring (hypoventilation possible)
2. **First-line immunotherapy (simultaneously):**
3. IV methylprednisolone 1g/day × 5 days
4. IVIG 2g/kg over 5 days
5. Consider plasmapheresis if no response
6. **Antiepileptics** for seizure control (levetiracetam preferred, no hepatic induction)

7. **Gynaecology referral:** Right ovarian cystic lesion → laparoscopic teratectomy (mandatory; dramatically improves outcomes)
 8. **Second-line if no improvement at 2–4 weeks:** Rituximab 375 mg/m² weekly × 4 doses ± cyclophosphamide
 9. **Symptomatic:** Low-dose haloperidol or quetiapine for agitation if absolutely necessary; reassess after immunotherapy
 10. **Monitor:** Antibody titres, functional recovery, ovarian pathology follow-up
- Prognosis:** >80% substantial recovery with treatment. Teratectomy is the single most impactful intervention.
-

Key Teaching Points:

- Anti-NMDAR encephalitis presents to **psychiatry first**, the psychiatric phase of 1–2 weeks precedes neurological signs
 - Any "first-episode psychosis" in a young woman with fever, seizures, or movement disorder → send CSF for anti-NMDAR antibodies immediately
 - The extreme delta brush on EEG is pathognomonic, learn to recognise it
 - Teratoma is the tumour source of antigen, its removal accelerates recovery
 - Do not anchor on schizophrenia, rapid onset, fever, normal premorbid function, seizures are all red flags
-

VIGNETTE 02: The Forgetful Professor

****PT-N19-02**

MALE, 52 YEARS

NEUROLOGY OPD**

Presentation:

Ramesh, a 52-year-old college professor, is brought by his wife. Over the past 18 months, he has become increasingly forgetful, he misplaces items, forgets appointments, and repeats himself in conversations. His wife notes that he seems slower in his thinking and takes longer to grade papers. He has also become increasingly withdrawn and lacks his previous enthusiasm for teaching.

He has a 6-year history of HIV infection, currently on tenofovir/lamivudine/efavirenz. His last CD4 count (4 months ago) was 380 cells/μL, viral load undetectable. No history of OIs. No substance use.

On examination: Alert, cooperative. MMSE 24/30 (loses points on serial 7s, delayed recall, and complex commands). Finger-tapping slow bilaterally. Mild psychomotor slowing on clinical observation. No focal deficits, no tremor, no gait abnormality.

IHDS score: 9/12 (motor speed 3/4, psychomotor speed 3/4, memory recall 3/4)

Investigations:

- MRI brain: Mild generalised cerebral atrophy, no focal lesions, no white matter changes, no ring-enhancing lesions
 - Comprehensive neuropsychological battery: Impairment in 3 domains (attention/working memory, psychomotor speed, executive function), all 1–1.5 SD below normative mean; IADL assessment shows difficulty managing complex financial tasks and calendar management
-

Questions:

1. What is the HAND diagnosis and why?
 2. What cognitive domains are affected and why does this pattern suggest subcortical rather than cortical dementia?
 3. Is efavirenz potentially contributing? What would you do?
 4. Outline management.
-

Diagnosis: HAND, Mild Neurocognitive Disorder (MND)

Reasoning:

- Neuropsychological impairment in ≥ 2 domains (3 domains affected here), each ≥ 1 SD below normative mean
- **Functional impairment is MILD**, he can still work but struggles with complex IADLs (managing finances, calendar), meets MND criteria
- IHDS = 9/12 (≤ 10 = positive screen for HAD, but formal battery needed to characterise; formal battery confirms MND not HAD as ADLs preserved)
- Viral load undetectable, HIV not actively replicating, yet HAND persists (common in cART era, "residual neuroinflammation")

Why subcortical pattern:

- Retrieval memory deficit (not encoding, would respond to cues)
- Psychomotor slowing (hallmark of subcortical)
- Executive dysfunction prominent
- Relatively spared language, praxis, and naming
- Contrast with Alzheimer's: encoding failure, aphasia, apraxia, agnosia

Efavirenz contribution:

- Efavirenz causes CNS symptoms including cognitive impairment ("mental fog") in up to 40–52%
- May be CONTRIBUTING to cognitive symptoms

- Action: Switch efavirenz to dolutegravir, dolutegravir has better CNS profile and minimal cognitive side effects
- Reassess cognitive function 3 months after switch

Management:

1. ART optimisation: Switch efavirenz → dolutegravir; ensure viral suppression maintained
2. Calculate CPE score of current regimen, optimise CNS penetration
3. Treat contributing factors: Address depression (withdrawal, anhedonia), optimise sleep
4. Cognitive rehabilitation: Memory strategies, compensatory aids (structured routines, calendars, pill organisers)
5. Monitor with 6-monthly IHDS; annual formal neuropsychological testing
6. Occupational health assessment if work impairment progresses

Key Teaching Points:

- HAND in the cART era: viral load undetectable ≠ no neurocognitive impairment (residual neuroinflammation continues)
- MND vs ANI distinction: both have cognitive impairment on testing; MND has MILD functional impact on IADLs
- Efavirenz is a modifiable contributor to cognitive symptoms in HIV, always review before attributing to HAND alone
- IHDS ≤10 is a screen, formal battery needed to stage HAND accurately

VIGNETTE 03: The Jealous Husband

PT-N19-03	MALE, 68 YEARS	PSYCHIATRY CLINIC, REFERRED BY NEUROLOGIST

Presentation:

Gopal, a 68-year-old retired bank manager with a 5-year history of Parkinson's disease, is brought by his daughter. He has been on levodopa/carbidopa 100/25 mg TDS and pramipexole 1 mg TDS for 3 years.

His daughter reports that over the past 6 months he has become increasingly suspicious of his wife, accusing her of being unfaithful and hiding money. He has questioned her about her phone calls, followed her when she leaves the house, and once struck her when she denied his accusations. He also admits to gambling online regularly over the past year, spending approximately ₹40,000–50,000 per month, something he had never done before. He has no insight into either behaviour.

On examination: Mild-to-moderate resting tremor, bradykinesia. MMSE 23/30 (mild impairment). Mood: guarded, suspicious. No auditory or visual hallucinations.

Current medications: Levodopa/carbidopa 100/25 TDS, pramipexole 1 mg TDS, pantoprazole, amlodipine.

Questions:

1. What are the two distinct neuropsychiatric problems in this vignette?
 2. What is the common pharmacological mechanism linking both problems?
 3. How would you manage the pathological jealousy specifically?
 4. What is the risk of simply adding an antipsychotic without addressing the dopamine agonist?
-

Diagnosis:

1. **Othello Syndrome (pathological/morbid jealousy)**, a delusional disorder with persecutory jealousy content
2. **Pathological gambling**, impulse control disorder (ICD) in PD

Common mechanism: Both are manifestations of **mesolimbic dopamine overstimulation** by pramipexole (dopamine agonist with high D3/D4 affinity in ventral striatum/reward circuit).

Management of pathological jealousy:

- **Step 1: Reduce and discontinue pramipexole**, primary intervention
- Taper slowly to avoid dopamine agonist withdrawal syndrome (dysphoria, anxiety, fatigue)
- Accept motor worsening; compensate with levodopa dose adjustment
- **Step 2: Antipsychotic if delusion persists after agonist reduction**
- **Clozapine** (first-line in PD, low dose 12.5–25 mg), does not worsen motor symptoms
- **Quetiapine**, alternative, no WBC monitoring needed
- **DO NOT use olanzapine, risperidone, haloperidol**, significant motor worsening in PD
- **Step 3: Safety assessment**, domestic violence risk; wife needs independent safety planning
- **Step 4: Carer education**, family must understand this is disease/medication-related, not moral failure

Risk of antipsychotic without addressing agonist:

- Will partially suppress the delusion but the underlying mesolimbic hyperdopaminergia continues

- Typical antipsychotics (haloperidol, risperidone) will cause severe EPS in PD
- Problem will recur or remain partially active
- Motor function will deteriorate significantly

Gambling management:

- Stop pramipexole (same mechanism, both ICD variants resolve with agonist reduction)
- Financial safeguards: Family takes over accounts
- CBT for gambling if residual behaviour persists after agonist reduction
- Naltrexone: Some evidence for ICD in PD; trial reasonable

Key Teaching Points:

- Othello syndrome + ICD in PD, same root cause (dopamine agonist), two clinical expressions
 - Pimavanserin would be ideal for psychosis in PD (no D2 blockade) but not available in India, clozapine is the accessible gold standard
 - Domestic violence assessment is mandatory when delusions involve infidelity accusations
 - Always screen PD patients on agonists with the QUIP questionnaire (Questionnaire for Impulsive-Compulsive Disorders in PD)
-

VIGNETTE 04: The Missing Months

PT-N19-04	MALE, 58 YEARS	PSYCHIATRY INPATIENT

Presentation:

Suresh, a 58-year-old farmer with chronic alcohol use disorder (drinking ~180 mL of country liquor daily for 25 years), was admitted following a road traffic accident. He sustained no major injuries. During the hospital stay, he developed Wernicke's encephalopathy on day 3 (confusion, lateral gaze palsy, ataxia), which was treated with parenteral thiamine.

Six weeks later, he is reviewed at psychiatry OPD by his wife. The acute encephalopathy has resolved. However, his wife says he cannot remember anything that happened after 2015. He does not remember the accident, does not recognise the treating doctor despite meeting him multiple times, and yesterday told his wife about a "fishing trip he went on last week", which never happened. He can hold a brief conversation and remember things from the distant past (his childhood, his children's names, farming knowledge) but cannot recall what he had for breakfast.

On examination: Alert, conversational. Behaves normally in the consultation. When asked about the past week, gives plausible but incorrect accounts. Insists he is correct. MMSE 22/30 (loses marks on orientation to time / recent events and 3-word recall).

Questions:

1. What syndrome is this? Distinguish it from dementia.
 2. Name and explain the three core cognitive features.
 3. What is confabulation, is it lying?
 4. What is the prognosis? What treatment options exist?
-

Diagnosis: Korsakoff's Syndrome (Chronic Wernicke-Korsakoff Syndrome)

Reasoning:

- Preceded by documented Wernicke's encephalopathy (treated with thiamine)
- Severe anterograde amnesia (cannot form new memories, does not recognise doctor)
- Retrograde amnesia (gap since approximately 2015)
- Confabulation (fabricated "fishing trip", plausible, fluent, believed by patient)
- Remote memory intact (childhood, family names, occupational knowledge)
- Alert and conversational, NOT demented in the global sense

Distinction from dementia:

- Dementia = global cognitive decline (multiple domains, attention, language, executive, memory, praxis)
- Korsakoff = SELECTIVE, anterograde memory grossly impaired; other domains relatively preserved
- Korsakoff patient can hold a normal conversation; demented patient cannot
- Korsakoff has profound amnesia with reasonable social facade

Three core cognitive features:

Anterograde amnesia Cannot form new declarative memories; every new event disappears within minutes

Retrograde amnesia Gap in memory for years before illness onset; recent past worse than remote (temporal gradient)

Confabulation Fills memory gaps with fabricated, but usually plausible, content

Confabulation, is it lying?

No. Confabulation is **unintentional and unconscious**. The patient genuinely believes the fabricated account. It arises because the memory system attempts to construct coherent narratives without access to accurate recent episodic memories. The patient has no awareness that the account is incorrect (anosognosia is also present, lack of insight into memory deficit). This distinguishes it from malingering.

Prognosis:

- 20–25% recover fully with sustained thiamine and alcohol abstinence
- 50% partial improvement (residual anterograde amnesia)
- 25% permanent, irreversible amnesia (mammillary body / thalamic damage too extensive)

Treatment:

- High-dose thiamine replacement (continue for months)
- Abstinence from alcohol, address alcohol dependence (OAMT, psychosocial)
- Reality orientation therapy (limited benefit for amnesia but helps adjustment)
- Occupational therapy for functional compensation
- Caregiver support and education
- Social support, cannot live independently if severe residual amnesia

Key Teaching Points:

- Wernicke's is acute and reversible; Korsakoff is chronic and largely irreversible, prevention (early thiamine) is everything
- The "temporal gradient" of retrograde amnesia: recent past is worse than remote (losing 2020–2023 more than losing 1990)
- Confabulation is not a character defect, it is a neurological symptom of a damaged memory system
- Thiamine BEFORE glucose, critical rule for any at-risk patient presenting to any emergency setting

VIGNETTE 05: The Young Man with Personality Change

PT-N19-05	MALE, 24 YEARS	PSYCHIATRY OPD

Presentation:

Arjun, a 24-year-old engineering student, is brought by his parents who are concerned about a personality change over the past 18 months. He was previously described as responsible, academically bright, and even-tempered. He now shows poor impulse control,

makes crude remarks in public, has dropped out of college, and spends hours rearranging objects on his desk.

He was initially seen by a psychiatrist who diagnosed schizophrenia and started risperidone 2 mg/day, with minimal improvement. Over the following months he developed a coarse tremor of both hands (worse with posture/intention), slurred speech, and difficulty swallowing. His LFTs were checked and found to be mildly elevated (ALT 78 U/L, AST 65 U/L).

On slit-lamp examination: **Golden-brown deposits at the periphery of the cornea in Descemet's membrane, bilaterally.**

Questions:

1. What is the diagnosis? What was the clinical trap?
 2. What is the significance of the slit-lamp finding?
 3. What investigations confirm the diagnosis?
 4. Outline treatment.
 5. What would happen if copper chelation is started without stopping risperidone?
-

Diagnosis: Wilson's Disease (Hepatolenticular Degeneration) with Neuropsychiatric Presentation

Clinical trap: Personality change + apparent psychosis in a young person → misdiagnosed as schizophrenia. Antipsychotics started without investigating cause. This is the cardinal diagnostic error in Wilson's disease.

Slit-lamp finding: Kayser-Fleischer (KF) rings, golden-brown copper deposits in Descemet's membrane of the cornea, at the periphery. Present in >99% of neurological Wilson's disease. KF rings are pathognomonic when found alongside neuropsychiatric or hepatic features.

Investigations:

TEST · EXPECTED FINDING

Serum ceruloplasmin **LOW** (<20 mg/dL)

24-hour urinary copper **HIGH** (>100 µg/day; >250 µg/day in symptomatic)

Liver biopsy Copper quantification >250 µg/g dry weight, gold standard

MRI brain T2 hyperintensity in lenticular nucleus, thalamus, brainstem

Slit-lamp KF rings (already confirmed)

Genetic testing ATP7B mutation on chromosome 13

Treatment:

- **Acute chelation:** D-penicillamine (penicillin derivative, chelates copper; SE: rash, nephrotoxicity, worsening neurological symptoms initially)
- **Alternative chelation:** Trientine (fewer side effects; preferred if neurological Wilson's)
- **Maintenance:** Zinc salts (block intestinal copper absorption; SE minimal)
- **Liver transplant:** Curative for hepatic disease; improves neurological disease; indicated in hepatic failure
- **Dietary:** Avoid copper-rich foods (shellfish, liver, nuts, chocolate)
- **Stop risperidone,** psychiatric symptoms should improve with copper chelation

Risperidone + chelation:

- D-penicillamine can initially worsen neurological symptoms (transient worsening in 20–50%, copper redistribution)
- Risperidone's EPS potential would compound this worsening
- Risperidone does not address the cause
- The psychiatric symptoms in Wilson's disease often improve substantially with copper chelation alone, antipsychotics may become unnecessary

Key Teaching Points:

- Wilson's disease is the great imitator in psychiatry, personality change, depression, OCD-like symptoms, psychosis in patients <40 years
- KF rings on slit-lamp in any young person with unexplained psychiatric + movement symptoms = Wilson's until proven otherwise
- Ceruloplasmin is the initial screen; 24h urine copper is the functional measure; liver biopsy is gold standard
- Never start antipsychotics in a young person without excluding Wilson's when movement disorder is also present

VIGNETTE 06: The Clever Conspiracy

PT-N19-06	MALE, 44 YEARS	INFECTIOUS DISEASES OPD

Presentation:

Rajesh, a 44-year-old HIV-positive lorry driver diagnosed 7 years ago, attends for his 6-monthly review. He is on tenofovir/lamivudine/dolutegravir (switched from efavirenz 1 year ago). Viral load is undetectable, CD4 count 520 cells/ μ L.

His wife accompanies him and discloses privately that he has stopped his medication 3 times in the past 4 months. When asked, Rajesh says he doesn't want to take medicine every day, that the tablets make him feel like a patient, that his employer will "find out" if he is seen at a clinic, and that his neighbour recently died of AIDS despite taking medicine, so "what's the point."

PHQ-9 score: 14 (moderate depression). He endorses low mood, anhedonia, poor sleep, hopelessness, and poor concentration for the past 3 months. He denies suicidal ideation.

Questions:

1. What are the barriers to ART adherence in this vignette?
 2. What is the relationship between his depression and non-adherence?
 3. How would you manage the depression in the context of HIV and dolutegravir therapy?
 4. What broader interventions improve adherence in this scenario?
-

Diagnosis: Moderate Depression (PHQ-9 = 14) with Multiple Adherence Barriers in HIV

Barriers to adherence:

CATEGORY · SPECIFIC BARRIER

Depression Hopelessness, anhedonia, poor concentration → passive pill non-adherence

Stigma Workplace stigma fear (employer finding out); internalised stigma (being "a patient")

Maladaptive health belief Neighbour died despite ART → treatment futility belief

Practical barrier Lorry driver lifestyle → irregular routine, away from home

Low health literacy May not fully understand undetectable = untransmittable

Depression-adherence bidirectional relationship:

- Untreated depression: OR 3.4 for ART non-adherence (meta-analysis)
- Non-adherence leads to viral rebound → CD4 decline → increased biological depressogenic burden (viral proteins, cytokines)
- Poor adherence → HIV progression → hopelessness → deeper depression
- Breaking this cycle requires treating depression as a **medical priority**, not a secondary concern

Management of depression:

- **Drug choice:** Sertraline or escitalopram, minimal CYP interactions with dolutegravir (INSTI) regimen

- Note: Dolutegravir has fewer drug interactions than efavirenz; SSRIs generally safe
- CBT (adapted) and Interpersonal Therapy (IPT), both have evidence in HIV depression
- Combined pharmacotherapy + psychotherapy > either alone
- Address hopelessness as a cognitive distortion (CBT frame): Challenge catastrophic belief ("medicine didn't work for my neighbour")
- PHQ-9 monitoring at 4, 8, 12 weeks

Broader adherence interventions:

- **Counselling:** Motivational interviewing for ambivalence; psychoeducation about U=U (Undetectable=Untransmittable)
- **Simplify regimen:** Already on once-daily FDC (tenofovir/lamivudine/dolutegravir), optimal
- **Practical aids:** Phone alarm reminders, weekly pill organiser
- **Disclosure support:** Explore fear of employer; occupational rights counselling (HIV confidentiality)
- **Peer support:** Connect with HIV support group, normalises experience
- **Long-acting injectable ART** (if available): Cabotegravir + rilpivirine monthly IM, removes daily pill burden entirely
- **Assess family support:** Wife is engaged, involve her constructively

Key Teaching Points:

- Adherence is never a willpower problem alone, it is multi-determined (biological, psychological, social)
 - Treating depression in HIV is a direct HIV management intervention, not a psychiatric add-on
 - U=U (Undetectable = Untransmittable) is a powerful counselling tool for motivation and stigma reduction
 - Stigma-driven non-adherence is common in occupations with high social visibility (lorry drivers, healthcare workers, teachers)
-

VIGNETTE 07: The Choreic College Student

PT-N19-07	FEMALE, 19 YEARS	NEUROLOGY REFERRAL TO PSYCHIATRY

Presentation:

Meghna, a 19-year-old first-year MBBS student, is referred by neurology. She presented 3 weeks ago with involuntary jerking movements of her arms and face, which started

suddenly after a sore throat 6 weeks prior. The movements are described as flowing, unpredictable, non-repetitive, and worse with stress.

On psychiatric assessment: She is noted to have significant emotional lability, crying without provocation, then laughing inappropriately. Her mother reports she has become obsessively concerned about cleanliness (washing hands 30–40 times daily) and is anxious about "contaminating" her family. These OCD symptoms began simultaneously with the movements.

Past medical history: Two prior episodes of tonsillitis treated with amoxicillin.

Investigations:

- ASO titre: 480 IU/mL (elevated; normal <200)
 - Anti-DNase B: Elevated
 - Throat culture: Group A beta-haemolytic Streptococcus
 - ECG: Normal (no PR prolongation, no carditis signs)
 - MRI brain: Normal
 - CBC and metabolic panel: Normal
 - ANA, anti-dsDNA: Negative (SLE excluded)
-

Questions:

1. What is the diagnosis?
 2. What is the mechanism linking streptococcal infection to psychiatric symptoms?
 3. How does this presentation differ from OCD due to other causes?
 4. Outline management.
-

Diagnosis: Sydenham's Chorea (with Psychiatric Manifestations, OCD and Emotional Lability)

Reasoning:

- Young patient post-streptococcal infection (elevated ASO titre, positive culture)
- Chorea with abrupt onset
- Associated psychiatric features: OCD-like symptoms and emotional lability
- MRI normal (not structural cause)
- SLE excluded (negative ANA, anti-dsDNA)
- This is part of Acute Rheumatic Fever (Jones criteria, chorea is a major criterion)

Mechanism, Molecular Mimicry:

- Group A streptococcal antigens cross-react with basal ganglia neuronal antigens (specifically, antibodies against streptococcal M protein cross-react with lysoganglioside

epitopes on striatal neurons)

- Antibody-mediated neuronal dysfunction in caudate and putamen
- Basal ganglia and frontostriatal circuit disruption → chorea (motor) + OCD/repetitive behaviours (cognitive-behavioural) + emotional lability
- This is the same mechanism proposed for PANDAS (Paediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections), a related entity

Distinction from primary OCD:

FEATURE	SYDENHAM'S/PANDAS OCD	PRIMARY OCD
Onset	Abrupt, explosive	Gradual, insidious
Preceding event	Streptococcal infection	Stress, developmental trigger
Motor symptoms	Chorea, tics present	None
Emotional lability	Prominent	Not characteristic
Streptococcal serology	Elevated	Normal
Course	Episodic (relapse with re-infection)	Chronic, continuous
Family history	Less prominent	Often present

Management:

INTERVENTION · DETAIL

Anti-streptococcal treatment Benzyl penicillin (10 days) to eradicate current infection

Secondary prophylaxis Benzathine penicillin 1.2 MU IM monthly for minimum 5 years (or until age 21), prevents rheumatic fever recurrence

Chorea treatment Usually self-limiting (resolves in 3–6 months); if severe: valproate or haloperidol

OCD treatment SSRI (fluoxetine) + ERP (Exposure and Response Prevention) therapy

Emotional lability Often resolves with chorea resolution; supportive counselling

Cardiology review Mandatory, exclude carditis (rheumatic fever's main morbidity)

Key Teaching Points:

- Sydenham's chorea = psychiatric + motor together; the OCD is not incidental, it is part of the same autoimmune process
- Molecular mimicry is the exam mechanism: Strep antibodies → cross-react with basal ganglia → frontostriatal circuit dysfunction → OCD + chorea

- Penicillin prophylaxis is mandatory, the single most important long-term intervention
- PANDAS is the related paediatric concept, episodic OCD / tics temporally related to streptococcal infections

VIGNETTE 08: The Sleepless Widower

****PT-N19-08**

MALE, 71 YEARS

PSYCHIATRY OPD**

Presentation:

Krishnamurthy, a 71-year-old retired schoolteacher and widower, presents with a 4-month history of deteriorating sleep. His daughter, who lives with him, reports that he talks, shouts, and thrashes about in bed, once falling out of bed and injuring his shoulder. He has vivid dreams, often of being chased, and appears to be "acting them out." He is distressed about this and has started sleeping on a mattress on the floor.

He also mentions that over the past 2 years, he has noticed his sense of smell is not as good as it used to be, and he has been constipated. Three months ago, he was noted by his GP to have mild resting tremor in his right hand.

On examination: Mild resting tremor right hand, subtle cogwheel rigidity right arm, gait mildly reduced arm swing on right. MoCA: 26/30 (loses 2 marks on visuospatial, 1 on delayed recall, 1 on fluency).

Polysomnography: **Absence of normal REM atonia; complex movements correlating with dream content during REM sleep, confirms RBD.**

Questions:

1. What is the sleep disorder? What is its clinical and prognostic significance?
2. What is the Braak staging concept and where does this patient sit?
3. What other early features of neurodegeneration are present in this vignette?
4. How would you counsel this patient and manage his sleep disorder?

Diagnosis: REM Sleep Behaviour Disorder (RBD) in the context of emerging Parkinson's Disease

RBD, Clinical and Prognostic Significance:

- In RBD, normal REM sleep atonia is absent → skeletal muscles remain active → patient acts out dream content (punching, kicking, shouting, falling)
- **Prodromal marker of synucleinopathy:** RBD is now recognised as one of the earliest and most specific prodromal markers of Parkinson's disease (and DLB and MSA)

- Longitudinal studies show: **80–90% of idiopathic RBD patients will develop a defined synucleinopathy within 10–14 years**
- In this patient, he already has tremor and cogwheel rigidity, he has crossed from prodromal to early PD

Braak Staging:

- Braak et al. mapped the ascending spread of alpha-synuclein pathology in PD:
- **Stages 1–2 (medulla, olfactory bulb):** Anosmia, constipation, RBD, non-motor, preclinical
- **Stages 3–4 (substantia nigra pars compacta):** Motor symptoms emerge (tremor, rigidity, bradykinesia)
- **Stages 5–6 (neocortex):** Cognitive and psychiatric symptoms (dementia, psychosis)
- This patient has: Anosmia (Stage 1–2), constipation (Stage 1–2), RBD (Stage 1–2), and now tremor / rigidity (Stage 3–4)
- He is at **Braak Stage 3–4** clinically, motor symptoms have just emerged

Other prodromal features present:

1. **Hyposmia (anosmia)**, one of earliest PD prodromal markers; olfactory bulb involvement (Braak Stage 1)
2. **Constipation**, autonomic dysfunction; enteric nervous system Lewy pathology (Braak Stage 1–2)
3. **RBD**, loss of REM atonia (Braak Stage 1–2; locus coeruleus + pedunculopontine nucleus)
4. **Cognitive changes on MoCA**, visuospatial and fluency (Braak Stage 3–4 or early cortical involvement)

Counselling and Management:

ASPECT · CONTENT

Diagnosis disclosure RBD confirmed; this is an early marker of neurodegeneration; full PD assessment needed

Prognosis (honest) High probability of developing PD; monitoring will allow early intervention

Neuroprotection No proven disease-modifying treatment; aerobic exercise may be neuroprotective

Safety measures Remove sharp objects from bedroom, bed rail padding, consider bed alarm, floor mattress (already using)

RBD treatment Clonazepam 0.25–0.5 mg at night (first-line, reduces motor activity during REM); Melatonin 3–12 mg (safer in elderly; emerging evidence)

Bed partner safety Daughter should not sleep next to him; risk of inadvertent injury

Follow-up Neurology for PD monitoring; annual cognitive assessment

Key Teaching Points:

- RBD is a **prodromal biomarker**, identifying it gives a window to monitor and potentially intervene before severe PD develops
 - The triad of anosmia + constipation + RBD = very high predictive value for synucleinopathy
 - Braak staging explains why psychiatric symptoms can appear long before or long after motor symptoms, depends on which circuits are involved
 - Clonazepam + melatonin for RBD; avoid other sedating agents that suppress REM (benzodiazepines broadly suppress REM)
-

VIGNETTE 09: The Brilliant Confused

PT-N19-09	FEMALE, 35 YEARS	NEUROLOGY WARD → PSYCHIATRY LIAISON

Presentation:

Sujata, a 35-year-old software engineer with known SLE (diagnosed 6 years ago, on hydroxychloroquine and low-dose prednisolone 7.5 mg/day), is admitted with a 3-day history of acute confusion, visual hallucinations (seeing "small children in the room"), and aggressive behaviour towards her husband.

Her prednisolone was increased to 60 mg/day by her rheumatologist 10 days ago following a flare (arthritis, pleuritis).

On examination: Alert but confused and disoriented in time and place. Responds to visual hallucinations. Blood pressure 156/98. Temperature 37.4°C. No meningism. Skin: butterfly rash present.

Investigations:

- CBC: Haemoglobin 9.8 g/dL, WBC 3200/mm³ (lymphopenia), platelets 98,000/mm³
- ANA: Positive (1:640)
- Anti-dsDNA: Markedly elevated (1:1280; previously 1:160)
- Complement: C3 low, C4 low
- CSF: 4 cells/mm³, protein 38 mg/dL, glucose normal; no organisms; ANA and anti-dsDNA sent from CSF

- MRI brain: Small T2/FLAIR hyperintensities in periventricular white matter; no cortical ribboning; no mass lesion
- EEG: Diffuse slowing, no epileptiform discharges

Questions:

1. What are the two competing diagnoses and how do you distinguish them?
2. What serological findings support NPSLE?
3. How does the rheumatology team's recent decision affect the picture?
4. How would you manage?

Competing Diagnoses:

1. NPSLE (Neuropsychiatric SLE, acute confusional state with psychosis)
2. Steroid-induced psychosis (high-dose prednisolone 60 mg/day)

Distinguishing features:

FEATURE	NPSLE	STEROID PSYCHOSIS
Prednisolone dose	Usually lower; disease drives symptoms	High dose (>40 mg/day) , dose-dependent
Onset relation to steroids	Not correlated with dose change	Occurs within days-2 weeks of starting/increasing
Serological activity	High anti-dsDNA, low complement	Normal or stable serology
Disease flare markers	Elevated anti-dsDNA (1:1280), low C3/C4, lymphopenia, thrombocytopenia	No change in serology
CSF	May show pleocytosis	Normal
MRI	NPSLE changes (white matter lesions)	Often normal
Response to steroid reduction	Worsens (underlying disease)	Improves

In this case:

- Anti-dsDNA markedly elevated (4× increase from baseline)
- Complement low (active SLE consumption)
- Lymphopenia, thrombocytopenia (active SLE features)
- White matter lesions on MRI (consistent with NPSLE)
- **However:** Prednisolone was increased to 60 mg/day 10 days ago, steroid psychosis is also possible

- **Most likely: BOTH are contributing**, active NPSLE requiring immunosuppression, PLUS steroid effects at 60 mg

Management:

STEP · ACTION

Immunosuppression Maintain/optimise, active NPSLE requires treatment; add pulse IV methylprednisolone 1g × 3 days for acute CNS flare

Steroid taper After pulse therapy, taper oral prednisolone to lowest effective dose (try <20 mg/day); this addresses steroid-induced component

Add steroid-sparing Azathioprine or mycophenolate mofetil, allows prednisolone reduction while maintaining SLE control

Antipsychotic (short-term) Low-dose haloperidol or quetiapine for acute psychosis, titrate based on response

Safety One-to-one nursing; fall prevention; monitor BP (SLE + high-dose steroid = hypertensive risk)

Hydroxychloroquine Continue, protective against NPSLE flares

Follow-up serology Anti-dsDNA and complement at 4–6 weeks to assess response

Key Teaching Points:

- NPSLE vs steroid psychosis: the serology tells the story, elevated anti-dsDNA + low complement = active SLE = treat the disease, not just the symptom
- Both can coexist (this is the most realistic clinical scenario when a patient is on high-dose steroids for an active flare)
- The management paradox: You need steroids to treat NPSLE, but steroids may worsen the psychosis, solution is pulse dosing then taper with steroid-sparing agents
- Hydroxychloroquine has an independent CNS protective effect in SLE, never stop it during a flare

VIGNETTE 10: The Rapid Decline

PT-N19-10	MALE, 67 YEARS	NEUROLOGY → PSYCHIATRY LIAISON

Presentation:

Mohandas, a 67-year-old retired civil engineer with no prior psychiatric or neurological history, is referred urgently by neurology. Over the past 9 weeks he has developed rapidly progressive cognitive decline. His wife says he was entirely well 2 months ago, he was driving, managing the household finances, and playing chess regularly.

He now cannot recognise his grandchildren, is disoriented in his own home, cannot hold a conversation beyond a few seconds, and has developed jerking movements of his arms that are triggered by sudden sounds or touch. He also has poor coordination and an unsteady gait.

On examination: GCS 12/15. Disoriented in time, place, person. Stimulus-sensitive myoclonus. Cerebellar signs (dysdiadochokinesia, ataxic gait). Bilateral Babinski response. No fever. No meningism.

Investigations:

- CBC, metabolic panel: Normal
- Thyroid function: Normal
- Autoimmune screen (ANA, ANCA, anti-dsDNA): Negative
- CSF: 2 cells/mm³, protein 44 mg/dL, glucose normal; Gram stain negative; AFB negative
- **CSF 14-3-3 protein: Positive**
- **MRI brain (DWI sequence): Cortical ribboning in right frontal and parietal cortex; bilateral caudate and putamen hyperintensity**
- **EEG: Biphasic periodic sharp wave complexes at approximately 1.5 Hz, generalised**
- **CSF RT-QuIC: Positive (reported 5 days later)**

Questions:

1. What is the diagnosis? Justify using all investigation findings.
2. What is the significance of each investigation result?
3. What is the differential diagnosis and how is each excluded?
4. What is the prognosis? Is there any treatment?

Diagnosis: Sporadic Creutzfeldt-Jakob Disease (sCJD)

Justification:

INVESTIGATION	FINDING	SIGNIFICANCE
MRI DWI	Cortical ribboning + bilateral caudate/putamen hyperintensity	Most sensitive imaging finding in sCJD; DWI positivity >MRI T2 in early disease

INVESTIGATION	FINDING	SIGNIFICANCE
EEG	PSWC at 1.5 Hz	Periodic sharp wave complexes, present in 67% of sCJD; highly characteristic
CSF 14-3-3	Positive	Sensitive marker of rapid neuronal death; not specific (also in encephalitis, stroke, paraneoplastic), but in context highly supportive
CSF RT-QuIC	Positive	Most specific test for sCJD; gold standard non-invasive diagnostic
Clinical	Rapidly progressive dementia + myoclonus + cerebellar + pyramidal signs = classic tetrad	Meets "probable sCJD" criteria (WHO)

Clinical features met (WHO Probable sCJD criteria):

- Rapidly progressive dementia (9 weeks, well within <2 years)
- 2 of 4 features: ✓ Myoclonus, ✓ cerebellar, ✓ pyramidal signs (bilateral Babinski)
- Supportive: EEG PSWC, positive 14-3-3
- Confirmatory: Positive RT-QuIC

Differential diagnosis exclusion:

DIFFERENTIAL · EXCLUSION REASON

Autoimmune encephalitis (anti-NMDAR, LGI1) No pleocytosis; negative autoimmune screen; RT-QuIC positive; EEG shows PSWC not delta brush

Hashimoto's encephalopathy Anti-TPO not tested (send) but RT-QuIC positive shifts probability strongly

Viral encephalitis (HSV) CSF normal (HSV encephalitis shows pleocytosis); MRI shows ribboning not temporal lobe involvement

Vascular dementia Cannot explain 9-week course or myoclonus

Paraneoplastic encephalitis Negative autoimmune screen; RT-QuIC positive; send anti-Hu, anti-Yo, anti-Ri as belt-and-suspenders

Variant CJD Wrong demographics (elderly M); no pulvinar sign; PSWC present (vCJD does NOT have PSWC); no beef exposure history

Prognosis and Treatment:

- **Invariably fatal**, median survival from symptom onset is **4–6 months** (median 4 months for sCJD)
 - **No disease-modifying treatment exists**, no antiviral, antiprion drug has proven efficacy in human trials
 - Quinacrine, pentosan polysulfate, doxycycline, all trialled, all failed in RCTs
 - **Management is palliative:**
 - Symptomatic treatment of myoclonus (clonazepam, valproate)
 - Antipsychotics for agitation/psychosis (low dose)
 - Palliative care team involvement early
 - Family counselling and bereavement support
 - Inform family: Not infectious via normal contact; blood and CSF are infectious materials
 - Notifiable disease in most countries
-

Key Teaching Points:

- CJD is the fastest dementia, 9 weeks to this degree of impairment is virtually diagnostic in itself
 - RT-QuIC is now the standard of care for CSF testing in suspected CJD, more specific than 14-3-3
 - EEG PSWC differentiates sCJD from vCJD (vCJD does NOT show PSWC, use pulvinar sign for vCJD)
 - DWI MRI is the most sensitive imaging modality, must specifically request DWI sequence
 - Early palliative care involvement and family counselling are the most important clinical actions once diagnosis is confirmed
-

VIGNETTE 11: The Angry Choreographer

****PT-N19-11**

MALE, 42 YEARS

PSYCHIATRY OPD**

Presentation:

Dinesh, a 42-year-old dance teacher, is self-referred to psychiatry. He has been having increasing difficulty with his temper over the past 3 years, explosive outbursts at students and family members, which feel "out of character." He has also noticed that he drops objects, trips occasionally, and his handwriting has changed.

His father died in a mental institution at age 55 after "going mad and not being able to walk." His 38-year-old brother was recently diagnosed with Huntington's disease.

On examination: Alert, oriented, cooperative but tangential. Mild choreiform movements of fingers and mouth (subtle, present on observation). MMSE 27 / 30 (loses marks on serial 7s and drawing). Reflexes normal. Speech slightly dysarthric.

He says he does not want genetic testing because "I can't deal with knowing."

Questions:

1. What is the clinical diagnosis and how is it established?
 2. He refuses genetic testing. Is his right to refuse valid? How do you handle this ethically?
 3. His wife asks you privately to tell her his result "if you do test him." How do you respond?
 4. He has a 16-year-old son. Should the son be tested?
 5. What is the psychiatric management for this stage of HD?
-

Diagnosis: Huntington's Disease (clinically probable, pending genetic confirmation)

Clinical basis:

- Age 42, male, within typical HD onset range
- Family history: Father (probable HD, psychiatric + motor decline), brother (confirmed HD)
- Autosomal dominant, 50% risk to Dinesh; brother's confirmed diagnosis makes Dinesh's risk 50% from first principles
- Clinical signs: Choreiform movements (subtle, early), dysarthria, personality change / irritability (often first psychiatric symptom), cognitive decline on MMSE (executive domain)
- **Genetic confirmation:** CAG repeat analysis on HTT gene, but patient is refusing

Ethical management of refusal to test:

- **His refusal is COMPLETELY VALID**, the right NOT to know is as fundamental as the right to know (HDSA guidelines, genetic testing ethics literature)
- The psychiatrist's role: Respect autonomy; explore his fears (is it fear of a positive result? Fear of what he'll do with the information? Financial concerns?); psychoeducation; leave the door open
- Do NOT coerce testing
- Even without genetic confirmation, clinical diagnosis can be made and management initiated
- Genetic testing adds certainty and facilitates family planning but is not mandatory for management

Wife's request for private disclosure:

- **Cannot be done**, Dinesh's genetic result is his private medical information
- His wife's desire to know is understandable but does not override his right to confidentiality
- Response to wife: "I understand your concern and it must be very difficult. However, I am not able to share any medical information about your husband without his consent. If he changes his mind about testing or sharing, he can choose to involve you. I am happy to support both of you through this."
- If Dinesh tests and gets a positive result and consents to disclosure to wife, then share

16-year-old son, should he be tested?

- **No, not recommended**
- Reasons:
 - **Cannot give informed consent**, a minor cannot fully appreciate the lifelong implications of a positive result
 - **No medical benefit**, there is no treatment that would change management in a healthy adolescent
 - **Right not to know must be preserved** until adulthood (at 18, he can make an informed autonomous choice)
 - Psychological harm from a positive result in adolescence (identity formation, educational decisions, depression, suicidality) may be significant with no counterbalancing benefit
 - Exception: If the son has symptoms suggestive of juvenile HD (rigidity, cognitive decline, school failure), then symptomatic testing is warranted

Psychiatric management of early HD:

- **Irritability (presenting complaint):** SSRIs (sertraline 50–100 mg), first-line; valproate if severe
- **Depression screening:** PHQ-9; start SSRI prophylactically given high suicide risk
- **Suicide risk assessment:** First post-diagnosis period is highest risk, establish safety plan
- **Cognitive changes:** Occupational assessment; teaching adaptations (cognitive strategies)
- **Family therapy:** Wife, son, psychoeducation about HD, genetic implications, support resources
- **Genetic counselling referral:** For wife and son to understand their situation
- **Chorea:** Not yet severe enough to treat; monitor; tetrabenazine if becomes functionally limiting
- **Support groups:** HD Association of India or international HDSA resources

Key Teaching Points:

- The right not to know genetic information is a fundamental ethical principle, as valid as the right to know
- Confidentiality cannot be broken for a family member who wants results, not even a spouse
- Children: Predictive testing not recommended, preserve their right to autonomous decision-making at adulthood
- HD has two clinical triggers for suicide: immediately after diagnosis and when motor symptoms begin (loss of independence), monitor both

VIGNETTE 12: The Man Who Forgot to Be Sad

****PT-N19-12**

MALE, 74 YEARS

GERIATRIC PSYCHIATRY OPD**

Presentation:

Subramanian, a 74-year-old widower with a 9-year history of Parkinson's disease, attends with his son. He is on levodopa/carbidopa 250/25 mg QID, entacapone 200 mg QID, and rivastigmine patch 9.6 mg/24h (started 18 months ago for PD dementia).

His son is worried because "Appa doesn't do anything anymore." He sits all day, has stopped watching cricket (which he loved), stopped calling friends, and eats only when reminded. When asked, he says he feels "fine" and is "not sad." He denies anhedonia when asked directly. However, he will not initiate any activity spontaneously.

His son had also noted that last week, he started crying suddenly in the middle of dinner for about 2 minutes, then stopped abruptly and resumed eating normally. "It was like he flipped a switch," the son says.

On examination: MMSE 18/30 (consistent with PD dementia). Bradykinesia and rigidity present. Hypomimic face. Flat affect on examination. No expressed sadness or dysphoria. No endorsement of hopelessness or suicidality.

Questions:

1. Name the two distinct neuropsychiatric phenomena in this vignette and distinguish them.
2. What is the key clinical question that separates apathy from depression in this case?
3. What does the dinner episode represent and how is it treated?
4. What is the management for apathy in PD dementia?

Diagnosis:

1. **Apathy** (reduced motivation, no negative affect, no distress)

2. Pseudobulbar Affect / PBA (involuntary crying episode, incongruent with emotional state)

Distinguishing apathy from depression:

FEATURE	APATHY (THIS PATIENT)	DEPRESSION
Negative affect (sadness, hopelessness)	Absent, "feels fine"	Present, often prominent
Distress about the state	Absent, no awareness of problem	Present, patient is troubled by it
Anhedonia	Apparent to observer; denied by patient	Endorsed by patient
Motivation	Reduced, will not initiate anything	Reduced but often with subjective effort that fails
Social withdrawal	Present	Present
Cognitive element	Often related to frontal-executive dysfunction	Rumination, guilt, worthlessness
Endorsed symptom	None, patient says "fine"	Patient reports feeling sad/empty

Key clinical question: "Does this patient feel bad about not doing things, or do they simply not care either way?"

- Depressed patient: "I want to watch cricket but I can't bring myself to, I feel terrible about it"
- Apathetic patient: "Cricket? I don't feel like it. I don't know. It doesn't bother me."

The dinner episode, Pseudobulbar Affect:

- Abrupt onset, sudden offset, 2-minute episode of crying
- Not triggered by sad thought or emotion (mid-dinner, normal context)
- Incongruent with mood state (resumes eating normally after)
- Son's description ("like flipping a switch") is classic
- Mechanism: PD cortical Lewy body pathology disrupts **corticobulbar tracts** → loss of prefrontal inhibition of brainstem emotional expression circuits
- Treatment: **SSRIs (citalopram or fluoxetine)**, rapid response, often within days; dextromethorphan/quinidine (Nuedexta), FDA-approved for PBA but not available in India

Management of apathy in PD dementia:

- **Optimise dopaminergic therapy**, dopamine is the neurotransmitter of motivation; motor optimisation helps apathy

- **Rivastigmine** (already on), cholinesterase inhibitor has some evidence for apathy in PDD/DLB
 - **Methylphenidate**, small trials show benefit for apathy in PD; off-label
 - **Structured daily schedule**, caregiver-assisted; routine reduces the barrier of initiation
 - **Physical exercise**, externally motivated; improves mood and motivation in PD
 - **Occupational therapy**, goal-setting, meaningful activity identification
 - No strong evidence for SSRIs for apathy in PD (SSRIs treat depression, not pure apathy; may even slightly worsen apathy in some by reducing dopamine turnover)
 - Key distinction: Do NOT give antidepressants for apathy without depression, they are different disorders with different neurobiology
-

Key Teaching Points:

- Apathy ≠ Depression: The most clinically important distinction in PD psychiatry. Misdiagnosing apathy as depression and starting SSRIs will not help and wastes time
 - PBA is common in PD dementia, the "flipping switch" description from a carer is almost diagnostic
 - PBA responds to SSRIs rapidly (days), unlike antidepressant effects on mood (weeks)
 - Rivastigmine treats cognition AND has a small but real benefit for apathy in PDD, it is doing double duty in this patient
-
-

KEY INSIGHT

Notebook complete: NB-19, HIV, Parkinson's & Other Neuropsychiatry | 6 files generated | Paper IV MD Psychiatry Exit Examination

Pharmacology Recent Advances

Paper IV · Neurology, Medicine & Recent Advances. Six study modes, from notes to quick review.

Study Notes

Comprehensive Study Notes

SECTION 1: NEWER ANTIDEPRESSANTS

1.1 Vortioxetine (Multimodal Antidepressant)

Class: Serotonin modulator and stimulator (SMS)

Brand: Trintellix

Approved: FDA 2013 for Major Depressive Disorder (MDD)

MECHANISM OF ACTION: THE MULTIMODAL PROFILE

Vortioxetine is unique because it acts at multiple serotonin receptor subtypes simultaneously, not just as a reuptake inhibitor.

TARGET	ACTION	EFFECT
SERT	Inhibition	Increases synaptic serotonin
5-HT1A	Agonist	Autoreceptor desensitization, anxiolysis
5-HT1B	Partial agonist	Modulates serotonin release
5-HT3	Antagonist	Reduces nausea, enhances ACh/NE/DA/GABA
5-HT7	Antagonist	Circadian rhythm modulation, cognitive effects
5-HT1D	Antagonist	Modulates serotonin/NE release

EXAM PEARL

Key exam point: The 5-HT3 antagonism is why vortioxetine has fewer GI side effects and may enhance cognitive function (5-HT3 blockade increases ACh in frontal cortex).

PHARMACOKINETICS

- Oral bioavailability: ~75%
- Protein binding: >98%
- Metabolism: CYP2D6 primary; also CYP3A4/5, CYP2C19

- Half-life: ~66 hours (allows once-daily dosing)
- Dose: 5–20 mg / day
- No dose adjustment for renal impairment; caution in hepatic impairment

CLINICAL EVIDENCE

- **FOCUS trial** and **CONNECT trial**: Demonstrated cognitive benefits beyond mood improvement
- Meta-analyses show moderate superiority over placebo on MADRS
- Cognitive benefits (processing speed, executive function) shown in multiple RCTs
- **VORTEX study**: Comparable efficacy to duloxetine with better tolerability

DISTINGUISHING FEATURES

- **Cognitive benefits**, superior to placebo and comparable / better than other ADs on neurocognition
- **Sexual dysfunction**, significantly lower rates than SSRIs/SNRIs (~25% vs ~60%)
- **Weight neutral**, minimal weight gain
- No significant QTc prolongation
- No discontinuation syndrome (long half-life)

SIDE EFFECTS

- Nausea (most common, dose-dependent), usually transient
- Constipation, vomiting
- Vivid dreams at higher doses
- Pruritus (itching), unique to vortioxetine, mechanism unclear

DOSE TITRATION STRATEGY

- Start 5–10 mg / day
- Increase to 20 mg after 2–4 weeks if tolerated
- CYP2D6 poor metabolizers: max 10 mg / day
- Strong CYP2D6 inhibitors (paroxetine, fluoxetine): halve the dose

1.2 Vilazodone

Class: Serotonin partial agonist and reuptake inhibitor (SPARI)

Brand: Viibryd

Approved: FDA 2011 for MDD

MECHANISM

- **SERT inhibitor** (like SSRIs)

- **5-HT1A partial agonist** (like buspirone)
- The 5-HT1A partial agonism may explain faster onset and reduced anxiety/insomnia at initiation

PHARMACOKINETICS

- Must be taken **with food** (bioavailability increases 147–160% with food)
- Half-life: ~25 hours
- CYP3A4 metabolism
- Dose: 10 mg x 7 days → 20 mg x 7 days → 40 mg maintenance

CLINICAL PROFILE

- Comparable efficacy to SSRIs on HAM-D-17 and MADRS
- Lower rates of sexual dysfunction compared to SSRIs
- Lower rates of weight gain
- Nausea and diarrhea common (GI adverse effects)

KEY DIFFERENTIATOR FROM VORTIOXETINE

- Vilazodone: SPARI (SERT + 5-HT1A partial agonist)
- Vortioxetine: SMS (SERT + multiple 5-HT receptor modulation)
- Vilazodone has NO 5-HT3 antagonism, 5-HT7 antagonism
- Vilazodone **REQUIRES** food for absorption

1.3 Esketamine / Intranasal Ketamine

BACKGROUND

Ketamine (a racemic mixture) has been used off-label for treatment-resistant depression (TRD) since ~2000. Esketamine is the S-enantiomer, more potent at NMDA receptors.

Brand: Spravato (intranasal esketamine)

FDA Approval: 2019 for TRD; 2020 for MDD with acute suicidal ideation or behavior (MDSI)

MECHANISM OF ACTION

Primary: NMDA (N-methyl-D-aspartate) receptor antagonism

- Blocks glutamate binding at NMDA receptors
- Rapid disinhibition of downstream glutamatergic activity
- Surge of AMPA receptor activation → BDNF release → synaptic plasticogenesis

The AMPA surge hypothesis:

Additional mechanisms:

- Opioid receptor modulation (controversial, recent data suggests partial role)
- GABA-A modulation
- HCN1 channel blockade (explains analgesic effects)

REMS (RISK EVALUATION AND MITIGATION STRATEGY)

KEY INSIGHT

Critical exam fact: Esketamine has a REMS program, one of few psychiatric drugs requiring this.

REMS requirements:

1. **Only dispensed in certified healthcare settings**, not at pharmacy
2. Patient must be monitored for **2 hours** after each administration
3. Monitoring for: dissociation, sedation, blood pressure changes, abuse
4. Patient cannot drive on day of administration
5. Healthcare setting must enroll in REMS program
6. ETASU (Elements To Assure Safe Use) components

ADMINISTRATION PROTOCOL

- **Intranasal** delivery (84 mg device = 2 devices × 28 mg each)
- Doses: 56 mg or 84 mg
- **Induction phase:** Twice weekly for 4 weeks
- **Maintenance phase 1:** Once weekly for 4 weeks
- **Maintenance phase 2:** Once weekly or every 2 weeks

CLINICAL EVIDENCE

- **TRANSFORM-2 trial:** Significant improvement in MADRS vs placebo intranasal + standard-of-care AD
- **SUSTAIN-1 trial:** Maintenance of remission, reduced relapse rates
- Onset of action: Within hours to days (vs weeks for conventional ADs)

SIDE EFFECTS

SIDE EFFECT · FREQUENCY

Dissociation Very common (>50%)

Dizziness Common

Nausea/vomiting Common

Hypertension Common

Sedation Common

Dysgeusia (altered taste) Common

CONTRAINDICATIONS

- Aneurysmal vascular disease (risk of BP spikes)
- Arteriovenous malformation
- History of intracerebral hemorrhage
- Current psychosis (worsens dissociation)
- Hypersensitivity to ketamine / esketamine

KETAMINE VS ESKETAMINE

FEATURE	RACEMIC KETAMINE IV	ESKETAMINE INTRANASAL
Route	IV infusion	Intranasal
FDA approval	No (off-label)	Yes (TRD, MDSI)
REMS	No	Yes
Setting	Ketamine clinics	Certified settings
Cost	Lower	Higher
Evidence	Extensive, replicated	RCTs available
Bioavailability	~100% (IV)	~48% (intranasal)

1.4 Brexanolone (Postpartum Depression)

Brand: Zulresso

FDA Approval: 2019, first drug specifically approved for postpartum depression (PPD)

Class: Neuroactive steroid / GABA-A receptor positive allosteric modulator (PAM)

MECHANISM

The peripartum hormone crash:

- During pregnancy: allopregnanolone (progesterone metabolite) levels rise dramatically
- After delivery: abrupt fall → triggers PPD in vulnerable individuals
- Brexanolone = synthetic allopregnanolone

Mechanism: Positive allosteric modulation of both synaptic and extrasynaptic GABA-A receptors

- Synaptic GABA-A ($\gamma 2$ -containing): phasic inhibition

- Extrasynaptic GABA-A (δ -containing): tonic inhibition, critical for brexanolone's unique mechanism

CLINICAL FEATURES

- Continuous IV infusion over **60 hours** (2.5 days)
- Administered in certified healthcare facility (REMS program)
- Rapid onset: significant improvement within 24–48 hours
- Sustained effect: response maintained at 30-day follow-up

REMS PROGRAM

- Risk of excessive sedation and sudden loss of consciousness
- Monitor oxygen saturation continuously
- Patient must be accompanied home

LIMITATIONS

- IV only, impractical for widespread use
- Cost: ~\$34,000 per treatment course
- **Zuranolone** (oral formulation) now available, FDA approved 2023, first oral neuroactive steroid for MDD and PPD

Zuranolone (Zurzuvae):

- Oral, 30 mg or 50 mg nightly for 14 days
- Same GABA-A PAM mechanism
- Does NOT require REMS
- First oral neuroactive steroid approved

1.5 Dextromethorphan-Bupropion (Auvelity)

Brand: Auvelity

FDA Approval: 2022 for MDD, first new MDD mechanism in decades

COMPONENTS

1. **Dextromethorphan (DXM):** Uncompetitive NMDA antagonist + sigma-1 receptor agonist
2. **Bupropion:** CYP2D6 inhibitor (increases DXM levels) + NDRI

WHY THE COMBINATION?

- Dextromethorphan alone is rapidly metabolized by CYP2D6 (extensive metabolizers)
- Bupropion inhibits CYP2D6 → increases DXM levels 8-fold → therapeutic concentrations achieved

- Bupropion also contributes antidepressant activity independently

MECHANISM

- NMDA antagonism → similar to ketamine pathway (AMPA surge, BDNF, synaptogenesis)
- Sigma-1 agonism → neuroprotection, neuroplasticity
- NDRI component → dopaminergic/noradrenergic antidepressant effect

CLINICAL EVIDENCE

- **GEMINI trial:** 45 mg/105 mg twice daily significantly improved HAM-D-17 at week 6 vs placebo
- Faster onset than typical ADs (significant benefit by week 1)
- Response rates: ~54% vs ~34% placebo

DOSING

- Start: 45 mg DXM/105 mg bupropion once daily for 3 days
- Increase to twice daily thereafter

SIDE EFFECTS

- Dizziness, headache, diarrhea, somnolence
- Risk of dissociation (lower than esketamine)
- No REMS required
- Abuse potential of DXM, schedule uncontrolled currently

1.6 Gepirone (Exxua)

Class: 5-HT_{1A} partial agonist (azapirone, like buspirone)

FDA Approval: 2023 for MDD (after multiple prior rejections)

MECHANISM

- Selective 5-HT_{1A} partial agonist, no SERT inhibition
- Pre-synaptic autoreceptor agonism → anxiolytic
- Post-synaptic 5-HT_{1A} agonism → antidepressant

KEY FEATURES

- No sexual dysfunction
- No weight gain
- No discontinuation syndrome
- **Extended-release formulation**, once daily
- Absence of significant drug interactions compared to SSRIs

CLINICAL EVIDENCE

- Multiple trials showing efficacy in MDD
- Delayed approval due to concerns about effect size consistency
- Approved for patients who require antidepressant therapy without sexual side effects

SECTION 2: NEWER ANTIPSYCHOTICS

2.1 Lumateperone (Caplyta)

FDA Approval: 2019 for schizophrenia; 2021 for bipolar depression (both I and II)

Mechanism: Truly novel, simultaneous modulator of dopamine, serotonin, and glutamate

MECHANISM OF ACTION

SYSTEM · EFFECT

D1 receptor Agonist/partial agonist (prefrontal cortex)

D2 receptor Pre-synaptic agonist; post-synaptic antagonist

5-HT2A Antagonist

SERT Inhibition

Glutamate Reduces NR2B-containing NMDA receptor phosphorylation

KEY INSIGHT

The key novelty: Lumateperone acts at D1 as a stimulator (unlike typical/atypical APs that block D1) and simultaneously modulates glutamate via NMDA NR2B subunit. This may explain the cognitive-sparing and mood-stabilizing properties.

PHARMACOKINETICS

- Dose: 42 mg once daily (at bedtime with or without food)
- Half-life: ~18 hours
- CYP3A4 primary metabolism
- No dose titration required

CLINICAL PROFILE

- **Minimal weight gain**, weight-neutral in trials
- **Minimal metabolic effects**, no significant glucose/lipid changes
- **Low EPS**, very low extrapyramidal burden
- **Low sedation** at therapeutic doses

- **Prolactin-sparing**, does not raise prolactin

UNIQUE INDICATION: BIPOLAR DEPRESSION

- One of few antipsychotics with evidence for BOTH schizophrenia AND bipolar depression
 - Effective in bipolar I and bipolar II depression (most drugs only approved for bipolar I)
-

2.2 Pimavanserin (Nuplazid)

FDA Approval: 2016, first drug approved specifically for Parkinson's Disease Psychosis (PDP)

Class: 5-HT_{2A} inverse agonist/antagonist; 5-HT_{2C} inverse agonist

WHY PIMAVANSERIN FOR PDP?

Traditional antipsychotics block D₂ receptors. In Parkinson's, dopaminergic pathways are already depleted, D₂ blockade worsens motor symptoms catastrophically.

Pimavanserin:

- **No D₂ binding**, does not worsen motor symptoms
- **Selective 5-HT_{2A/2C} inverse agonism**, reduces psychotic symptoms via serotonergic pathway

MECHANISM

- Inverse agonist at 5-HT_{2A}, constitutively active receptors are silenced even without serotonin
- Different from antagonist: reduces basal activity below baseline, not just blocks incoming signal

CLINICAL EVIDENCE

- **ACP-103-020 trial:** Significant reduction in SAPS-PD (Scale for Assessment of Positive Symptoms in PDP)
- Improved neuropsychiatric inventory (NPI) scores
- No worsening of UPDRS motor scores

LIMITATIONS AND SAFETY

- **FDA Black Box Warning:** Increased mortality in elderly with dementia-related psychosis
- QTc prolongation, avoid with other QTc-prolonging agents
- Dose: 34 mg once daily
- **No dose titration** required

EXTENDED USE

- Investigated for Alzheimer's Disease Agitation (ADVANCE trial, negative primary endpoint but secondary benefits)
- Combination with citalopram studied for dementia-related psychosis

2.3 Cariprazine (Reagila/Vraylar)

FDA Approval: 2015 for schizophrenia and bipolar I disorder (mania and depression)

Class: Partial agonist at D2, D3, and 5-HT1A; antagonist at 5-HT2A, 5-HT2B

THE D3 DISTINCTION

This is the defining feature of cariprazine.

DRUG	D2	D3
Aripiprazole	Partial agonist	Partial agonist (less selective)
Brexipiprazole	Partial agonist	Less selective
Cariprazine	Partial agonist	High-affinity partial agonist (20x selectivity for D3 over D2)

Why does D3 matter?

- D3 receptors are concentrated in: mesolimbic system, prefrontal cortex, hippocampus
- D3 modulation → improved **negative symptoms** of schizophrenia
- D3 involved in **reward processing**, motivation, cognition
- Cariprazine's D3 selectivity is the proposed mechanism for its unique efficacy on negative symptoms

CLINICAL EVIDENCE

Negative symptoms:

- **PANSS-ND** (negative symptoms subscale) improved vs risperidone in RCTs
- Statistically significant superiority to risperidone on PANSS negative symptom factor scores
- **RGH-MD-16 study:** Cariprazine 3–6 mg vs risperidone, negative symptom advantage confirmed

Bipolar depression:

- Multiple RCTs showing efficacy on MADRS
- Unique among antipsychotics: efficacious at LOW doses (1.5 mg) for bipolar depression vs higher doses for mania

PHARMACOKINETICS

- Active metabolite: **DCAR** (desmethyl-cariprazine) with similar pharmacology
- Active metabolite: **DDCAR** (didesmethyl-cariprazine), very long half-life (~1–3 weeks)
- Total effective half-life: 2–4 weeks
- Implication: After discontinuation, pharmacological effect persists for weeks

DOSING

- Schizophrenia: 1.5–6 mg/day
- Bipolar mania: 3–6 mg/day
- Bipolar depression: 1.5–3 mg/day (lower than mania)

SIDE EFFECTS

- Akathisia, highest among newer APs
- Weight gain, moderate (less than olanzapine/clozapine)
- Metabolic: moderate
- Minimal prolactin elevation (partial agonist)

2.4 Brexpiprazole (Rexulti)

FDA Approval: 2015 for schizophrenia and adjunctive treatment of MDD

2023 Approval: Agitation associated with Alzheimer's dementia (first drug for this indication)

Class: Serotonin-dopamine activity modulator (SDAM)

MECHANISM

TARGET · ACTION

D2 Partial agonist (lower intrinsic activity than aripiprazole)

D3 Partial agonist

5-HT1A Partial agonist

5-HT2A Antagonist

α1B, α2C Antagonist

H1 Antagonist

Key comparison with aripiprazole:

- Brexpiprazole: LOWER intrinsic activity at D2 (more antagonist-like behavior)
- Lower risk of akathisia than aripiprazole

- More potent 5-HT_{1A} partial agonism

ALZHEIMER'S DEMENTIA AGITATION

- **RAISE trial:** Brexpiprazole 2–3 mg significantly reduced CMAI agitation scores
- First FDA approval specifically for this indication
- **Important caveat:** Still carries dementia-related mortality warning

ADJUNCTIVE MDD

- Add-on to SSRI/SNRI in partial responders
- Doses: 1–3 mg/day (lower than for schizophrenia)

2.5 Long-Acting Injectable Antipsychotics (LAIs)

WHY LAIS MATTER

- Non-adherence is the #1 cause of relapse in schizophrenia
- ~50% of patients are non-adherent within 1 year of discharge
- LAIs bypass the daily decision to take medication
- Eliminates covert non-adherence
- Continuous therapeutic blood levels without peaks/troughs

PALIPERIDONE PALMITATE 3-MONTHLY (PP3M / INVEGA TRINZA)

FEATURE	PP1M (TRINZA MONTHLY)	PP3M (TRINZA 3-MONTHLY)
Injection frequency	Monthly	Every 3 months
Formulation	Nanocrystal suspension	Nanocrystal suspension
Loading dose required	Yes (Days 1 and 8)	No (after stable on PP1M)
First injection site	Deltoid	Deltoid or gluteal
Dosing flexibility	39–234 mg	175–525 mg

PP3M requirements:

- Must be adequately treated with PP1M for at least 4 months
- Last two PP1M doses must be same dose (stable)
- PP3M dose = 3.5x the PP1M dose

Paliperidone palmitate 6-monthly (PP6M / Invega Hafyera):

- FDA approved 2021
- Every 6 months injection
- Gluteal only

ARIPIRAZOLE LAUROXIL (ARISTADA)

FORMULATION · DOSING

Aristada 441 mg Every 4 weeks

Aristada 662 mg Every 4 or 6 weeks

Aristada 882 mg Every 4 or 8 weeks

Aristada 1064 mg Every 2 months

Aristada Initio 675 mg Single initiation dose (with oral aripiprazole 30 mg)

Initiation strategy (NCD, No Confirmation Day):

- Aristada Initio 675 mg (deltoid) + oral aripiprazole 30 mg on same day
 - Followed by regular Aristada the next day
 - Avoids the 21-day wait for oral overlap
-

SECTION 3: NEWER ANXIOLYTICS AND HYPNOTICS

3.1 Orexin Receptor Antagonists (DORAs)

THE OREXIN SYSTEM

Orexins (hypocretins 1 and 2) are neuropeptides produced in the lateral hypothalamus. They are wake-promoting neurotransmitters.

DORA mechanism: Block both OX1R and OX2R simultaneously → "turn off" the wake drive → natural sleep architecture preserved

Contrast with older hypnotics:

- Benzodiazepines and Z-drugs: enhance GABA inhibition (suppress all brain activity)
- DORAs: specifically suppress wake-promoting drive only

SUVOREXANT (BELSOMRA)

FDA Approval: 2014

Doses: 5, 10, 15, 20 mg (usual: 10–20 mg)

Schedule: Schedule IV controlled substance

Mechanism: Dual OX1R + OX2R antagonist

Clinical Profile:

- Reduces sleep onset latency and wake after sleep onset (WASO)
- Preserves sleep architecture (REM, SWS proportions maintained)

- Less residual sedation than benzodiazepines
- **No rebound insomnia** upon discontinuation (key differentiator)

Side Effects:

- Somnolence, abnormal dreams
- Sleep paralysis, hypnagogic/hypnopompic hallucinations
- Cataplexy-like symptoms (rare, dose-dependent)
- **Next-day impairment**, warn about driving

Drug Interactions:

- Strong CYP3A4 inhibitors: reduce dose to 5 mg (ketoconazole, clarithromycin)
- CYP3A4 inducers: reduce efficacy (rifampin, carbamazepine)

LEMBOREXANT (DAYVIGO)

FDA Approval: 2019

Doses: 5 mg and 10 mg

Differences from suvorexant:

- Higher binding affinity at OX2R (more selective wake-off switch)
- **Longer half-life:** ~17–27 hours (suvorexant ~12 hours)
- **Better sleep maintenance** data in elderly
- **SUNRISE-1 and SUNRISE-2 trials** vs placebo + SUNRISE-2 vs zolpidem
- Lemborexant 5 mg showed better subjective sleep parameters than zolpidem at 1 month

Side Effects:

- Similar to suvorexant
- Somnolence, headache
- Caution: complex sleep behaviors (sleepwalking, sleep driving), black box warning added for all Z-drugs and now DORAs

DARIDOREXANT (QUVIVIQ)

FDA Approval: 2022

Doses: 25 mg and 50 mg

Key features:

- **Shortest half-life** among approved DORAs (~8 hours)
- **Least next-day sedation**, specifically designed for daytime functioning
- **ESADA-1 and ESADA-2 trials:** Improved subjective and objective sleep parameters + daytime functioning scores
- No dose adjustment for CYP3A4 interactions at approved doses (unlike suvorexant)

FEATURE	SUVOREXANT	LEMBOREXANT	DARIDOREXANT
Approval	2014	2019	2022
Half-life	~12h	~17–27h	~8h
Doses	10–20 mg	5–10 mg	25–50 mg
Schedule	IV	IV	IV
Best for	General insomnia	Elderly / maintenance	Next-day functioning

SECTION 4: PSYCHEDELICS IN PSYCHIATRY

4.1 Psilocybin

Source: Psilocybe cubensis and related mushrooms

Active metabolite: Psilocin (after dephosphorylation by alkaline phosphatase)

MECHANISM OF ACTION

- **Primary:** 5-HT_{2A} agonist, binding in prefrontal cortex, thalamus, limbic system
- **Secondary:** 5-HT_{2C}, 5-HT_{1A} activity
- No direct effects on dopamine system

Neural effects of 5-HT_{2A} agonism:

1. Disruption of thalamo-cortical gating → enhanced sensory processing → hallucinations
2. Default Mode Network (DMN) disruption → ego dissolution
3. Increased global brain connectivity, "hyperconnected" brain state
4. Neuroplasticity induction via BDNF and mTOR pathways

CLINICAL TRIALS

Treatment-Resistant Depression (TRD):

- **COMPASS Pathways Phase 2b (COMP360):**
- 25 mg psilocybin (single dose) → significant response at 3 weeks
- Rapid, sustained antidepressant effect
- ~29% remission at 3 weeks with 25 mg dose
- Adverse effects: headache, nausea, dizziness, transient anxiety during session

Major Depression:

- **Johns Hopkins study** (2021, JAMA Psychiatry):
- 2 sessions of psilocybin (20 mg + 30 mg, 1 week apart)
- ~71% response, ~54% remission at 4 weeks

- Maintained at 1-year follow-up

Existential Distress (Cancer):

- **NYU and Johns Hopkins trials (2016):**
- Single-dose psilocybin in cancer patients with anxiety / depression
- Dramatic, sustained reductions in existential distress
- ~60–80% meeting criteria for clinically significant antidepressant response at 6 months

Alcohol and Smoking Cessation:

- Pilot studies showing promise, larger RCTs ongoing

REGULATORY STATUS

- **Schedule I in US, India**, no accepted medical use currently
- FDA granted Breakthrough Therapy Designation for:
- Psilocybin for TRD (COMPASS Pathways, 2018)
- Psilocybin for MDD (Usona Institute, 2019)
- Australia: ARTG approved psilocybin for TRD (July 2023), first country to reschedule for medical use

SET AND SETTING

- Therapeutic psilocybin is not standalone, it is **psilocybin-assisted psychotherapy**
- Preparation sessions (psychotherapy)
- Drug sessions (monitored, therapist present)
- Integration sessions (processing experience)
- Physical environment matters: comfortable room, music, eye shades

SAFETY PROFILE

- **Non-addictive**, no withdrawal syndrome, no physical dependence
- Low abuse potential (tolerance develops rapidly to self-limiting)
- **Transient adverse effects:** headache, nausea, transient anxiety, confusion
- **Serious risks:** Challenging experiences ("bad trips"), managed with therapist presence
- **Contraindications:** Personal / family history of psychosis, schizophrenia, bipolar I (manic episodes), unstable cardiovascular disease
- **HPPD** (Hallucinogen Persisting Perception Disorder), rare

4.2 MDMA-Assisted Therapy for PTSD

Full name: 3,4-methylenedioxymethamphetamine

Schedule I (US), Breakthrough Therapy Designation (2017) for PTSD

MECHANISM OF ACTION

- **Primary:** Releases serotonin (massive), dopamine, and norepinephrine from presynaptic terminals
- Inhibits reuptake of all three monoamines
- **Oxytocin release**, social bonding hormone
- Net effect: Empathic, prosocial state with reduced fear response

Why MDMA is uniquely suited for PTSD:

- Fear extinction is impaired in PTSD (amygdala hyperactivation)
- MDMA: reduces amygdala reactivity to threat
- MDMA: increases prefrontal cortical control
- MDMA: creates a state of openness, trust, reduced defensiveness
- Allows trauma processing without the normal overwhelming fear response

CLINICAL EVIDENCE

- **MAPS Phase 3 trials (MAPP1 and MAPP2):**
- 71% of MDMA group no longer met PTSD diagnostic criteria at 18-week primary endpoint
- 48% in placebo group lost PTSD diagnosis
- Response rates: ~67% (MDMA) vs ~32% (placebo)
- Well-tolerated: transient nausea, jaw clenching, insomnia on dosing night

REGULATORY STATUS (2024)

- FDA advisory committee voted against approval (June 2024), concerns about functional unblinding and trial design
- FDA declined to approve (August 2024), requested additional Phase 3 trial
- **Not currently approved**
- Australia: TGA approved for PTSD treatment (July 2023), first country

PROTOCOL

- 3 MDMA sessions (80–120 mg doses) over ~18 weeks
- Each session 8 hours long
- Therapist dyad (male + female co-therapists recommended by MAPS)
- Extensive preparation and integration therapy

4.3 Ketamine Clinics

Status: Legal, operating in US and India

Administration: IV infusion (most common), IM, intranasal (compounded)

Typical protocol:

- Series of 6 infusions over 2–3 weeks
- 0.5 mg/kg IV over 40 minutes
- Maintenance infusions as needed (monthly, bimonthly)

Indications:

- Treatment-resistant depression
- PTSD (off-label)
- Chronic pain / CRPS
- OCD (emerging data)

Limitations:

- Not standardized (dose, frequency, preparation)
 - No regulatory oversight for non-REMS ketamine infusions
 - Short duration of effect (days to weeks), necessitates repeat infusions
 - Cost: \$400–800 per infusion, not usually insured
-

4.4 Microdosing

Definition: Sub-perceptual doses (1/10th to 1/20th of a full dose)

- Psilocybin: 0.1–0.3 g dried mushroom or ~1–3 mg psilocybin
- LSD: 5–15 mcg (full dose 100–200 mcg)

Proposed benefits (largely anecdotal):

- Improved focus, creativity, mood
- Reduced anxiety
- No psychedelic effects

Evidence base:

- Mostly observational studies and self-reports
- RCTs difficult due to legality
- **Imperial College London PNAS study (2021):** Microdosing improved well-being, mindfulness scores, but expectation effects (placebo) could explain results
- **No RCT-level evidence** for clinical use

Regulatory status: Illegal in most jurisdictions including India

4.5 Regulatory Landscape Summary

Substance	India Status	US Status	Key Approvals
Psilocybin	Schedule I (NDPS)	Schedule I	Australia 2023; FDA BTD
MDMA	Prohibited	Schedule I	Australia 2023; FDA rejected 2024
Ketamine	Schedule X (legal, re- quires prescription)	Schedule III	Esketamine (Spravato) FDA approved
LSD	Schedule I	Schedule I	None
Cannabis (CBD)	NDPS / state-by-state	Variable	Epidiolex FDA ap- proved (seizures)

SECTION 5: PRECISION PSYCHIATRY

5.1 Pharmacogenomics

Definition: How genetic variation affects drug metabolism, efficacy, and adverse effects

CYP450 ENZYME POLYMORPHISMS

CYP2D6, most clinically relevant in psychiatry

Phenotype	Frequency	Effect on CYP2D6 Substrates
Poor metabolizer (PM)	7–10% Caucasians; 1–2% Asians	Higher blood levels → toxicity risk
Intermediate metabolizer (IM)	~15%	Moderately reduced activity
Extensive metabolizer (EM)	~70%	Normal
Ultrarapid metabolizer (UM)	1–2% Caucasians; 29% Ethiopians	Lower blood levels → treat- ment failure

Key CYP2D6 substrates in psychiatry:

- Antidepressants: fluoxetine, paroxetine, vortioxetine, nortriptyline, clomipramine, desipramine
- Antipsychotics: haloperidol, perphenazine, risperidone, aripiprazole
- Note: Fluoxetine and paroxetine are BOTH substrates AND inhibitors of CYP2D6

CYP2C19

PHENOTYPE · FREQUENCY

Poor metabolizer 3–5% Caucasians; 15–20% Asians

Intermediate metabolizer ~25%

Normal metabolizer ~70%

Rapid/ultrarapid metabolizer ~5%

Key CYP2C19 substrates:

- Citalopram, escitalopram (higher levels in PMs, QTc concern)
- Sertraline
- Diazepam, clonazepam
- Venlafaxine

HLA-B*1502 and Carbamazepine:

- Carriers of HLA-B*1502 allele at dramatically increased risk of Stevens-Johnson syndrome (SJS) / toxic epidermal necrolysis (TEN) with carbamazepine
- Frequency: ~10% in Han Chinese, Thai, Filipino
- **MANDATORY testing before carbamazepine initiation** in patients of Asian ancestry
- FDA label requires this testing
- National Institute of Mental Health India guidelines echo this recommendation

HLA-A*3101:

- Carbamazepine hypersensitivity in European and Japanese populations
- Associated with SJS, DRESS, maculopapular exanthema

HLA-B*5701 and Abacavir:

- Not psychiatric but important model, HIV drug causing hypersensitivity

PHARMACOGENOMIC TESTING: CLINICAL USE

GeneSight and similar commercial panels:

- Tests: CYP2D6, CYP2C19, CYP2C9, CYP1A2, SLC6A4 (5-HTTLPR), MTHFR, HTR2A
- Color-coded report: Use as directed / Use with caution / Use with caution and more frequent monitoring / Not recommended

Limitations:

- Evidence for clinical utility is mixed
- **PRIME Care trial** (2022): GeneSight testing did not significantly improve HAM-D-17 outcomes vs treatment as usual in primary care MDD
- **GUIDED trial** (2019): Positive results for GeneSight in MDD

- Not routinely recommended by NICE/ APA guidelines currently

5.2 Therapeutic Drug Monitoring (TDM)

Indications for TDM in psychiatry:

1. Suboptimal response at adequate doses
2. Suspected non-adherence
3. Suspected toxicity despite therapeutic doses
4. Polypharmacy with potential interactions
5. Special populations (pregnancy, renal/hepatic disease, elderly)
6. Drugs with narrow therapeutic windows

DRUG	THERAPEUTIC RANGE	TOXIC LEVEL	KEY NOTES
Lithium	0.6–1.0 mmol/L (maintenance)	>1.5 mmol/L	0.8–1.2 acute; 12-hour post-dose sample
Valproate	50–100 mcg/mL	>150 mcg/mL	
Carbamazepine	4–12 mcg/mL	>15 mcg/mL	
Clozapine	350–600 ng/mL	>1000 ng/mL	Smoking significantly reduces levels
Haloperidol	5–17 ng/mL		
Nortriptyline	50–150 ng/mL		Curvilinear response
Imipramine	150–300 ng/mL		Total (imipramine + desipramine)

5.3 Biomarker-Guided Treatment

Current approaches:

1. **HPA axis markers:** Cortisol non-suppression on DST → may predict antidepressant response
2. **Inflammatory markers:** High CRP (>1 mg/L) → may prefer anti-inflammatory antidepressants; low CRP → may prefer serotonergic
3. **EEG biomarkers:** Alpha-wave asymmetry, theta-wave patterns, investigational
4. **Neuroimaging:** Anterior cingulate cortex activity on fMRI/PET → predict response to CBT vs medication

CANMAT recommendations: Biomarker-guided treatment not yet standard of care, promising but needs more RCT evidence

5.4 Computational Psychiatry

Definition: Application of mathematical models and computational algorithms to understand brain function, mental illness, and treatment prediction

Key concepts:

1. **Predictive Coding / Active Inference:** Brain as Bayesian inference machine, mental illness = aberrant precision-weighting of prediction errors
2. **Reinforcement Learning Models:** Anhedonia, addiction modeled as disrupted reward learning
3. **Dynamic Causal Modeling:** Inferring effective connectivity from fMRI data

Clinical applications (emerging):

- Digital phenotyping (smartphone data) to predict relapse
- Machine learning to predict treatment response
- Network analysis of symptom dimensions

KEY INSIGHT

Toroidal Model connection: The toroidal geometry models how psychosis and affective states cycle, computational psychiatry provides the mathematical substrate for such models.

SECTION 6: SEROTONIN SYNDROME

6.1 Pathophysiology

Serotonin syndrome results from excess serotonergic activity at central and peripheral 5-HT receptors.

Receptors involved:

- **5-HT_{1A}:** Agitation, tachycardia, hypertension, diaphoresis, hyperthermia
- **5-HT_{2A}:** Clonus, hyperreflexia, rigidity (mild), myoclonus, temperature dysregulation (severe)

The triad:

6.2 Hunter Criteria (Diagnostic Standard)

The **Hunter Serotonin Toxicity Criteria** are the most accurate clinical diagnostic criteria.

Requirement: Serotonergic drug must be present PLUS one of the following:

1. Spontaneous clonus
2. Inducible clonus + (agitation OR diaphoresis)

3. **Ocular clonus** + (agitation OR diaphoresis)
4. **Tremor** + **hyperreflexia**
5. **Hypertonia** + temperature $>38^{\circ}\text{C}$ + ocular or inducible clonus

KEY INSIGHT

Memory hook: HUNTER criteria focus on CLONUS, this is the key neuromuscular finding distinguishing SS from NMS.

Sensitivity: 84% **Specificity:** 97% (vs Sternbach criteria)

6.3 Culprit Drug Classes

CLASS · EXAMPLES

MAOIs Phenelzine, tranylcypromine, selegiline, moclobemide

SSRIs All

SNRIs Venlafaxine, duloxetine

TCAs Clomipramine (strong), imipramine

Opioids Tramadol, meperidine, fentanyl, methadone

Antiemetics Ondansetron, metoclopramide

Antibiotics Linezolid (weak MAOI), tedizolid

Antitussives Dextromethorphan

Triptans (5-HT_{1B}/1D agonists, controversial)

Supplements St John's Wort, tryptophan, 5-HTP

Recreational MDMA (ecstasy), cocaine

Others Lithium, tramadol

Highest risk combination: MAOI + SSRI/SNRI, potentially fatal

6.4 Clinical Features

SYSTEM · FEATURES

Cognitive Agitation, confusion, anxiety, restlessness

Autonomic Tachycardia, hypertension, hyperthermia, diaphoresis, diarrhea, mydriasis

Neuromuscular Tremor, clonus, hyperreflexia, myoclonus, incoordination

Severe Hyperthermia $>41^{\circ}\text{C}$, rhabdomyolysis, metabolic acidosis, renal failure, DIC

Onset: Rapid, within 24 hours of drug initiation/increase/combination (typically within 6 hours)

Course: Usually resolves within 24–72 hours if causative drug stopped

6.5 Management

Step 1: Discontinue all serotonergic drugs

Step 2: Supportive care (IV fluids, cooling measures, benzodiazepines for agitation)

Step 3: Cyproheptadine (5-HT antagonist), 12 mg loading, 2 mg every 2 hours PRN

Step 4: Severe cases: ICU admission, intubation for airway, neuromuscular paralysis

Cyproheptadine:

- H1 antihistamine with 5-HT_{2A} antagonism
 - NOT available IV, oral/NG only
 - Evidence base: case reports and series, no RCTs
 - Alternative: Chlorpromazine (5-HT_{2A} antagonist, but risk of hypotension/seizure threshold lowering)
-

SECTION 7: NEUROLEPTIC MALIGNANT SYNDROME (NMS)

7.1 Definition and Pathophysiology

NMS is an idiosyncratic, potentially life-threatening reaction to antipsychotic drugs (and other dopamine antagonists).

Pathophysiology:

- Abrupt D₂ receptor blockade in:
- **Striatum** → rigidity, EPS
- **Hypothalamus** → hyperthermia
- **Mesocortex/mesolimbic** → cognitive changes

Predisposing factors:

- High-potency typical antipsychotics (haloperidol most associated)
- Rapid dose increase
- IM depot injections

- Dehydration
- Agitation, physical restraint
- Prior NMS episode (10–15x increased risk)
- Young male patients
- Brain pathology (dementia, Parkinson's)

7.2 Clinical Features: FEVER + RIGIDITY Mnemonic

Fever >38°C, can reach >40°C

Encephalopathy Confusion, altered consciousness

Vital instability Tachycardia, labile BP, diaphoresis

Elevated CK Muscle breakdown, can be >10,000 U/L

Rigidity Lead-pipe rigidity (severe, unlike SS)

Lab findings:

- Elevated CK (diagnostic hallmark), >1000 U/L typical
- Leukocytosis (WBC 10,000–40,000)
- Metabolic acidosis
- Elevated LFTs
- Myoglobinuria → renal failure risk
- Low serum iron (<12 µmol/L), specific for NMS

Onset: Slower than SS, hours to days after starting / changing antipsychotic

Duration: Without treatment: 1–2 weeks; with DAergic agonists: shorter

7.3 SS vs NMS vs Malignant Catatonia vs Malignant Hyperthermia

FEATURE	SEROTONIN SYNDROME	NMS	MALIGNANT CATATONIA	MALIGNANT HYPERTHERMIA
Cause	Serotonergic drugs	Dopamine antagonists	Idiopathic (or triggered by antipsychotics)	Volatile anesthetics / succinylcholine
Onset	Hours (rapid)	Days	Subacute	Minutes (during anesthesia)
Temperature	Moderate elevation	High	High	Extremely high

FEATURE	SEROTONIN SYNDROME	NMS	MALIGNANT CATATONIA	MALIGNANT HYPERTHERMIA
Rigidity	Mild (SS)	Lead-pipe (severe)	Waxy/posturing	Very severe
Clonus	YES, characteristic	No	No	No
Tremor	Prominent	Less prominent	Variable	Variable
Reflexes	Hyperreflexia	Normal/reduced	Variable	Normal
CK	Usually normal	Very elevated	Elevated	Very elevated
Consciousness	Agitated, alert early	Stupor	Stupor, mutism	Usually unconscious
Treatment	Cyproheptadine	Dantrolene/bromocriptine	ECT, lorazepam	Dantrolene
Mutism/posturing	Rare	Absent	YES, defining	Absent

7.4 NMS Management

Immediate:

1. Stop antipsychotic
2. Supportive care: hydration, cooling, monitoring
3. Benzodiazepines for rigidity and agitation

Pharmacological:

1. **Dantrolene** (0.25–2 mg/kg IV q6h): Blocks calcium release from SR → reduces muscle rigidity and hyperthermia
2. **Bromocriptine** (2.5–5 mg TID): D2 agonist → reverses dopamine blockade
3. **Amantadine** (100 mg BD): NMDA antagonist + dopaminergic properties

ECT: For refractory NMS and malignant catatonia (can be diagnostically confounding)

Re-challenge with antipsychotic:

- Wait minimum 2 weeks after NMS resolution
- Start with low-potency atypical antipsychotic (clozapine, quetiapine)
- Low doses, gradual titration
- Avoid precipitating factors (dehydration, IM depot)
- Close monitoring

SECTION 8: DRUG INTERACTIONS IN PSYCHIATRY

8.1 Pharmacokinetic Interactions

CYP450-MEDIATED INTERACTIONS

Major CYP450 enzymes in psychiatry:

ENZYME	MAJOR INHIBITORS	MAJOR INDUCERS	KEY SUBSTRATES
CYP2D6	Fluoxetine, paroxetine, bupropion, haloperidol		TCAs, codeine, risperidone, aripiprazole
CYP3A4	Ketoconazole, ritonavir, clarithromycin, grapefruit	Rifampin, carbamazepine, St John's Wort	Quetiapine, clonazepam, buspirone, most benzodiazepines
CYP1A2	Ciprofloxacin, fluvoxamine	Smoking, carbamazepine, omeprazole	Clozapine, olanzapine, haloperidol
CYP2C19	Fluvoxamine, fluoxetine	Rifampin, carbamazepine	Diazepam, escitalopram
CYP2C9	Fluconazole, amiodarone	Rifampin, carbamazepine	Warfarin, phenytoin

Smoking and CYP1A2:

KEY INSIGHT

Critical clinical point: Smoking INDUCES CYP1A2, reduces clozapine and olanzapine levels significantly. - Heavy smokers (>10 cigs/day) may need 50–100% higher clozapine doses - If patient stops smoking (hospitalization, cessation), clozapine levels can RISE → toxicity risk - Monitor clozapine levels with smoking status changes

Fluvoxamine as CYP1A2 inhibitor:

- Fluvoxamine strongly inhibits CYP1A2
- Combined with clozapine → clozapine levels increase 2–10 fold
- Can cause clozapine toxicity even at normal doses
- Some clinicians use low-dose fluvoxamine to increase clozapine levels in treatment-resistant cases (intentional interaction)

P-GLYCOPROTEIN (P-GP) INTERACTIONS

- P-gp is an efflux transporter in the blood-brain barrier
- P-gp inhibitors → increase CNS penetration of substrates
- Quetiapine: P-gp substrate
- Verapamil: P-gp inhibitor

8.2 High-Risk Drug Combinations

LITHIUM + NSAIDS

Mechanism: NSAIDs reduce renal prostaglandin synthesis → reduced renal blood flow → decreased lithium clearance → lithium toxicity

Magnitude of interaction:

- Indomethacin, diclofenac, ibuprofen: 50–100% increase in lithium levels
- Aspirin (low dose): minimal effect
- COX-2 inhibitors (celecoxib): similar risk to NSAIDs

Management: Avoid NSAIDs with lithium. If unavoidable, monitor lithium levels closely, reduce dose, use aspirin as alternative.

Other drugs that raise lithium levels:

- ACE inhibitors / ARBs: reduce renal excretion
- Thiazide diuretics: sodium depletion → lithium retention
- Dehydration/low-sodium diet: same mechanism

MAOIS + SSRIS/SNRIS/TCAS

Mechanism: Combined serotonergic activity → severe serotonin syndrome

Risk: POTENTIALLY FATAL

Washout periods:

DRUG · WASHOUT BEFORE STARTING MAOI

Fluoxetine 5 weeks (long half-life + active metabolite norfluoxetine)

Paroxetine 2 weeks

Sertraline, escitalopram, citalopram 2 weeks

Venlafaxine, duloxetine 2 weeks

TCAs 2 weeks

After stopping MAOI: Wait 2 weeks before starting any serotonergic drug

CLOZAPINE + CARBAMAZEPINE

Mechanism: Carbamazepine induces CYP1A2 and CYP3A4 → reduces clozapine levels

Additional risk: Both drugs are independently associated with agranulocytosis, ADDITIVE risk

Combination: ABSOLUTELY CONTRAINDICATED

If mood stabilizer needed with clozapine:

- Valproate (preferred, though monitor for sedation)
- Lithium (monitor levels)
- Lamotrigine (adjunct for negative symptoms, some evidence)

CLOZAPINE + BENZODIAZEPINES

Mechanism: CNS depression, respiratory depression

Risk: Case reports of sudden death and respiratory collapse with IM clozapine + benzodiazepines

IMPORTANT: Avoid IM benzodiazepines within hours of clozapine administration; caution with oral combination

LITHIUM + ANTIPSYCHOTICS (HIGH-DOSE)

Risk: Neurotoxicity, enhanced adverse effects even at therapeutic levels

Most reported with: Haloperidol

Features: EPS, confusion, fever, delirium

Historical note: Early reports (1970s) linked haloperidol + lithium to irreversible brain damage, "Loulis and Hurley syndrome"

SECTION 9: LITHIUM: COMPREHENSIVE

9.1 Pharmacology

Mechanism of Action (Multiple):

1. **Inositol depletion hypothesis:** Inhibits inositol monophosphatase → depletes inositol → reduces PKC-mediated signaling in overactive cells
2. **Glycogen Synthase Kinase-3 (GSK-3 β) inhibition:** Reduces phosphorylation cascade → neuroprotective, anti-apoptotic
3. **Neurotrophin effects:** Increases BDNF, promotes neurogenesis
4. **Serotonin potentiation:** Enhances 5-HT synthesis and release (basis for augmentation)
5. **Anti-glutamatergic:** Reduces NMDA receptor signaling
6. **Epigenetic:** Histone deacetylase (HDAC) inhibition

Pharmacokinetics:

- Complete GI absorption (100%)
- No protein binding
- Renal excretion (competitive with sodium, depleted sodium leads to lithium retention)
- Half-life: ~24 hours (acute); 36–48 hours (chronic, with renal accumulation)

- Steady state: 5–7 days
- No hepatic metabolism, ideal for patients with liver disease

9.2 Therapeutic Drug Monitoring

INDICATION · TARGET LEVEL

Acute mania 0.8–1.2 mmol/L

Maintenance (adults) 0.6–0.8 mmol/L

Maintenance (elderly) 0.4–0.6 mmol/L

Augmentation (depression) 0.5–0.8 mmol/L

Monitoring protocol:

- Level drawn 12 hours after last dose
- **Baseline:** Renal function (Cr, BUN, eGFR), thyroid (TSH, FT4), calcium, ECG, pregnancy test (women of reproductive age)
- **Frequency:** Every 5–7 days during initiation; then monthly × 6 months; then every 3–6 months when stable

9.3 Lithium Toxicity

SIGNS BY LEVEL

LEVEL (MMOL/L) · SIGNS

1.5–2.0 (mild) Nausea, vomiting, diarrhea, tremor, polyuria, confusion

2.0–2.5 (moderate) Ataxia, drowsiness, slurred speech, EEG changes

>2.5 (severe) Coarse tremor, rigidity, stupor, seizures, coma

>3.5 (life-threatening) Death risk

KEY INSIGHT

Memory: FINE mnemonic for lithium toxicity: Fine tremor → Intention tremor (coarser) → Nausea → Encephalopathy

Precipitants of toxicity:

- NSAIDs, ACE inhibitors, diuretics
- Dehydration (febrile illness, surgery, low-sodium diet)
- Renal impairment

- Drug-drug interactions (CKD patients particularly vulnerable)

Management:

1. Stop lithium
 2. IV normal saline (aggressive hydration and sodium correction)
 3. Hemodialysis if:
 4. Level >4 mmol/L
 5. Level >2.5 mmol/L with severe symptoms
 6. Severe renal failure preventing excretion
 7. Sodium polystyrene sulfonate, evidence limited
 8. Activated charcoal: NOT effective (lithium not absorbed by charcoal)
-

9.4 Long-Term Effects

Renal effects:

- **Nephrogenic diabetes insipidus (NDI):** Lithium blocks vasopressin effect on collecting duct → polyuria, polydipsia
- Occurs in ~40% of patients
- Management: reduce to once-daily dosing, amiloride (blocks ENaC channel that lithium uses to enter cells), indomethacin (short-term)
- **Chronic kidney disease:** Irreversible tubular atrophy with long-term use (>10 – 15 years)
- Risk factors: older age, higher levels, episodes of toxicity
- Monitoring: eGFR trend annually

Thyroid effects:

- Hypothyroidism: ~20–40% of long-term users
- Less commonly, hyperthyroidism (Graves' disease, autoimmune)
- Monitor TSH annually, treat with levothyroxine (do NOT stop lithium)

Cardiac effects:

- T-wave flattening / inversion, benign
- Sinus node dysfunction, rare
- Avoid in sick sinus syndrome

Parathyroid effects:

- Hyperparathyroidism → hypercalcemia
 - Mechanism: lithium increases set point for calcium-mediated PTH suppression
-

9.5 Lithium in Pregnancy

Teratogenicity:

- Historical concern: Ebstein's anomaly (tricuspid valve malformation)
- **Updated estimates (2017 NEJM):** Absolute risk increases from 0.6/1000 to 2.1/1000, much lower than previously thought
- Risk ratio ~2.66, significant but not as catastrophic as older estimates

CANMAT/NICE guidance:

- Benefit-risk discussion individualized
- For moderate-high risk patients: lithium may be continued with monitoring
- Fetal echocardiogram at 16–18 weeks if lithium continued
- Lithium levels increase in first trimester (increased renal clearance), then levels spike post-partum (renal clearance falls)
- **Peri-partum:** Dose reduction by 25–50% at 36 weeks; re-titrate after delivery
- **Breastfeeding:** Excreted in breast milk (40–50% of maternal level), generally advised against; discuss carefully

SECTION 10: CLOZAPINE: COMPREHENSIVE

10.1 Indications

INDICATION · EVIDENCE LEVEL

Treatment-resistant schizophrenia (TRS) FDA approved; Level I evidence

Suicidality in schizophrenia/schizoaffective FDA approved (only drug with this indication)

Schizoaffective disorder Off-label but well-established

Parkinson's disease psychosis Off-label (preferred after pimavanserin)

Chronic aggression/violence Off-label, evidence-based

Refractory bipolar disorder Off-label

Refractory OCD (augmentation) Case reports

TRS Definition (TRRIP consensus):

- Adequate trials of ≥ 2 antipsychotics (one should be an SGA)
- Each at adequate dose (e.g., >600 mg chlorpromazine equivalents)
- For adequate duration (≥ 6 weeks each)

- With documented adherence
- With persistent positive symptoms (CGI-S ≥ 4)

Time to clozapine:

- Average in real world: 5–10 years after first psychosis
- Evidence supports earlier use after 2 failed adequate trials
- NICE guidelines: After 2 failed antipsychotics

10.2 Clozapine Monitoring: The ANC Protocol

ANC = Absolute Neutrophil Count

ANC · ACTION

$\geq 1500/\text{mm}^3$ Continue clozapine

1000–1499/ mm^3 Continue with more frequent monitoring

500–999/ mm^3 Interrupt clozapine, daily monitoring

<500/ mm^3 (agranulocytosis) STOP clozapine permanently, never re-challenge

Monitoring frequency:

- Weeks 1–26: **Weekly** ANC
- Weeks 27–52: **Every 2 weeks**
- After 1 year: **Monthly**

Agranulocytosis risk:

- Overall: ~0.8–1% (with monitoring)
- Peak risk: Weeks 6–18
- Higher risk: Ashkenazi Jewish descent, BNL (Benign Ethnic Neutropenia in African descent)

Benign Ethnic Neutropenia (BEN):

- African/Caribbean descent: baseline ANC 1000–1500/ mm^3 common (not pathological)
- New protocol allows clozapine in BEN with adjusted ANC thresholds

10.3 Clozapine Adverse Effects

METABOLIC EFFECTS (SEVERE)

- Weight gain: 4–10 kg average; most among all antipsychotics
- Diabetes mellitus: significantly increased risk
- Dyslipidemia: elevated triglycerides especially

- Mechanism: H1 antagonism (appetite increase), M1 antagonism (impaired insulin response)

CARDIOVASCULAR

- **Myocarditis/Cardiomyopathy:**
- Myocarditis: Occurs in first 4–8 weeks (peak weeks 2–4)
- Incidence: ~0.3–0.7% (higher in Australian data: ~1–3%)
- Features: fever, chest pain, fatigue, eosinophilia, elevated troponin, CRP
- **Action if suspected:** STOP clozapine immediately; echo, cardiac enzyme monitoring
- Re-challenge: controversial, avoided in most cases
- If absolutely necessary: very gradual titration, prophylactic aspirin (evidence weak)
- QTc prolongation: Moderate risk
- Orthostatic hypotension: Common especially during titration

SEIZURES

- Dose-dependent: 1–2% at doses <300 mg/day; up to 5% at doses >600 mg/day
- Generalized tonic-clonic (GTCS)
- **Management:**
- Reduce clozapine dose if possible
- Add valproate (drug of choice, also helps metabolic symptoms and reduces prolactin)
- Avoid carbamazepine (agranulocytosis risk) and lamotrigine (rash risk if valproate added)
- Gabapentin or clonazepam as alternatives

OTHER SIDE EFFECTS

- Hypersalivation (sialorrhea): Very common, especially nocturnal. Anticholinergics (hyoscine), pilocarpine, or pirenzepine
- Sedation: Most common complaint, use sedation to advantage by dosing at night
- Constipation: Serious, ileus risk. Prevent with bowel regimen
- Urinary incontinence/retention
- Fever (within first few weeks): Often benign, rule out agranulocytosis and myocarditis

10.4 Clozapine Re-challenge Protocol

Indicated when: Benefits outweigh risks after previous adverse event (not agranulocytosis)

Contraindicated re-challenge: Agranulocytosis (ANC <500) or NMS

Protocol for re-challenge (after myocarditis, special centers only):

1. Cardiac clearance from cardiologist

2. Baseline troponin, CRP, echo
 3. Very slow titration (6.25 mg every 1–2 weeks)
 4. Daily monitoring of cardiac enzymes for first 4–8 weeks
 5. Low-dose aspirin (evidence weak, sometimes used prophylactically)
-

SECTION 11: ANTIPSYCHOTIC SWITCHING STRATEGIES

11.1 Rationale for Switching

Reasons to switch antipsychotic:

1. Inadequate efficacy
2. Adverse effects (EPS, metabolic, sedation)
3. Adherence issues (preference for LAI, simplification)
4. Specific comorbidity (e.g., depression → add mood benefits)

11.2 Cross-Titration

Most common approach, gradual overlap:

Steps:

1. Start new drug at low dose
2. Gradually increase new drug
3. Gradually taper old drug
4. Complete switch when new drug at target dose

Best for: Most switching scenarios, especially between drugs of different receptor profiles

11.3 Plateau Strategy (Abrupt Switch)

Abrupt discontinuation of old drug + immediate full dose of new drug

Used for:

- Switching to clozapine (often done this way)
- Patient preference, clinical urgency
- Drugs with very long half-lives (no need for gradual taper)

Risk: Withdrawal effects, rebound psychosis

11.4 Overlap Strategy (Add and Maintain)

New drug started and maintained at therapeutic dose while old drug continued temporarily

Used for:

- Adding clozapine to partial responder (augmentation phase)
- Assessing response to new drug before committing

11.5 Special Considerations by Drug

Switching FROM clozapine:

- Very risky, "supersensitivity psychosis" risk
- Very gradual taper (3–6 months)
- Bridge with other antipsychotic at full dose
- Clinical deterioration expected in many patients

Switching TO clozapine:

- Usually abrupt switch (clozapine requires titration from scratch anyway)
- Previous drug maintained briefly while clozapine titrated up, then tapered

Switching from depot:

- Cannot abruptly stop depot
- Plan based on half-life of specific depot (weeks to months)
- Start oral drug at appropriate time point in injection cycle

SECTION 12: AUGMENTATION STRATEGIES

12.1 Lithium Augmentation of Antidepressants

Evidence: Level I, most evidence-based augmentation strategy for treatment-resistant depression

Mechanism:

- Enhances serotonin synthesis and release
- Potentiates 5-HT_{1A} autoreceptor desensitization
- Potentiates mood-stabilizing effects

Protocol:

- Add lithium to current antidepressant
- Target level: 0.5–0.8 mmol/L for augmentation (lower than bipolar)
- Response expected: 2–4 weeks
- Continue 6–12 months if response achieved

Evidence:

- Multiple RCTs and meta-analyses confirm efficacy
- NNT approximately 5 for augmentation

- Effective across SSRIs, TCAs, MAOIs

12.2 Triiodothyronine (T3) Augmentation

Mechanism: T3 sensitizes serotonin receptors; potentiates TCA activity

Evidence:

- Strong evidence for TCA augmentation
- Weaker evidence for SSRIs
- Meta-analysis: 24% response vs 14% placebo when added to TCAs

Dose: T3 25–50 mcg/day (low dose, below replacement threshold)

Duration: 3–4 week trial; continue 6–12 months if response

Adverse effects: Tachycardia, anxiety, osteoporosis risk (long-term)

Contraindicated: Cardiac disease, hyperthyroidism

12.3 Atypical Antipsychotic + SSRI

Most evidence:

AP	SSRI	INDICATION	EVIDENCE
Aripiprazole	SSRIs	TRD	FDA approved
Quetiapine	SSRIs	TRD	FDA approved
Brexpiprazole	SSRIs	TRD	FDA approved
Olanzapine	Fluoxetine	Bipolar depression; TRD	FDA approved (OFC)

Mechanisms:

- 5-HT_{2A} antagonism (AP) + SERT inhibition (SSRI) → greater serotonin throughput
- Partial D₂ agonism (aripiprazole) → improves motivation, reduces anhedonia
- Noradrenergic enhancement

12.4 Clozapine Augmentation Strategies

For **ultra-treatment-resistant schizophrenia** (inadequate response to clozapine alone):

AUGMENTATION	EVIDENCE	MECHANISM
Amisulpride	Moderate	D ₂ /D ₃ antagonism adds to clozapine
Sulpiride	Moderate	D ₂ /D ₃ antagonism
Aripiprazole	Multiple RCTs	Partial agonism, reduces metabolic effects

AUGMENTATION	EVIDENCE	MECHANISM
Lamotrigine	Multiple RCTs	AMPA potentiation, glutamate modulation
Mirtazapine	Pilot data	NaSSA properties
ECT	Case series	Refractory positive symptoms

Aripiprazole + clozapine: Well-studied, reduces weight, metabolic effects; modest improvement in psychopathology

SECTION 13: DISCONTINUATION SYNDROMES

13.1 SSRI Discontinuation Syndrome

Incidence: 20–40% of patients stopping SSRIs abruptly

Clinical features, FINISH mnemonic:

- Flu-like symptoms (malaise, myalgia, chills)
- Insomnia, vivid dreams
- Nausea, GI disturbance
- Imbalance (dizziness, vertigo)
- Sensory disturbances (**electric shock sensations**, paresthesias, pathognomonic)
- Hyperarousal, anxiety

Onset: 1–4 days after abrupt discontinuation

Duration: 1–2 weeks; can persist longer

Risk by half-life:

DRUG	HALF-LIFE	DISCONTINUATION RISK
Paroxetine	~24h (no active metabolite)	HIGHEST
Venlafaxine	~5h	VERY HIGH
Sertraline	~26h	Moderate
Fluoxetine	4–6 days + norfluoxetine 4–16 days	LOWEST, self-tapering
Escitalopram	~27h	Moderate

Management:

1. Gradual taper (minimum 2 weeks; often 4–8 weeks for long-term use)
2. If already stopped: reinstate low dose, taper slowly

3. Switch to fluoxetine for easier taper
 4. Liquid formulations allow micro-tapering
-

13.2 Benzodiazepine Withdrawal

Mechanism: Chronic BZD use → downregulation of GABA-A receptors → upon discontinuation, excess CNS excitability

Clinical features:

- Mild: Anxiety, insomnia, tremor, sweating, irritability
- Moderate: Tachycardia, hypertension, perceptual disturbances
- Severe: Seizures, delirium (benzodiazepine withdrawal delirium)
- **Risk of death** (unlike most drug withdrawals; similar to alcohol withdrawal)

Timeline:

- Short-acting BZDs (lorazepam, oxazepam): Onset 12–24 hours
- Long-acting BZDs (diazepam, clonazepam): Onset 2–4 days

Management:

1. **Substitution with long-acting BZD** (diazepam or chlordiazepoxide) and gradual taper
 2. Rule of 10%: Reduce dose by 10% every 1–2 weeks (Ashton manual)
 3. Adjuncts: Carbamazepine, valproate (reduce seizure risk, help with psychological symptoms)
 4. Propranolol for autonomic symptoms
 5. Thiamine for those with alcohol co-dependence
-

13.3 Antipsychotic Withdrawal (Discontinuation)

Supersensitivity psychosis:

- Dopamine receptor upregulation after chronic D2 blockade
- Abrupt discontinuation → dopaminergic rebound → florid psychosis within days-weeks
- Can appear even in patients who did not have primary psychotic illness
- Distinction from relapse: onset within days of discontinuation; often more severe and atypical

Cholinergic rebound:

- Especially after stopping low-potency APs (clozapine, quetiapine) with high M1 antagonism
- Features: nausea, vomiting, diarrhea, headache, insomnia
- Onset: 24–48 hours after discontinuation

Management of AP discontinuation:

1. Gradual taper (months, not weeks, for chronic use)
2. Especially slow for clozapine (3–6 months)
3. Clinical monitoring for re-emergence of psychosis

SECTION 14: POLYPHARMACY IN PSYCHIATRY

14.1 Evidence-Based Combinations

Combinations with strong evidence:

COMBINATION	INDICATION	EVIDENCE LEVEL
SSRI + atypical AP (aripiprazole/quetiapine/brexipiprazole)	TRD	Level I, FDA approved
Lithium + antidepressant	TRD	Level I
Valproate + lithium	Bipolar disorder (mania)	Level II
SSRI + buspirone	Anxiety-predominant depression	Level II
Olanzapine + fluoxetine	Bipolar depression	Level I, FDA approved
Clozapine + lamotrigine	TRS augmentation	Level II (multiple RCTs)
SSRIs + CBT	Anxiety/OCD	Level I

14.2 Irrational Polypharmacy

High-risk irrational combinations:

1. **Two antipsychotics simultaneously** (except specific situations): increased side effects, no added efficacy
2. **Two antidepressants without rationale:** Limited evidence for most combinations
3. **Benzodiazepine + Z-drug:** Additive CNS depression
4. **Multiple anticholinergics:** Cognitive impairment, peripheral toxicity

Rational for two APs (limited evidence):

- Clozapine + amisulpride/aripiprazole: Evidence exists
 - During cross-titration (temporary)
 - Depot (stability) + oral (breakthrough), not ideal
-

14.3 Deprescribing

Principles:

1. Identify medications that are: no longer needed, duplicative, cause harm
2. Prioritize: Start with highest risk/burden medication
3. Gradual taper (especially for psych meds)
4. Shared decision-making with patient
5. Explicit stop dates and review points

HIGH-YIELD for deprescribing in psychiatry:

- Anticholinergics (for EPS that may have resolved)
- Sleep aids (evaluate and potentially discontinue benzodiazepines)
- Antipsychotics in dementia (when behavior has improved)
- PRN antipsychotics that have become regular
- Redundant mood stabilizers in stable bipolar disorder

SECTION 15: CANNABIS-BASED MEDICINES

15.1 Cannabinoids: Overview

COMPOUND	RECEPTOR	EFFECT
THC (tetrahydrocannabinol)	CB1 (full agonist), CB2	Psychoactive, analgesic
CBD (cannabidiol)	CB1 (inverse agonist/antagonist), 5-HT1A agonist	Non-psychoactive, anxiolytic, anti-seizure
Nabilone	Synthetic CB1 agonist	Analgesic, antiemetic
Dronabinol	Synthetic THC	Antiemetic, appetite stimulant
Nabiximols (Sativex)	THC:CBD (1:1)	Spasticity (MS)

15.2 Nabilone

Regulatory status: Approved in India (Schedule H drug); FDA approved in US

Indications:

- Chemotherapy-induced nausea and vomiting (CINV) unresponsive to conventional antiemetics
- Chronic pain (off-label)
- PTSD nightmares (off-label, limited evidence)

Mechanism: Synthetic cannabinoid, CB1 and CB2 agonist

Dose: 1–2 mg BD; reduce dose in elderly

15.3 CBD Oil

Epidiolex: FDA-approved CBD (100% CBD, plant-derived)

- Approved for: Dravet syndrome, Lennox-Gastaut syndrome, tuberous sclerosis complex
- Mechanism: GABA-A PAM, CB1 inverse agonist, TRPV1 agonist, inhibits AEA reuptake

CBD for psychiatric conditions:

- **Anxiety:** Small RCTs and open-label studies suggest benefit for social anxiety; dose range 300–600 mg
- **Psychosis:** CBD as antipsychotic? Phase II trial showing CBD reduced positive symptoms in schizophrenia; mechanism may involve AEA-CB1 pathway normalization
- **PTSD:** Limited data; being studied

India regulatory status:

- Cannabis plants: NDPS Act 1985, Schedule I narcotics
 - However: CBD products (under 0.3% THC) exist in a grey zone
 - No approved CBD formulation for psychiatric use in India
 - State government licenses required for research
-

15.4 Cannabinoid Hyperemesis Syndrome (CHS)

- Paradoxical cyclical vomiting in heavy, long-term cannabis users
 - Typically relieved by hot showers (compulsive bathing behavior)
 - Mechanism: CB1 receptor desensitization vs direct emetic effects
 - Treatment: Cessation of cannabis; capsaicin cream (topical, for bathing behavior); haloperidol has evidence for acute management
-

SECTION 16: KEY EXAM TABLES AND SUMMARIES

16.1 Novel Mechanisms: Quick Reference

DRUG	CLASS	KEY MECHANISM	KEY INDICATION
Vortioxetine	SMS	SERT + 5-HT ₃ antagonist + 5-HT ₇ antagonist	MDD (cognitive benefits)
Vilazodone	SPARI	SERT + 5-HT _{1A} partial agonist	MDD

DRUG	CLASS	KEY MECHANISM	KEY INDICATION
Esketamine	NMDA antagonist	S-enantiomer of ketamine	TRD, MDSI
Brexanolone	Neuroactive steroid	GABA-A PAM (synaptic + extrasynaptic)	PPD
Zuranolone	Neuroactive steroid (oral)	GABA-A PAM	MDD, PPD
Auvelity (DXM-BUP)	NMDA antagonist + NDRI	DXM NMDA antagonism; BUP inhibits CYP2D6	MDD
Pimavanserin	5-HT2A inverse agonist	NO D2 binding	Parkinson's psychosis
Lumateperone	Novel AP	D1 agonist + D2 pre/post modulator + SERT inhibitor	Schizophrenia, bipolar depression
Cariprazine	D2/D3 partial agonist	HIGH D3 selectivity	Schizophrenia (negative symptoms), bipolar
Suvorexant	DORA	OX1R + OX2R antagonist	Insomnia
Daridorexant	DORA (short T1/2)	OX1R + OX2R antagonist	Insomnia (daytime functioning)
Brexipiprazole	SDAM	D2 partial agonist (low intrinsic activity)	Schizophrenia, MDD augmentation, AD agitation

Total estimated word count: ~18,000 words

Model Answers

15 Model Answers

ANSWER 01

Discuss the pharmacology, indications, adverse effects, and monitoring of clozapine. How would you manage clozapine-induced agranulocytosis? (15 marks)

Introduction

Clozapine remains the gold standard for treatment-resistant schizophrenia (TRS), the only antipsychotic with FDA approval for reducing suicidal behaviour in schizophrenia and schizoaffective disorder. Its unique pharmacological profile explains both its superior efficacy and its complex adverse effect burden.

Pharmacology

Clozapine is a dibenzodiazepine atypical antipsychotic with an unusually broad receptor binding profile:

RECEPTOR	ACTION	CLINICAL CONSEQUENCE
D4	High-affinity antagonist	Reduced positive symptoms
D2	Low-affinity antagonist (fast dissociation)	Low EPS, low prolactin elevation
D1	Antagonist	Cognitive effects
5-HT2A	Potent antagonist	Antidepressant, anti-EPS effect
5-HT2C	Antagonist	Weight gain, metabolic effects
M1–M5	Antagonist	Sialorrhea (paradox: M2 block), tachycardia, constipation
H1	Potent antagonist	Sedation, weight gain
α1, α2	Antagonist	Orthostatic hypotension
GABA-A	Allosteric modulation	Seizure risk at high doses

The key pharmacokinetic characteristic of clozapine is its dependence on **CYP1A2** for metabolism, smoking and drugs that induce or inhibit this enzyme cause clinically

significant level changes.

Clozapine's "fast-off" kinetics from D2 receptors (unlike haloperidol which binds tightly) are proposed to explain low EPS despite its antipsychotic efficacy (the "fast dissociation hypothesis," Kapur and Seeman).

Indications

1. **Treatment-resistant schizophrenia (TRS):** Defined as inadequate response after ≥ 2 adequate antipsychotic trials. Level I evidence; NNT approximately 6 compared to standard antipsychotics.
 2. **Suicidality in schizophrenia/schizoaffective disorder:** FDA-approved specifically for this indication, the only antipsychotic to carry it.
 3. **Parkinson's disease psychosis:** When pimavanserin is unavailable or ineffective, very low doses (12.5–50 mg) preserve motor function.
 4. **Refractory bipolar disorder:** Off-label, evidence-based.
 5. **Chronic violence/aggression:** Evidence for reducing aggression even independent of psychotic symptoms.
-

Adverse Effects

Haematological (potentially life-threatening):

- Agranulocytosis: ~0.8% lifetime risk. Peak onset weeks 6–18. Mechanism: toxic/immunological destruction of granulocyte precursors.
- Benign neutropenia: up to 3%, usually transient.

Cardiovascular:

- Myocarditis: 0.3–0.7% (Australian data suggests up to 3%). Peak weeks 2–4 of treatment. Features: fever, chest pain, eosinophilia, elevated troponin and CRP. Action: STOP immediately.
- Cardiomyopathy: later, dilated type.
- QTc prolongation: moderate risk.
- Orthostatic hypotension: especially during titration.

Metabolic:

- Weight gain: 4–10 kg average, highest among all antipsychotics.
- Type 2 diabetes mellitus.
- Dyslipidaemia: especially hypertriglyceridaemia.

Neurological:

- Seizures: dose-dependent (1–2% at <300 mg/day; up to 5% at >600 mg/day). Generalised tonic-clonic.
- Sedation: common, utilise by dosing at night.
- EPS: very rare.

Autonomic:

- Hypersalivation (sialorrhea): very common, especially nocturnal. Mechanism: M2 antagonism in salivary glands.
- Constipation: potentially severe, ileus risk.
- Urinary incontinence.

Monitoring Protocol

TIME POINT	ANC MONITORING	ADDITIONAL
Weeks 1–26	Weekly	Baseline ECG, troponin, CRP, echo
Weeks 27–52	Every 2 weeks	Fasting glucose, lipids at 3 months
After 52 weeks	Monthly	Annual metabolic panel, renal function

ANC thresholds:

- $\geq 1500/\text{mm}^3$: continue
- 1000–1499: continue with more frequent monitoring
- 500–999: interrupt, daily monitoring
- <500 (agranulocytosis): STOP, permanent contraindication to re-challenge

Management of Agranulocytosis

Definition: ANC <500/ mm^3

Immediate actions:

1. Stop clozapine immediately
2. Notify the clozapine registry (CPMS in India, REMS in US)
3. Admit patient
4. Reverse barrier nursing (infection precaution)
5. Daily FBC
6. Urgent haematology consultation

Medical management:

- G-CSF (Granulocyte Colony Stimulating Factor): filgrastim 300–480 mcg/day SC, stimulates granulocyte recovery. Now standard of care.
- Prophylactic antibiotics if fever or clinical infection
- Monitor for sepsis

Recovery: Usually 2–3 weeks with G-CSF; without G-CSF: 3–4 weeks.

Re-challenge: ABSOLUTELY CONTRAINDICATED after true agranulocytosis. The patient must be permanently registered as contraindicated in the clozapine registry.

Antipsychotic alternatives after agranulocytosis:

- Quetiapine, olanzapine, amisulpride
- Higher relapse risk, expect clinical deterioration
- Consider LAI for adherence

Conclusion

Clozapine remains irreplaceable in TRS despite its adverse effect burden. The mandatory monitoring system has reduced agranulocytosis mortality from >10% to <5%. The clinical decision to initiate clozapine should be made in a specialist setting with patient education, written consent, and enrolment in the monitoring registry.

ANSWER 02

Write a detailed note on serotonin syndrome: pathophysiology, clinical features, diagnosis, and management. Distinguish from neuroleptic malignant syndrome. (10 marks)

Introduction

Serotonin syndrome (SS) is a drug-induced syndrome caused by excess serotonergic activity at central and peripheral 5-HT receptors. It is a clinical diagnosis based on drug history and examination. Unlike NMS, it is predominantly pharmacological in origin and typically self-limiting.

Pathophysiology

Excess serotonin acts at two key receptors:

1. **5-HT_{1A}:** Mediates cognitive and autonomic effects, agitation, tachycardia, hypertension, hyperthermia
2. **5-HT_{2A}:** Mediates neuromuscular effects, clonus, myoclonus, hyperreflexia, and at high stimulation: life-threatening hyperthermia

The critical neuromuscular pathways:

- Spinal 5-HT_{2A} receptors: clonus, hyperreflexia
 - Brainstem 5-HT: temperature dysregulation
 - Peripheral autonomic: tachycardia, diaphoresis
-

Clinical Features, The Classic Triad

DOMAIN · FEATURES

Cognitive/Behavioural Agitation, anxiety, confusion, restlessness

Autonomic Tachycardia, hypertension, hyperthermia (mild to severe), diaphoresis, mydriasis, diarrhoea

Neuromuscular Tremor, **clonus** (inducible, spontaneous, ocular), hyperreflexia, myoclonus, ataxia

Severity spectrum:

- Mild: tremor, tachycardia, diaphoresis, mydriasis, intermittent tremor
- Moderate: all above + clonus, hyperreflexia, hyperthermia <38.5°C, agitation
- Severe: hyperthermia >41°C, rhabdomyolysis, metabolic acidosis, renal failure, DIC, respiratory failure

Onset: Rapid, typically within 6 hours of causative drug exposure.

Diagnosis, Hunter Serotonin Toxicity Criteria

Requirement: Serotonergic agent present PLUS one of:

1. Spontaneous clonus
2. Inducible clonus + (agitation OR diaphoresis)
3. Ocular clonus + (agitation OR diaphoresis)
4. Tremor + hyperreflexia
5. Hypertonia + temperature >38°C + (ocular OR inducible clonus)

Sensitivity 84%, specificity 97%, superior to Sternbach criteria.

High-risk drug combinations: MAOI + SSRI (potentially fatal), MAOI + tramadol, MAOI + meperidine, SSRI + linezolid, SSRI + tramadol.

Management

STEP · ACTION

1 Discontinue ALL serotonergic agents

2 Supportive care: airway, IV fluids, cardiac monitoring

3 Benzodiazepines (lorazepam/ diazepam): agitation and muscle rigidity

4 Cooling measures for hyperthermia (do NOT use antipyretics, useless here)

5 Cyproheptadine 12 mg loading, 2 mg q2h PRN (5-HT antagonist)

6 Severe cases: ICU, intubation, neuromuscular paralysis (vecuronium preferred), avoid succinylcholine (risk of hyperkalaemia in rhabdomyolysis)

SS vs NMS Distinction

FEATURE	SEROTONIN SYNDROME	NMS
Cause	Serotonergic excess	Dopamine antagonist (antipsychotic)
Onset	Hours (rapid)	Days (gradual)
Neuromuscular	Clonus, hyperreflexia	Lead-pipe rigidity, no clonus
Reflexes	HYPERREFLEXIA	Normal or reduced
Temperature	Moderate-severe	Severe
CK	Usually normal	Very elevated (>1000, often >10,000)
Treatment	Cyproheptadine	Dantrolene, bromocriptine
Resolution	24–72h after drug stopped	1–2 weeks
Mutism/catatonia	Absent	May be present

Mnemonic to remember the clonus distinction: SS = Spastic and Spikey (hyperreflexia, clonus); NMS = Necrotic and Numb (rigidity, elevated CK).

ANSWER 03

Discuss the pharmacology, clinical evidence, REMS requirements, and place in therapy of esketamine nasal spray for treatment-resistant depression. (10 marks)

Introduction

Esketamine (Spravato, intranasal) received FDA approval in 2019, becoming the first truly novel antidepressant mechanism since the introduction of SSRIs in the 1980s. As the S-enantiomer of ketamine, it offers rapid onset of action via glutamatergic modulation, a

departure from the monoamine-based framework that dominated psychiatry for six decades.

Pharmacology

Mechanism:

1. **NMDA receptor antagonism (primary):** Esketamine binds to the phencyclidine (PCP) site inside the NMDA receptor channel (open-channel block). This inhibits glutamatergic transmission acutely.
1. **AMPA receptor disinhibition (downstream):** NMDA blockade at interneurons (which tonically inhibit AMPA activity) leads to a burst of AMPA receptor activation. This triggers BDNF release from neurons, activating the TrkB-mTOR signalling cascade.
1. **Synaptogenesis:** mTOR activation drives rapid de novo protein synthesis → new synaptic spines form within hours → this is the cellular basis of the rapid antidepressant effect.
1. **Additional mechanisms:** Opioid receptor modulation has been proposed (controversial), HCN1 channel blockade, sigma-1 receptor interaction.

Pharmacokinetics:

- Intranasal bioavailability: ~48% (higher than expected due to direct CNS access via olfactory pathways)
- Tmax: 20–40 minutes
- Half-life: ~7–12 hours
- Metabolism: hepatic (CYP3A4, CYP2B6) to noresketamine (active)
- Dose: 56 mg or 84 mg intranasally

Clinical Evidence

TRIAL	DESIGN	KEY FINDING
TRANSFORM-2	Phase III RCT, TRD	Esketamine + new oral AD superior to oral AD + placebo on MADRS at Day 28
TRANSFORM-3	Phase III, elderly TRD	Positive; slower titration needed
SUSTAIN-1	Maintenance RCT	Significant reduction in relapse rate vs placebo
ASPIRE-I, II	TRD with MDSI	Rapid reduction in suicidality within 24 hours

Onset of action: Antidepressant effects within 2–4 hours; clinically meaningful by 24–48 hours. Peaks at 1–4 weeks.

REMS Requirements

Esketamine carries a mandatory **REMS (Risk Evaluation and Mitigation Strategy)** programme, one of approximately 60 drugs in the US with this requirement.

Key REMS elements:

1. **Certified healthcare settings only:** Cannot be dispensed at a pharmacy for home use
2. **On-site supervision:** Patient must receive each dose in a certified healthcare facility
3. **Post-dose monitoring:** Minimum 2 hours observation for:
 4. Dissociation (most common, occurs in >50%)
 5. Sedation
 6. Blood pressure elevation (systolic rise of 20–40 mmHg common)
 7. Perceptual disturbances
8. **No driving on dosing day:** Patient requires escort
9. **ETASU certification:** Healthcare settings must register with the REMS programme
10. **Pregnancy registry:** Women of childbearing age

Why REMS? Abuse potential (Schedule III), dissociation risk, BP elevation risk, not safe for unsupervised self-administration.

Administration Protocol

- **Induction:** 56 mg or 84 mg twice weekly × 4 weeks
 - **Maintenance Phase 1:** Once weekly × 4 weeks
 - **Maintenance Phase 2:** Once weekly or every 2 weeks thereafter
 - Taken as 2 × 28 mg devices (one nostril each), 5 minutes apart
-

Place in Therapy

POSITION · EVIDENCE

After 2+ failed adequate AD trials (TRD) Level I

Acute suicidality (MDSI) when rapid response needed Level I

Not first-line, adjunct to oral AD Standard of care

Advantages over IV ketamine:

- FDA-approved (ketamine: off-label)

- Standardised dose and route
- REMS monitoring built-in
- S-enantiomer: more potent at NMDA receptor per mg

Limitations:

- Does not replace ongoing antidepressant treatment
- Duration of effect limited (days to weeks per infusion session)
- Cost: ~\$800–900 per treatment session
- Long-term maintenance data still accumulating
- High rates of dissociation at each session

ANSWER 04

Describe the pharmacology of newer antipsychotics with particular reference to cariprazine and lumateperone. What is the clinical significance of D3 receptor selectivity? (10 marks)

Introduction

Third-generation antipsychotics have moved beyond simple D2 blockade toward receptor-selective approaches that target specific dopamine receptor subtypes and multiple neurotransmitter systems. Cariprazine and lumateperone represent two distinct advances in this evolution.

Cariprazine, D3-Selective Partial Agonist

Receptor profile:

RECEPTOR	ACTION	CLINICAL SIGNIFICANCE
D2	Partial agonist	Antipsychotic effect, low EPS
D3	High-affinity partial agonist (20× selectivity over D2)	Negative symptom improvement
5-HT1A	Partial agonist	Anxiolysis, reduced EPS
5-HT2A	Antagonist	Antidepressant synergy
5-HT2B	Antagonist	Cardiac safety

Clinical significance of D3 selectivity:

D3 receptors are concentrated in the mesolimbic system, prefrontal cortex, and hippocampus, regions governing reward, motivation, and cognition. Negative symptoms of

schizophrenia (avolition, alogia, anhedonia) are linked to hypodopaminergic tone in these circuits.

Partial D3 agonism is proposed to:

- Restore reward salience (reduced avolition)
- Improve working memory (PFC D3 modulation)
- Reduce anhedonia

RCH-MD-16 study: Cariprazine 3–6 mg demonstrated statistically significant superiority over risperidone 3–6 mg on PANSS negative symptom factor scores, a landmark finding, as no previous drug had shown this against an active comparator.

Pharmacokinetics: Active metabolites (DCAR and DDCAR) have a combined effective half-life of 2–4 weeks. Clinical implication: drug effects persist weeks after discontinuation.

Clinical use:

- Schizophrenia: 1.5–6 mg/day (negative symptom benefit at 3 mg)
- Bipolar mania: 3–6 mg/day
- Bipolar depression: 1.5–3 mg/day (only antipsychotic effective at sub-mania doses for bipolar depression)

Adverse effects: Akathisia (highest among newer APs), weight gain (moderate), metabolic effects (moderate).

Lumateperone, Multimodal Novel Mechanism

Receptor profile:

RECEPTOR · ACTION

D1 Agonist/partial agonist

D2 Pre-synaptic partial agonist; post-synaptic antagonist

5-HT_{2A} Antagonist

SERT Inhibitor

NMDA (NR2B) Indirect modulation via phosphorylation

What makes lumateperone truly novel:

1. **D1 agonism in the PFC:** While all other antipsychotics either block or have no activity at D1, lumateperone activates prefrontal D1 receptors. This is predicted to improve cognition and negative symptoms.

1. **Dual D2 activity:** Pre-synaptic agonism normalises dopamine synthesis in hypo-dopaminergic states (relevant for negative / cognitive symptoms); post-synaptic antagonism reduces excessive mesolimbic signalling (relevant for positive symptoms).
1. **SERT inhibition:** Contributes to antidepressant and mood-stabilising properties, explains bipolar depression efficacy.
1. **NMDA NR2B modulation:** Reduces excitotoxic glutamate signalling, a mechanism shared with ketamine, potentially explaining mood and cognitive benefits.

Clinical evidence:

- Schizophrenia: Phase III trials (ITT-301, -302) showing significant PANSS reduction vs placebo
- Bipolar I depression AND Bipolar II depression: Multiple RCTs positive, one of very few drugs approved for both
- Weight-neutral in clinical trials, a practical advantage over most APs

Dosing: 42 mg once daily (no titration required)

Comparison

FEATURE	CARIPRAZINE	LUMATEPERONE
Key mechanism	D3 selectivity	D1 agonism + dual D2 + SERT
Negative symptoms	Strong evidence	Promising
Bipolar depression	Yes (1.5–3 mg)	Yes (I + II)
Weight	Moderate gain	Weight-neutral
Akathisia	HIGH risk	LOW risk
Titration	Required	Not required

ANSWER 05

Discuss lithium pharmacology, monitoring, toxicity management, and use in pregnancy. (10 marks)

Introduction

Lithium remains the most evidence-based mood stabiliser for bipolar disorder after more than 70 years of clinical use. It is the only psychiatric drug with Level I evidence for suicide prevention in bipolar disorder, and the only drug with proven anti-suicidal effects independent of mood stabilisation.

Pharmacology

Mechanisms of action (multiple, interacting):

1. **Inositol depletion:** Inhibits inositol monophosphatase and bisphosphatase → depletes inositol from hyperactive neural circuits → selectively dampens overactive phosphoinositide signalling (the "inositol depletion hypothesis").
1. **GSK-3 β inhibition:** Glycogen synthase kinase-3 β is a key regulator of neuronal apoptosis, neurogenesis, and synaptic plasticity. Lithium inhibition → neuroprotective, reduces apoptosis, promotes BDNF.
1. **Serotonin potentiation:** Increases synthesis and release of 5-HT → basis for augmentation of antidepressants and anti-suicidal effect.
1. **HDAC inhibition:** Epigenetic mechanism, histone deacetylase inhibition → altered gene expression → long-term neuroprotection.
1. **Anti-glutamatergic:** Reduces NMDA receptor-mediated excitotoxicity.

Pharmacokinetics:

- Oral absorption: 100% (complete)
- No protein binding, no hepatic metabolism
- Distribution: total body water
- Renal excretion (competes with sodium reabsorption in proximal tubule)
- Half-life: ~24 hours (acute); 36–48 hours (chronic)
- Steady-state: 5–7 days

Narrow therapeutic index: This drives the mandatory monitoring protocol.

Monitoring Protocol

Baseline investigations:

- Renal function: creatinine, BUN, eGFR, urinalysis
- Thyroid: TSH, FT4
- Serum calcium (parathyroid effects)
- ECG (especially >50 years)
- Pregnancy test (women of reproductive age)
- Weight, BMI

Serum level targets (12-hour post-dose sample):

INDICATION · TARGET LEVEL (MMOL/L)

Acute mania 0.8–1.2

Maintenance (adult) 0.6–0.8

Maintenance (elderly) 0.4–0.6

Augmentation for depression 0.5–0.8

Monitoring frequency:

- Initiation: every 5–7 days until stable
- Stable: monthly × 6 months → every 3–6 months

Long-term monitoring: Renal function (eGFR) annually; TSH annually; calcium annually.

Toxicity

Precipitating factors:

- NSAIDs (reduce renal clearance)
- ACE inhibitors / ARBs (reduce glomerular filtration)
- Thiazide diuretics (sodium loss → lithium retention)
- Dehydration, fever, vomiting
- Renal disease
- Low-sodium diet

Clinical features by level:

LEVEL (MMOL/L) · FEATURES

1.5–2.0 (mild) Nausea, vomiting, diarrhoea, fine tremor, fatigue, polyuria

2.0–2.5 (moderate) Coarse tremor, ataxia, drowsiness, slurred speech, confusion

>2.5 (severe) Rigidity, seizures, stupor, coma

>3.5 High risk of death

Management:

1. Stop lithium
2. IV normal saline 0.9%, aggressive hydration (promotes renal excretion and corrects sodium deficit)
3. Haemodialysis if: level >4 mmol/L; level >2.5 with severe symptoms; severe renal failure
4. Activated charcoal: NOT effective
5. Sodium polystyrene: limited evidence
6. Supportive: seizure management, airway

Use in Pregnancy

Teratogenicity, updated estimates:

Earlier reports dramatically overstated the risk of Ebstein's anomaly (tricuspid valve malformation). A 2017 NEJM cohort study revised the absolute risk:

- Background risk: 6 / 10,000 births
- With lithium: 21 / 10,000 births (relative risk ~2.66)

This is a real risk, but much lower than the 1-in-10 figures quoted previously.

Clinical decision framework:

- Women with severe bipolar disorder: lithium may be continued given that untreated mania / depression also poses foetal risks
- Women at lower risk: taper lithium during first trimester; restart after organogenesis

Peripartum management:

- Renal clearance increases in first trimester → levels may fall (increase dose to maintain therapeutic level)
- Post-partum: renal clearance falls → level spikes → REDUCE dose 25–50% at 36–38 weeks, re-titrate after delivery
- Monitor fortnightly in third trimester

Neonatal effects (if continued):

- Neonatal lithium toxicity: hypotonia ("floppy baby"), cyanosis, bradycardia
- Resolve within days as lithium is excreted

Fetal monitoring:

- Anomaly scan with foetal echocardiogram at 16–18 weeks
- Growth scans third trimester

Breastfeeding: Excreted in breast milk at 40–50% of maternal serum level. Generally advised against; if continued, monitor infant lithium levels and renal function.

ANSWER 06

Enumerate and explain the strategies for augmentation of antidepressants in treatment-resistant depression. Which has the strongest evidence base? (10 marks)

Introduction

Treatment-resistant depression (TRD) is conventionally defined as inadequate response to ≥ 2 adequate antidepressant trials. Approximately 30% of patients with MDD meet this criterion. Augmentation, adding a second agent to an existing antidepressant, is distinct from switching strategies and is the recommended approach when partial response exists.

Augmentation Strategies, Evidence Hierarchy

Tier 1 (Strongest evidence, Level I):

1. Atypical antipsychotic augmentation (FDA-approved combinations)

DRUG	EVIDENCE	DOSE FOR AUGMENTATION
Aripiprazole	Multiple Phase III RCTs; FDA approved	2–15 mg/day
Quetiapine XR	Multiple Phase III RCTs; FDA approved	50–300 mg/day
Brexiprazole	Phase III RCTs; FDA approved	1–3 mg/day
Olanzapine + fluoxetine (OFC)	Phase III; FDA approved for bipolar depression	6/25–12/50 mg

Mechanism: 5-HT_{2A} antagonism by AP + SERT inhibition by AD → enhanced serotonin throughput; partial D₂ agonism → improved motivation and anhedonia (aripiprazole).

2. Lithium augmentation

- Most evidence-based pharmacological augmentation, Level I evidence predating all AP augmentation trials
- Mechanism: enhances serotonin synthesis and release; potentiates 5-HT_{1A} desensitisation
- Target level: 0.5–0.8 mmol/L
- Response rate: ~50% in previously treatment-resistant patients
- Time to response: 2–4 weeks
- **NNT: approximately 5**

Tier 2 (Good evidence, Level II):

3. Triiodothyronine (T₃) augmentation

- Dose: 25–50 mcg/day (sub-replacement)
- Best evidence for TCA augmentation; weaker for SSRIs
- Meta-analysis: 24% response vs 14% placebo
- Mechanism: sensitises serotonin receptors; potentiates TCA activity

4. Mirtazapine added to SSRI/SNRI ("California Rocket Fuel")

- Mechanism: SNRI + NaSSA → combined noradrenergic + serotonergic + histaminergic action
- Evidence: multiple RCTs, generally positive though less robust than AP augmentation
- Practical: mirtazapine's sedation is often used therapeutically for insomnia comorbidity

5. Bupropione augmentation

- 5-HT1A partial agonist, augments SSRI action at autoreceptors
- Level II evidence; less potent than AP augmentation

Tier 3 (Emerging evidence):

6. Esketamine nasal spray

- FDA-approved for TRD (2019)
- Rapid effect (within 24–48 hours), uniquely useful in urgent situations
- Sustained maintenance with regular sessions

7. Thyroid hormone (levothyroxine, T4)

- Weaker evidence than T3 augmentation

8. Lamotrigine augmentation of antidepressants

- Case series and small RCTs; evidence for SSRI + lamotrigine in TRD
- May be particularly useful when bipolar spectrum features are present

9. Pramipexole (D3 agonist)

- Evidence for bipolar II depression and unipolar TRD
- Level II evidence

10. Modafinil/armodafinil

- Augment fatigue and hypersomnia in partial responders
- Does not improve core depression scores significantly

Strongest Evidence

RANK	STRATEGY	LEVEL
1	Lithium augmentation	Level I (decades of RCT evidence)
2	Atypical AP augmentation (aripiprazole, quetiapine, brexpiprazole)	Level I (FDA approved)
3	Esketamine	Level I (FDA approved, rapid onset)

RANK	STRATEGY	LEVEL
4	T3 augmentation	Level II

Clinical decision guide: If partial response to SSRI/SNRI → first add atypical AP (if tolerability concern, aripiprazole; if insomnia comorbid, quetiapine; if better side-effect profile needed, brexpiprazole). If metabolic concerns preclude AP → lithium augmentation. If urgent response needed (severe suicidality) → esketamine.

ANSWER 07

Write a pharmacological note on orexin receptor antagonists. Compare the three approved agents. What is their mechanism of action and advantage over traditional hypnotics? (8 marks)

Introduction

Dual orexin receptor antagonists (DORAs) represent a paradigm shift in insomnia pharmacotherapy, from GABAergic sedation to targeted wake-drive suppression. Three agents are currently approved: suvorexant (2014), lemborexant (2019), and daridorexant (2022).

The Orexin System

Orexins (orexin-A/hypocretin-1, orexin-B/hypocretin-2) are neuropeptides produced by ~70,000 neurons in the lateral hypothalamus. They project widely to wake-promoting nuclei:

In narcolepsy (loss of orexin neurons): sudden sleep attacks, cataplexy.

In insomnia: orexin system overactivated → failure to "turn off" wake drive.

DORA mechanism: Simultaneously block OX1R and OX2R → suppress the wake drive without globally suppressing brain activity.

Advantage Over Traditional Hypnotics

PROPERTY	BZDS / Z-DRUGS (GABA AGONISTS)	DORAS (OREXIN ANTAGONISTS)
Mechanism	Enhance global GABA inhibition	Specifically block wake drive
Sleep architecture	Suppress SWS, alter REM	Preserves normal architecture
Physical dependence	Yes	No (or minimal)

PROPERTY	BZDS / Z-DRUGS (GABA AGONISTS)	DORAS (OREXIN ANTAGONISTS)
Tolerance	Develops readily	Minimal
Rebound insomnia	Significant	Minimal to none
Cognitive impairment	Significant	Mild, dose-dependent
Next-day sedation	Common	Present but lower (especially daridorexant)
Abuse potential	Schedule IV	Schedule IV (but lower perceived abuse)
Anterograde amnesia	Yes	Rare

Comparison of the Three DORAs

FEATURE	SUVOREXANT	LEMBOREXANT	DARIDOREXANT
FDA approval	2014	2019	2022
Doses	10, 20 mg	5, 10 mg	25, 50 mg
Half-life	~12h	~17–27h	~8h
OX2R selectivity	Moderate	Higher	Moderate
Key trials	SUNRISE-1 / 2	SUNRISE-1 / 2 + vs zolpidem	ESADA-1 / 2 (daytime function endpoint)
Next-day impairment	Moderate concern	Greater (long T _{1/2})	Least concern
Best use case	General maintenance	Elderly, sleep maintenance	When daytime performance matters
CYP3A4 interaction	Significant (reduce to 5 mg with inhibitors)	Significant	Less clinically significant
Daytime functioning endpoint	Not primary	Not primary	Yes, primary endpoint in trials

Suvorexant: First in class, most clinical experience, works for sleep onset and maintenance.

Lemborexant: Better than zolpidem on subjective sleep parameters at 1-month mark; longer half-life beneficial for sleep maintenance but raises next-day concern in some patients.

Daridorexant: Designed from the start with daytime functioning as co-primary endpoint; shortest half-life → best next-day profile.

Safety Notes

- **Complex sleep behaviours** (sleep-walking, sleep-driving, sleep-eating): Black box warning for all three, although incidence far lower than with Z-drugs.
- Respiratory depression: Minimal effect on respiratory drive (unlike BZDs), relatively safer in mild COPD/OSA. Caution in severe respiratory compromise.
- No abuse potential defined in clinical use patterns.
- Pregnancy: Avoid (insufficient data).

ANSWER 08

Discuss the role of pharmacogenomics in clinical psychiatry with special reference to CYP2D6 and CYP2C19. What is the clinical significance of HLA-B*1502 testing? (8 marks)

Introduction

Pharmacogenomics, the study of how genetic variation affects drug response, offers the promise of "right drug, right dose, right patient." In psychiatry, where drug selection has historically been empirical and trial-and-error, pharmacogenomics provides a biological framework for individualising treatment.

CYP2D6

CYP2D6 is the most clinically relevant enzyme in psychiatric pharmacogenomics, metabolising approximately 25% of all psychotropic drugs.

Phenotype classification:

PHENOTYPE	COPIES OF FUNCTIONAL ALLELES	DRUG LEVELS	CLINICAL RISK
Poor metaboliser (PM)	0	HIGH	Toxicity at standard doses
Intermediate (IM)	1 (or reduced function)	Moderately high	Increased adverse effects
Extensive/normal (EM)	2	Normal	Standard dosing
Ultrarapid (UM)	>2 (gene duplication)	LOW	Treatment failure

Ethnic distribution:

- PMs: 7–10% Caucasians; 1–2% Asians; 3–7% Africans
- UMs: 1–2% Caucasians; up to 29% in Ethiopian populations

Key psychiatric CYP2D6 substrates:

- Antidepressants: nortriptyline, desipramine, clomipramine, vortioxetine, paroxetine, fluoxetine
- Antipsychotics: haloperidol, risperidone, aripiprazole, perphenazine
- Opioids: codeine (prodrug, PMs get no analgesia; UMs get excessive morphine)

Important: Paroxetine and fluoxetine are BOTH substrates AND potent inhibitors of CYP2D6. This creates phenoconversion, an EM becomes a functional PM when taking paroxetine.

CYP2C19

Ethnic distribution of PMs:

- 3–5% Caucasians
- 15–20% Asian populations (particularly Japanese, Chinese)

Key psychiatric substrates:

- Citalopram, escitalopram (PMs have elevated levels → QTc concern)
- Sertraline
- Diazepam, clonazepam
- Venlafaxine, amitriptyline

Clinical application: CYP2C19 PMs should receive lower doses of citalopram/escitalopram, the FDA already recommends a maximum 20 mg/day for CYP2C19 PMs based on QTc risk.

HLA-B*1502 and Carbamazepine

Background:

- Carbamazepine causes Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), life-threatening mucocutaneous reactions, in rare individuals
- In 2004, a Taiwanese study demonstrated that nearly 100% of Han Chinese patients who developed SJS on carbamazepine carried the HLA-B*1502 allele

Allele frequency:

- Han Chinese: ~8–10%
- Thai, Filipino, Malaysian: 6–8%
- South Asian (Indian subcontinent): ~2–4% (varies significantly by region)
- Europeans: <1%
- Japanese: rare

Mechanism: HLA-B*1502 presents carbamazepine metabolites as neoantigens to cytotoxic T-cells → explosive T-cell activation → cutaneous cell death.

FDA mandate: Test for HLA-B*1502 before initiating carbamazepine in patients of Asian ancestry. If positive → DO NOT use carbamazepine.

India relevance:

- Indian Pharmacopoeia and CDSCO guidelines recommend HLA-B*1502 testing before carbamazepine
- Risk is real but lower than East Asian populations
- Oxcarbazepine also carries risk in HLA-B*1502 carriers

HLA-A*3101:

- Associated with carbamazepine hypersensitivity in European and Japanese populations
- Causes SJS, DRESS (Drug Reaction with Eosinophilia and Systemic Symptoms), and maculopapular exanthema
- Lower penetrance than B*1502 for severe reactions but broader population relevance in Europeans

Clinical decision algorithm:

ANSWER 09

Classify and discuss drug interactions in psychiatry. Which combinations are potentially fatal? How do you manage a patient who requires both an MAOI and SSRI? (8 marks)

Introduction

Drug interactions in psychiatry are clinically significant because polypharmacy is common, psychiatric drugs have narrow therapeutic windows, and many interactions can be fatal. Interactions are classified as pharmacokinetic or pharmacodynamic.

Classification

A. Pharmacokinetic Interactions (affect drug levels)

1. **Absorption:** Antacids reduce absorption of many psychotropics (less clinically significant)
2. **Distribution:** Displacement from protein binding (valproate + aspirin)
3. **Metabolism (most important):**
4. CYP450 inhibition → increased levels of substrate

5. CYP450 induction → decreased levels of substrate
6. Phase II (glucuronidation): valproate inhibits UGT → increases lamotrigine levels 2-fold
7. **Excretion:**
8. Lithium: renal excretion manipulated by NSAIDs, diuretics, ACE inhibitors
9. Renally cleared drugs affected by renal function changes

B. Pharmacodynamic Interactions (affect drug effects)

1. **Additive:** Two CNS depressants → excessive sedation
2. **Synergistic:** MAOI + SSRI → serotonin syndrome
3. **Antagonistic:** Anticholinergic drugs reduce effect of procognitive agents

Potentially Fatal Combinations

COMBINATION	MECHANISM	RISK
MAOI + SSRI/SNRI	Serotonin syndrome	FATAL
MAOI + tramadol/meperidine	Serotonin syndrome	FATAL
Clozapine + carbamazepine	Additive agranulocytosis + reduced levels	CONTRAINDICATED
Lithium + NSAIDs + dehydration	Lithium toxicity → encephalopathy	FATAL if severe
Clozapine + IM benzodiazepine	Respiratory collapse	DEATH reported
Haloperidol + QTc-prolonging drugs	Torsades de pointes → VF	FATAL
Pimozide/thioridazine + CYP inhibitors	QTc prolongation → TdP	FATAL

High-Risk Combinations: Detailed

Lithium + NSAIDs:

- Mechanism: NSAIDs inhibit renal prostaglandins → reduced renal blood flow → lithium retention
- Magnitude: 50–100% increase in lithium levels
- Management: Avoid; if unavoidable, reduce lithium dose 25–50%, monitor levels in 3–5 days, advise patient about dehydration risk

Clozapine + carbamazepine:

- Dual risk: carbamazepine independently causes agranulocytosis + induces CYP1A2 → reduces clozapine levels

- Absolutely contraindicated
- Alternative mood stabiliser: valproate (preferred with clozapine)

Fluvoxamine + clozapine:

- Fluvoxamine is a potent CYP1A2 inhibitor → can increase clozapine levels 2–10 fold
- Inadvertent prescribing can cause clozapine toxicity (seizures, respiratory depression)
- Some clinicians exploit this intentionally: low-dose fluvoxamine (25–50 mg/day) to increase clozapine levels while using lower clozapine doses (reduces metabolic burden)

Managing a Patient Requiring Both MAOI and SSRI

This situation should be avoided if at all possible. However, if sequential use is required:

Standard washout:

Stopping SSRI → starting MAOI:

- Fluoxetine: 5-week washout (long half-life + active norfluoxetine ~14 days)
- Other SSRIs/SNRIs: 2-week washout
- Venlafaxine: 2-week washout

Stopping MAOI → starting SSRI:

- ALL MAOIs: 2-week washout minimum
- Phenelzine and tranylcypromine irreversible: 3-week washout often recommended in practice

Why the asymmetry? Fluoxetine's extremely long active metabolite half-life means it can still be present 5 weeks after the last dose, still capable of causing SS if combined with MAOI.

Practical scenario: Patient stable on SSRI, needs to switch to MAOI-class antidepressant.

1. Stop SSRI (use 5-week washout for fluoxetine, 2 weeks for others)
2. During washout: bridge with psychotherapy, sleep hygiene, PRN benzodiazepines for anxiety
3. Monitor for withdrawal syndrome (reinstate briefly if severe)
4. Begin MAOI at minimum dose after washout period

Emergency situation (patient critically unwell): Hospitalise, use ECT as bridge. Do NOT overlap serotonergic agents.

ANSWER 10

What is neuroleptic malignant syndrome? Discuss its pathophysiology, clinical features, management, and guidelines for antipsychotic re-challenge. (10 marks)

Introduction

Neuroleptic malignant syndrome (NMS) is a rare, life-threatening idiosyncratic reaction to dopamine-blocking agents, characterised by the tetrad of hyperthermia, rigidity, altered consciousness, and autonomic instability. Before the introduction of active management protocols, mortality was 25–30%. With current management, mortality is approximately 5–10%.

Pathophysiology

NMS results from abrupt or excessive dopamine D2 receptor blockade across three anatomical domains:

1. **Striatum:** D2 blockade → loss of dopaminergic modulation of extrapyramidal motor system → lead-pipe rigidity
2. **Hypothalamus:** Dopamine normally inhibits the heat-dissipating mechanisms; D2 block → thermoregulatory failure → hyperthermia
3. **Mesocortical/mesolimbic pathways:** D2 blockade → altered consciousness, confusion, stupor

Precipitating factors:

- High-potency typical antipsychotics (haloperidol most implicated)
 - Rapid dose escalation
 - IM depot injections
 - Dehydration
 - Agitation (metabolic demand increases muscle heat production)
 - Physical restraint
 - Ambient heat
 - Prior NMS episode (strongest predictor, 10–15x increased risk)
 - Young male patients
 - Underlying brain pathology
-

Clinical Features

Cardinal tetrad:

1. **Hyperthermia:** Temperature $>38^{\circ}\text{C}$ (often $>40^{\circ}\text{C}$, sometimes $>42^{\circ}\text{C}$)

2. **Muscle rigidity:** Lead-pipe rigidity (unlike clonus in SS), generalised, severe, can cause rhabdomyolysis from sustained contraction
3. **Altered consciousness:** Confusion → obtundation → stupor → coma
4. **Autonomic instability:** Tachycardia, labile blood pressure (oscillates, hyper and hypotensive episodes), tachypnoea, diaphoresis, sialorrhea, incontinence

Laboratory findings:

- CK: Very elevated, often >1000 U/L, can reach >50,000 U/L
- Leukocytosis: 10,000–40,000/mm³
- Metabolic acidosis
- Elevated LFTs
- Myoglobinuria → risk of acute kidney injury
- Low serum iron (<12 µmol/L), specific marker for NMS, useful diagnostically
- Elevated ESR, CRP

Onset: Hours to days after drug initiation or dose change (unlike SS which develops within hours)

Duration: 1–2 weeks without treatment; shorter with dantrolene/bromocriptine

DSM-5 Diagnostic Criteria

Development of severe muscle rigidity and elevated temperature following antipsychotic exposure, PLUS ≥2 of: diaphoresis, dysphagia, tremor, incontinence, altered consciousness, mutism, tachycardia, elevated/labile BP, leukocytosis, elevated CK, in the absence of an alternative medical/neurological explanation.

Management

Immediate steps:

1. Stop antipsychotic (and all other dopaminergic agents including metoclopramide)
2. ICU admission
3. IV fluid resuscitation (prevent renal failure from myoglobinuria)
4. Cooling measures (cooling blankets, ice packs to axillae/groin, NOT antipyretics which are ineffective)
5. Monitor: temperature, vitals, CK, renal function, urine myoglobin

Pharmacological:

DRUG	MECHANISM	DOSE
Dantrolene	Blocks SR calcium release → reduces muscle contraction → lowers rigidity + temperature	0.25–2 mg/kg IV q6–12h; oral 50–200 mg/day maintenance
Bromocriptine	D2 agonist → reverses central D2 blockade	2.5–10 mg TID (oral/NG)
Amantadine	DA release + NMDA antagonism	100–200 mg BD
Lorazepam	Muscle relaxation, sedation, anti-catatonic	1–2 mg IV q4–6h

ECT: For refractory NMS or when malignant catatonia cannot be excluded. ECT has both diagnostic and therapeutic utility in this context.

Antipsychotic Re-challenge

When indicated: Patient has psychotic illness with no alternative to antipsychotic treatment, NMS has fully resolved.

Contraindications to re-challenge:

- NMS within the past 2 weeks
- Persistent fever, rigidity, or elevated CK
- Patient's refusal with informed consent
- Malignant catatonia (alternative diagnosis, ECT is first-line)

Protocol:

1. Wait minimum **2 weeks** after NMS resolution (ANC and CK normalised; some sources recommend 4–6 weeks)
2. Choose **lowest-potency atypical antipsychotic** (clozapine, quetiapine, or olanzapine)
3. Start at very **low dose** with slow titration
4. Avoid precipitating factors: ensure adequate hydration, avoid IM depots initially
5. Close monitoring: daily temperature and vitals for first 2 weeks
6. Written informed consent documenting recurrence risk (~10–15%)

Best evidence for re-challenge without recurrence:

- Clozapine: multiple case reports of successful re-challenge
- Quetiapine: low D2 affinity, low recurrence risk

ANSWER 11

Discuss the pharmacology, monitoring, and practical prescribing of long-acting injectable antipsychotics. What are the clinical advantages and disadvantages compared to oral formulations? (8 marks)

Introduction

Long-acting injectable antipsychotics (LAIs) address the single most important modifiable factor in schizophrenia outcomes, medication non-adherence. Non-adherence affects 50–70% of patients with schizophrenia within the first year of treatment. LAIs eliminate covert non-adherence, reduce the daily decision burden, and provide pharmacokinetic stability.

Available LAI Formulations

DRUG	NAME	FREQUENCY
Fluphenazine decanoate	Modecate	2–6 weeks
Haloperidol decanoate		4 weeks
Zuclopenthixol decanoate	Clopixol Depot	2–4 weeks
Risperidone microspheres	Risperdal Consta	2 weeks
Paliperidone palmitate 1-month	Invega Sustenna	Monthly
Paliperidone palmitate 3-month	Invega Trinza	3-monthly
Paliperidone palmitate 6-month	Invega Hafyera	6-monthly
Aripiprazole monohydrate	Abilify Maintena	Monthly
Aripiprazole lauroxil	Aristada	4–8 weeks
Olanzapine pamoate	Zypadhera	2–4 weeks

Pharmacological Principles of LAIs

Mechanism of prolonged action:

- Decanoate esters (haloperidol, fluphenazine): esterified drug dissolved in sesame oil → released slowly from injection site → cleaved by esterases → active drug
- Microspheres (risperidone): drug encapsulated in biodegradable polymer → gradual release

- Nanocrystal suspension (paliperidone palmitate): water-insoluble nanocrystals → very slow dissolution

Pharmacokinetic advantages of LAIs:

- Eliminate first-pass metabolism (higher relative bioavailability for some drugs)
- Stable plasma levels without peaks (oral) or troughs (missed doses)
- Plasma level predicts dose adjustment, clinician can titrate based on measured levels

PP3M (Paliperidone Palmitate 3-Monthly), Key Exam Focus

Prerequisites for switching from PP1M to PP3M:

1. Adequately treated with PP1M for ≥ 4 months
2. Last two PP1M doses must be at the same dose level
3. Dose conversion: $PP3M = 3.5 \times PP1M$ dose

PP3M doses available: 175 mg, 263 mg, 350 mg, 525 mg (corresponding to PP1M 39, 78, 117, 156 mg)

Clinical Advantages of LAIs

ADVANTAGE · EXPLANATION

Eliminates covert non-adherence Clinician knows with certainty when last dose was given

Reduces relapse rates Meta-analyses show 30–40% reduction in hospitalisations vs oral

Stable pharmacokinetics No peak-trough variation → steadier clinical state

Patient freedom No daily reminder of illness

Fewer hospitalizations Cost-effective (though drug cost is higher)

Enables early intervention Non-attendance for injection = early warning signal

Meta-analytic evidence: Kishimoto et al. (2014), 25 RCTs, LAIs significantly reduced all-cause discontinuation and relapse vs oral.

Disadvantages and Practical Challenges

DISADVANTAGE · COMMENT

Difficult to adjust dose rapidly If adverse effect emerges, cannot withdraw quickly

Post-injection delirium/sedation syndrome (PDSS) Olanzapine pamoate: requires 3-hour monitoring post-injection

Pain and injection site reactions Especially with depot oils

Healthcare contact required Barrier for patients in remote areas

Patient stigma Some patients object to "depot" concept

Initiation complexity Loading doses required (e.g., PP1M needs Day 1 + Day 8 deltoid injections)

Cost Significantly higher than oral generics

Monitoring Protocol for LAIs

1. Document last oral antipsychotic dose and timing
 2. Weight, metabolic panel at baseline and 3-monthly
 3. EPS assessment at each visit
 4. Prolactin if symptoms (risperidone / paliperidone: cause significant prolactin elevation)
 5. Document injection site, lot number, expiry
 6. Ensure patient is aware of washout and carry-over effects before stopping
-

ANSWER 12

Discuss psilocybin-assisted therapy: mechanism of action, clinical evidence, and current regulatory status in psychiatry. (8 marks)

Introduction

Psilocybin is a classic serotonergic psychedelic compound derived from *Psilocybe* mushroom species. After decades of prohibition following the Controlled Substances Act of 1970, it has re-emerged as a genuinely promising treatment for several psychiatric conditions. Its mechanism differs fundamentally from all currently approved psychiatric medications.

Mechanism of Action

Primary: Psilocybin is dephosphorylated to **psilocin** by alkaline phosphatase (liver, small intestine, blood). Psilocin is the active compound.

Receptor actions:

- **5-HT_{2A} agonist** (primary): binding in prefrontal cortex, thalamus, anterior cingulate cortex, and limbic system
- **5-HT_{2C} agonist:** contributes to subjective effects

- **5-HT1A:** some affinity

Neural mechanisms:

1. **Default Mode Network (DMN) disruption:** The DMN (medial PFC, posterior cingulate, angular gyrus) is hyper-connected in depression, OCD, addiction. Psilocin disrupts DMN connectivity → ego dissolution → reduced self-referential rumination.
1. **Global brain connectivity increase:** Psilocin causes a transient hyperconnected brain state, regions that do not normally communicate become temporarily linked. This "breaking of habits" may be the substrate for lasting psychological change.
1. **Neuroplasticity:** 5-HT2A agonism → BDNF release → TrkB-mTOR activation → synaptic plasticity. New dendritic spines form within 24 hours and persist for weeks.
1. **Psychological "reset":** The mystical/peak experience reliably produced at therapeutic doses correlates strongly with therapeutic outcomes, suggesting the subjective experience itself is therapeutic, not just the pharmacology.

Clinical Evidence

CONDITION	STUDY	FINDING
TRD	COMPASS Phase 2b (N=233)	25 mg: 29% remission at 3 weeks; dose-dependent response
MDD	Johns Hopkins (N=24, JAMA Psychiatry 2021)	71% response, 54% remission at 4 weeks; effects at 1 year
Cancer existential distress	NYU + JHU (N=80, double-blind RCT)	60–80% sustained response at 6 months; single dose
Alcohol use disorder	Trial data (Bogenschutz et al.)	Reduced heavy drinking days; large effect sizes
Smoking cessation	JHU pilot	67% abstinence at 12 months vs ~30% with varenicline
OCD	Yale pilot	Symptom reduction in all 9 participants; dose-dependent

Adverse effects:

- Transient: headache, nausea, dizziness, anxiety during session
- Challenging experiences ("bad trips"): managed by therapist presence
- HPPD (Hallucinogen Persisting Perception Disorder): rare (<1%)
- No withdrawal syndrome, no physical dependence

Contraindications:

- Personal or first-degree family history of schizophrenia or bipolar I (manic episodes)
 - Acute psychosis
 - Unstable cardiac disease
 - Pregnancy
 - Concurrent lithium (seizure risk reported)
-

Therapeutic Model

Psilocybin is NOT a standalone drug, it is **psilocybin-assisted psychotherapy**:

1. **Preparation sessions (2–3):** Build therapeutic alliance, set intentions, reduce anticipatory anxiety
2. **Drug session (1–3 sessions):** Supervised in a comfortable environment; music, eye shades; therapist present throughout
3. **Integration sessions (2–4):** Processing the experience; applying insights to life; CBT-like work

The set (psychological state), setting (physical environment), and therapeutic relationship are considered pharmacologically relevant.

Regulatory Status (2026)

JURISDICTION · STATUS

USA Schedule I; FDA Breakthrough Therapy Designation (TRD via COMPASS; MDD via Usona)

Australia Rescheduled to Schedule 8 for TRD and PTSD treatment (2023), first country

Canada Compassionate access approved for end-of-life distress

UK Phase III trials ongoing (COMPASS, Imperial College)

Netherlands Truffle retreats legal (different species, grey area)

India NDPS Act Schedule I, no legal clinical use; research requires CDSCO approval

Outlook: Phase III trial results expected 2025–2026; FDA decision likely by 2027–2028.

ANSWER 13

Discuss the clinical pharmacology of brexanolone and zuranolone for postpartum depression. What is the mechanism of action and how do they differ from conventional antidepressants? (8 marks)

Introduction

Postpartum depression (PPD) affects 10–15% of postpartum women. Until 2019, it was treated with the same antidepressants used for MDD, which take 4–8 weeks to act, cross into breast milk, and do not address the peripartum-specific neurobiological mechanism. Brexanolone (2019) and zuranolone (2023) are the first drugs targeting the specific pathophysiology of PPD.

The Peripartum Neurobiological Hypothesis

During pregnancy:

- Progesterone levels rise massively ($\times 100$ above baseline)
- Progesterone is metabolised to **allopregnanolone** (3α -hydroxy- 5α -pregnan-20-one)
- Allopregnanolone is a potent positive allosteric modulator of GABA-A receptors
- Chronically elevated allopregnanolone $\rightarrow$ GABA-A receptor adaptations (downregulation, subunit changes)

At delivery:

- Progesterone and allopregnanolone fall precipitously within 24–48 hours
- GABA-A receptors, adapted to high allopregnanolone, are suddenly deprived
- Neuronal excitability surges $\rightarrow$ PPD in vulnerable individuals

The vulnerability model: Women with PPD may have GABA-A receptors that respond abnormally to allopregnanolone fluctuations, a trait rather than purely a state phenomenon.

Brexanolone (Zulresso)

Class: Synthetic allopregnanolone (neuroactive steroid)

Approval: FDA 2019, first drug specifically approved for PPD

Mechanism: Positive allosteric modulation of both:

- **Synaptic GABA-A receptors** ($\gamma 2$ -subunit containing): phasic inhibition
- **Extrasynaptic GABA-A receptors** (δ -subunit containing): tonic inhibition

The extrasynaptic GABA-A modulation is particularly important, these receptors, largely concentrated in limbic and corticolimbic regions, mediate sustained inhibitory tone. Allopregnanolone (and brexanolone) are among the only endogenous/exogenous substances that modulate extrasynaptic GABA-A at physiological concentrations.

Administration:

- IV infusion over 60 hours (2.5 days), continuous
- Hospital admission required

- Doses: 30 mcg/kg/hour for 4 hours → 60 mcg/kg/hour for 20 hours → 90 mcg/kg/hour for 28 hours → taper down

REMS requirements:

- Administered only in certified healthcare facilities
- Risk: excessive sedation and sudden loss of consciousness
- Continuous oxygen saturation monitoring
- Patient must be accompanied when discharged

Clinical evidence:

- HUMMINGBIRD trial: 73.7% Hamilton Depression Rating Scale response at 60 hours (vs 47.8% placebo)
- 94 hours post-infusion: 83.3% response rate vs 64.5% placebo
- Effect sustained at 30 days

Limitations: IV only, 60-hour infusion, cost ~USD 34,000, requires hospitalisation, limited global availability.

Zuranolone (Zurzuvae)

Class: Same mechanism as brexanolone (neuroactive steroid, GABA-A PAM), but oral

Approval: FDA August 2023, first oral neuroactive steroid for both MDD and PPD

Pharmacokinetics:

- Oral bioavailability: moderate-high (better with fatty meal)
- Half-life: ~16–19 hours
- CYP3A4 metabolism
- Dose: 30 mg or 50 mg once daily at bedtime for 14 days

Clinical evidence:

- ROBIN trial (PPD): 50 mg zuranolone → significant reduction in HAM-D-17 at Day 15
- LANDSCAPE / SHORELINE (MDD): Both trials positive
- Onset: significant separation from placebo within 3 days

No REMS required, can be prescribed from pharmacy for home use

Comparison with Conventional Antidepressants

FEATURE	SSRIS/SNRIS	BREXANOLONE	ZURANOLONE
Mechanism	Monoamine reuptake	GABA-A PAM	GABA-A PAM
Onset	4–8 weeks	24–48 hours	3 days

FEATURE	SSRIS/SNRIS	BREXANOLONE	ZURANOLONE
PPD-specific	No	Yes	Yes
Route	Oral	IV (60h)	Oral (14 days)
Breast milk	Yes (generally low)	Minimal data	Avoid breastfeeding
Driving restriction	Minimal	Yes (hospital stay)	Yes (8 hours post-dose)
Discontinuation syndrome	Yes (SSRIs)	No	No
Treating postpartum neuro	No	Yes (directly)	Yes (directly)

ANSWER 14

Discuss discontinuation syndromes in psychiatry: focusing on SSRI discontinuation, benzodiazepine withdrawal, and antipsychotic supersensitivity psychosis. How do you manage each? (10 marks)

Introduction

Discontinuation syndromes arise when drugs that alter receptor density, signalling cascades, or neurotransmitter homeostasis are stopped. They differ from drug withdrawal in mechanism (not mediated by physical dependence per se) but share clinical urgency. In psychiatry, three syndromes are clinically most important: SSRI discontinuation, benzodiazepine withdrawal, and antipsychotic supersensitivity psychosis.

1. SSRI Discontinuation Syndrome

Pathophysiology:

Chronic SSRI use → adaptive changes in serotonin receptors (down-regulation of 5-HT_{1A}, up-regulation of post-synaptic receptors) + serotonin transporter upregulation. Abrupt withdrawal → sudden reduction in synaptic serotonin → transient serotonergic deficit.

FINISH mnemonic:

- Flu-like symptoms: malaise, myalgia, lethargy
- Insomnia, vivid dreams/nightmares
- Nausea, vomiting, diarrhoea
- Imbalance: dizziness, ataxia, vertigo
- Sensory: **electric shock sensations** (paraesthesias, "brain zaps"), pathognomonic
- Hyperarousal: anxiety, irritability, agitation

Onset and duration:

- Short half-life drugs (paroxetine, venlafaxine): within 24–48 hours of stopping; duration 1–2 weeks
- Longer half-life (sertraline, escitalopram): 2–4 days; usually milder
- Fluoxetine: rarely causes syndrome due to ~4-6 day half-life + norfluoxetine active metabolite

Risk by drug:

Paroxetine > Venlafaxine > Sertraline > Escitalopram > Fluoxetine (lowest risk)

Management:

1. Gradual taper: Reduce by 25% every 1–2 weeks minimum. For long-term use (>2 years): taper over months.
 2. If syndrome has started: reinstate at half the previous dose, stabilise for 2–4 weeks, then taper more slowly
 3. Switch to fluoxetine 20 mg (self-tapering due to long half-life), taper fluoxetine over 2–4 weeks
 4. Liquid formulations (sertraline oral solution): enable micro-taper protocols (the Horowitz/Taylor method: hyperbolic taper)
 5. Inform patient: distinguish from relapse of depression (SSRI discontinuation ≠ return of depression, but can be confused)
-

2. Benzodiazepine Withdrawal Syndrome**Pathophysiology:**

Chronic BZD → GABA-A receptor downregulation + subunit composition changes (from $\gamma 2$ to δ subunits) + compensatory NMDA upregulation. Withdrawal → generalised CNS excitability.

Clinical features:

- Mild: anxiety, insomnia, tremor, sweating, irritability, hypersensitivity to sensory stimuli
- Moderate: tachycardia, hypertension, perceptual disturbances (visual/auditory)
- Severe: grand mal seizures, delirium (benzodiazepine withdrawal delirium)

Life-threatening: Benzodiazepine withdrawal (like alcohol withdrawal) can cause death. This is NOT the case with most other psychotropic drugs.

Timeline:

- Short-acting (lorazepam, oxazepam, alprazolam): onset 12–24 hours; peak 36–72 hours
- Long-acting (diazepam, clonazepam): onset 3–4 days; peak 5–7 days; prolonged course

Protracted withdrawal syndrome: Anxiety, insomnia, cognitive fog persisting for months, true or psychological?; evidence supports neurobiological basis in some patients.

Management:

1. **Substitution:** Convert all short-acting BZDs to equivalent diazepam dose (or chlordiazepoxide)
 2. Example: Lorazepam 4 mg/day = diazepam ~40 mg/day
 3. **Gradual taper:** 10% reduction every 1–2 weeks (Ashton Protocol)
 4. For high-dose long-term users: may take 6–18 months
 5. **Adjuncts:**
 6. Carbamazepine or valproate: reduce seizure risk, improve completion rates
 7. Propranolol: autonomic symptoms
 8. Hydroxyzine, pregabalin: adjunct anxiolytics
 9. Flumazenil infusion: specialist use only for protracted withdrawal
 10. Inpatient if: high dose, history of seizures, concurrent alcohol dependence, medical comorbidity
-

3. Antipsychotic Discontinuation, Supersensitivity Psychosis

Pathophysiology:

Chronic D2 receptor blockade → compensatory D2 receptor upregulation (increase in number and sensitivity). Abrupt discontinuation → dopaminergic rebound → florid psychosis even in patients who may not have had psychosis as primary presentation.

Features:

- Rapid onset: hours to days after discontinuation (distinguishes from relapse of underlying illness)
- Severity: often more severe and atypical than original episode
- Features: hallucinations, agitation, excitement, often more florid than original illness
- Can occur even after gradual taper if years of AP exposure

Distinguishing from relapse:

- Supersensitivity: onset within days; very rapid; may be atypical symptoms
- Relapse: onset over weeks to months; similar to original presentation

Cholinergic rebound:

- Stopping low-potency APs (clozapine, quetiapine) with high anticholinergic properties
- Features: nausea, vomiting, diarrhoea, headache, insomnia within 24–48 hours

Management:

1. **Prevention:** Gradual taper is mandatory, never abrupt for long-term AP users
2. Minimum taper: 3–6 months for decade-long use; some sources recommend hyperbolic taper
3. Clozapine: even slower, 6–12 months taper
4. **If supersensitivity has occurred:** Reinstate AP promptly (do not wait)
5. If AP reinstatement fails: different AP class; consider clozapine
6. Manage cholinergic rebound: antiemetics, symptomatic treatment for 1–2 weeks

ANSWER 15

Write a critical note on rational prescribing and deprescribing in psychiatric practice. What constitutes irrational polypharmacy? (8 marks)

Introduction

Polypharmacy in psychiatry is a double-edged reality. Evidence-based combinations exist and save lives (lithium augmentation, clozapine + lamotrigine). Irrational polypharmacy, adding drugs reflexively, defensively, or due to inertia, harms patients through adverse effects, drug interactions, reduced adherence, and increased cost.

Rational Polypharmacy, Evidence-Based Combinations

COMBINATION	CLINICAL BASIS	EVIDENCE
SSRI + aripiprazole	Augmentation for TRD	Level I, FDA approved
SSRI + quetiapine	TRD augmentation + insomnia	Level I, FDA approved
Lithium + antidepressant	TRD	Level I
Olanzapine + fluoxetine	Bipolar depression	Level I, FDA approved
Clozapine + lamotrigine	Ultra-treatment-resistant schizophrenia	Level II, multiple RCTs
Valproate + antipsychotic	Acute mania with agitation	Level I
SSRI + buspirone	Anxiety-predominant depression	Level II

Irrational Polypharmacy, Definitions and Examples

Irrational polypharmacy is defined as the concurrent use of multiple drugs without adequate clinical justification, where:

- The evidence does not support the combination

- The combination adds risk without proportionate benefit
- The combination resulted from sequential addition without review ("prescribing cascade")
- The combination creates dangerous interactions

Examples:

1. **Two antipsychotics simultaneously (excluding specific combinations):** Meta-analyses show no benefit over optimised monotherapy for most combinations. Exception: clozapine augmentation with amisulpride / aripiprazole, some RCT evidence.
1. **Two drugs from the same class:** Two SSRIs, two SNRIs, no clinical rationale; additive adverse effects and serotonin toxicity risk.
1. **Unnecessary anticholinergic drugs:** Procyclidine or trihexyphenidyl prescribed for EPS that has resolved, patient continues on it for years. Results in cognitive impairment, constipation, urinary retention in elderly.
1. **Benzodiazepine + Z-drug:** Additive CNS depression without additive efficacy; both work on GABA-A.
1. **Prescribing cascade:** Drug A causes side effect → Drug B added to treat side effect → Drug B causes new side effect → Drug C added...
1. **The "defensive add-on":** A drug is added "just in case" without evidence-based indication. Example: standing lorazepam added indefinitely after acute agitation episode.

Principles of Deprescribing

Deprescribing is the planned, supervised reduction or discontinuation of medications that are no longer needed, causing harm, or where benefit-risk ratio has shifted.

STOPP/START criteria (Ireland): Widely used tool, STOPP identifies potentially inappropriate prescriptions; START identifies omissions.

Five-step deprescribing process:

1. **Reconcile:** Comprehensive medication review, list ALL drugs, doses, durations, indications
2. **Identify targets:** Highest risk / lowest benefit first (anticholinergics in elderly, long-term BZDs, redundant antipsychotics)
3. **Assess feasibility:** Can this drug be stopped? What is the taper plan?
4. **Patient engagement:** Shared decision-making, patient must agree and understand withdrawal risk
5. **Monitor:** Explicit review date after each deprescription

Specific deprescribing in psychiatry:

DRUG CLASS	WHEN TO DEPRESCRIBE	METHOD
Benzodiazepines	After 4 weeks of use; dependency established	Ashton Protocol, slow diazepam taper
Anticholinergics	EPS resolved or not present	Gradual reduction, check for recurrence
Antipsychotics in dementia	After 3 months of behavioural stabilisation	25–50% dose reduction; monitor for 2 weeks
Sedative ADs (mirtazapine for sleep)	Sleep hygiene now adequate	25% taper every 2 weeks
Mood stabilisers in stable bipolar	After 5+ years remission (high controversy)	Only with full patient understanding of relapse risk

Monitoring After Deprescription

- Explicit withdrawal monitoring schedule
- Patient and family education on discontinuation syndrome features vs relapse features
- Clear re-entry plan if needed
- Documentation of reason for deprescription (legal protection)

Mnemonics & Memory Tricks

15+ Mnemonics

MNEMONIC 01

FINISH: SSRI Discontinuation Syndrome

How to use it: Any question about SSRI discontinuation asks for this triad. The sensory "brain zaps" are the only truly pathognomonic feature, nothing else causes them.

Risk order (high to low): Paroxetine > Venlafaxine > Sertraline > Escitalopram > Fluoxetine

Memory hook: "Parrots Vomit Suddenly; Eventually Fine"

MNEMONIC 02

FEVER: NMS Core Features

Companion memory: NMS = "Never Move Suddenly" (Neuroleptic / Malignant / Syndrome)

CK elevation + lead-pipe rigidity = NMS

Clonus + hyperreflexia = Serotonin Syndrome

MNEMONIC 03

CLONUS: Serotonin Syndrome vs NMS Differentiator

The single most important differentiating sign:

Full Hunter Criteria trigger: "Spontaneous Inducible Ocular Tremor Hypertonia"

SIOTHS, each needs clonus or hyperreflexia present

- Spontaneous clonus → SS
 - Inducible clonus + agitation/diaphoresis → SS
 - Ocular clonus + agitation/diaphoresis → SS
 - Tremor + hyperreflexia → SS
 - Hypertonia + temp >38 + clonus → SS
-

MNEMONIC 04

VORTEX: Vortioxetine Receptor Profile

Exam shortcut: "Vortioxetine = the one with 5 different receptor actions, not just SERT"

The **3 antagonist** (5-HT₃) is why nausea is less and cognition improves.

The **7 antagonist** (5-HT₇) is why circadian rhythm and sleep improve.

MNEMONIC 05

CLOZAPINE MONITORING: "Every Week, Every Two, Monthly"

Memory: "1st half year = weekly watch; 2nd half = fortnight; after that = monthly forever"

ANC thresholds, "Green / Amber / Red / STOP"

- ≥ 1500 = Green (continue)
 - 1000–1499 = Amber (more frequent monitoring)
 - 500–999 = Red (interrupt + daily)
 - < 500 = STOP, PERMANENT contraindication
-

MNEMONIC 06

NMS MANAGEMENT: "STOP, DRIP, DAN-BRO"

Add-on: Lorazepam for agitation/muscle relaxation

ECT for refractory NMS or when malignant catatonia cannot be excluded

Dantrolene dose: 0.25–2 mg/kg IV every 6–12 hours

Bromocriptine dose: 2.5–10 mg TID

MNEMONIC 07

LITHIUM TOXICITY LEVELS: "Fine to Seizing"

Memory hook: "One-Five Fine; Two-Zero Drowsy; Two-Five Dying"

Haemodialysis triggers:

- Level > 4.0 mmol/L (any symptoms)
 - Level > 2.5 mmol/L + severe symptoms
 - Anuric renal failure + any toxic level
-

MNEMONIC 08

CYP2D6 PHENOTYPES: "PURE UM"

PURE UM, the two extremes are the clinical problems

Key CYP2D6 substrates to memorise: "Risky Antidepressants Halt Perfectly"

- Risperidone
- Aripiprazole
- Haloperidol
- Paroxetine, nortriptyline (TCAs)

Paroxetine + fluoxetine = substrate AND inhibitor (phenoconversion from EM to functional PM)

MNEMONIC 09

HLA-B*1502: "Asians Before Carbamazepine"

Memory sentence: "Before Carbamazepine, Check Blood in Asians"

- HLA-B*1502: East/South Asian → SJS/TEN with carbamazepine
 - HLA-A*3101: European/Japanese → DRESS + milder reactions
 - If positive: use valproate or lamotrigine instead
-

MNEMONIC 10

ESKETAMINE REMS: "CASH In Hand"

Esketamine schedule: Induction → 2x/week × 4 weeks; Maintenance 1 → weekly × 4 weeks; Maintenance 2 → weekly or every 2 weeks

REMS reason: Abuse potential + dissociation + BP spikes + no safe self-administration

MNEMONIC 11

OREXIN ANTAGONIST COMPARISON: "SLD: Short Long Daytime"

Memory: "Sleeping pills get better with time, Suvorexant, then Lemborexant, then Daridorexant"

Key distinguisher: Daridorexant was the first DORA with **daytime functioning** as a co-primary endpoint in trials. Use it when next-day performance matters most.

MNEMONIC 12

CARIPRAZINE D3 SELECTIVITY: "D3 = Dopamine for Drive and Desire"

Why cariprazine is unique: 20× selectivity for D3 over D2 → targets negative symptoms

Evidence: RGH-MD-16 trial: cariprazine superior to risperidone on PANSS negative symptoms

Dosing by indication:

- **Negative symptoms / schizophrenia:** 3–6 mg
 - **Bipolar depression:** 1.5–3 mg (LOWER than schizophrenia)
 - **Bipolar mania:** 3–6 mg
-

MNEMONIC 13

LUMATEPERONE: "D1 Activator, Not Just Blocker"

Every other antipsychotic = D1 neutral or blocker

Lumateperone = **D1 AGONIST** in PFC (the key novelty)

Memory: "**Luma Turns D1 ON**"

Plus: Lumateperone is the only AP approved for **Bipolar I AND Bipolar II** depression (most only approved for Bipolar I).

Side effect advantage: "**LAMP**"

- Low EPS
 - Anti-metabolic (weight-neutral)
 - Minimal prolactin rise
 - Preserved cognition (D1 agonism)
-

MNEMONIC 14

LITHIUM DRUG INTERACTIONS: "NADS Raise Lithium Levels"

Aspirin (low dose): Minimal effect, safe to use

Loop diuretics (frusemide): Less effect than thiazides, still caution

Reverse direction (REDUCE lithium levels): Theophylline, sodium loading, osmotic diuretics

MNEMONIC 15

CLOZAPINE CONTRAINDICATIONS: "BONE MARROW PROBLEMS"

The **ONE absolute combination to never do**: Clozapine + Carbamazepine

Reason: **DOUBLE** agranulocytosis risk + carbamazepine induces CYP1A2 → reduces clozapine levels to sub-therapeutic

MNEMONIC 16

PSILOCYBIN CONTRAINDICATIONS: "SPAS"

Plus: **Pregnancy, Lithium concurrent use** (seizure risk combination)

Memory addition: "SET and SETTING matter, bad set = bad outcome"

Set = psychological preparation

Setting = physical environment + therapist relationship

MNEMONIC 17

BREXANOLONE vs ZURANOLONE: "IV vs PO, Both GABA"

Memory: "**Brex needs the DRIP; Zuran takes a TRIP home**"

Both: GABA-A PAM (positive allosteric modulator)

Both: approved for PPD

Zuranolone: **ALSO** approved for MDD (broader indication)

Mechanism unique point: **extrasynaptic δ -GABA-A receptors**, different from benzodiazepines which act on synaptic γ -GABA-A receptors

MNEMONIC 18

PHARMACOGENOMICS QUICK RECALL: "Poor UltraRapid EATS"

CYP2D6 clinically important phenotypes:

High-yield exam fact: CYP2C19 PMs in Asians → high escitalopram/citalopram levels → QTc risk → dose reduction to 20 mg max

MNEMONIC 19

DISCONTINUATION WASHOUT: "5 WEEKS FOR FLUOX"

Memory: "**Fluoxetine takes FIVE, the rest take TWO**"

Why 5 weeks for fluoxetine: norfluoxetine active metabolite has ~14-day half-life → fully eliminated at 5 half-lives = ~70 days → practically 5 weeks is the clinical minimum

MNEMONIC 20 (BONUS)

AUVELITY (DXM-BUP): "DXM Needs BUP to Survive"

Without bupropion: DXM metabolised too fast by CYP2D6 → no therapeutic levels

With bupropion: CYP2D6 inhibited → DXM levels ↑8-fold → NMDA antagonism achieved

Memory: "**Bupropion saves Dextromethorphan from being eaten by CYP2D6**"

Result: Antidepressant effect via:

1. NMDA antagonism (ketamine-like pathway)
2. NDRI effect (bupropion)
3. Sigma-1 agonism (DXM)

First oral NMDA-targeting antidepressant approved (FDA 2022)

QUICK MNEMONIC REFERENCE TABLE

#	MNEMONIC	TOPIC
01	FINISH	SSRI discontinuation syndrome
02	FEVER	NMS core features
03	CLONUS vs RIGIDITY	SS vs NMS differentiator
04	VORTEX	Vortioxetine receptor profile
05	Weekly / Fortnightly / Monthly	Clozapine ANC monitoring
06	STOP DRIP DAN-BRO	NMS management
07	Fine-Drowsy-Dying levels	Lithium toxicity levels
08	PURE UM	CYP2D6 phenotypes
09	Asians Before Carbamazepine	HLA-B*1502
10	CASH In Hand	Esketamine REMS
11	SLD: Short Long Daytime	Orexin antagonist comparison
12	D3 = Drive Desire Dexterity	Cariprazine D3 selectivity
13	Luma Turns D1 ON	Lumateperone
14	NADS	Lithium drug interactions
15	BONE MARROW	Clozapine contraindications

#	MNEMONIC	TOPIC
16	SPAS	Psilocybin contraindications
17	DRIP vs TRIP	Brexanolone vs zuranolone
18	Poor UltraRapid EATS	Pharmacogenomics
19	5 WEEKS FOR FLUOX	MAOI washout
20	DXM Needs BUP	Auvelity mechanism

High-Yield Comparisons

10 Comparison Tables

TABLE 01

Serotonin Syndrome vs NMS vs Malignant Catatonia vs Malignant Hyperthermia

FEATURE	SEROTONIN SYNDROME	NEUROLEPTIC MALIGNANT SYNDROME	MALIGNANT CATATONIA	MALIGNANT HYPERTHERMIA
Causative agent	Serotonergic drugs (MAOIs, SSRIs, opioids, tramadol)	Dopamine antagonists (antipsychotics, metoclopramide)	Idiopathic; may be triggered by antipsychotics	Volatile anaesthetics (halothane, sevoflurane); succinylcholine
Context	Drug initiation, combination, or dose increase	AP initiation, dose increase, or switch	Psychiatric illness (often schizophrenia, mood disorder)	Intraoperative, within minutes of induction
Onset	Rapid: within 6 hours	Subacute: 24–72 hours	Subacute to gradual	Extremely rapid: minutes
Temperature	Moderate–severe elevation; can reach >41°C	High: >38°C commonly >40°C	High: similar to NMS	Extremely high: >42°C; fastest rise of all four
Muscle tone/rigidity	Mild rigidity; clonus is dominant	Lead-pipe rigidity (severe)	Waxy flexibility; posturing; catalepsy	Generalised rigidity, masseter spasm prominent
Reflexes	Hyperreflexia (increased)	Normal or decreased	Variable	Normal
Clonus	YES, pathognomonic (spontaneous, inducible, ocular)	Absent	Absent	Absent
Tremor	Prominent; coarse myoclonus	Less prominent	Variable	May occur
Autonomic features	Diaphoresis, tachycardia, hypertension, mydriasis, diarrhoea	Tachycardia, labile BP, diaphoresis, incontinence	Tachycardia, hyperhidrosis	Tachycardia, CO2 rise, metabolic acidosis

FEATURE	SEROTONIN SYNDROME	NEUROLEPTIC MALIGNANT SYNDROME	MALIGNANT CATATONIA	MALIGNANT HYPERTHERMIA
Consciousness	Agitated and alert early; can deteriorate	Stupor → coma	Mutism , stupor; psychomotor features	Unconscious (under anaesthesia)
Mutism/posturing	Rare	Absent	YES, defining features	Absent
Serum CK	Usually normal	Very elevated (>1000–50,000 U/L)	Elevated (moderate)	Very elevated
Serum iron	Normal	Low (<12 µmol/L), specific marker	Low	Normal
Leukocytosis	Absent	Yes (10,000–40,000)	Variable	Absent
ECG changes	Tachycardia	Tachycardia, occasional QTc changes	Variable	Tachyarrhythmias
Key treatment	Cyproheptadine; benzodiazepines; stop serotonergic drugs	Dantrolene; bromocriptine; stop antipsychotic	ECT (first-line); IV lorazepam	Dantrolene (immediate); cooling; stop triggering agent
Cyproheptadine effective	YES	No	No	No
Dantrolene effective	Limited	YES	Partial	YES
ECT effective	No	Partial (refractory)	YES, first-line	No
Mortality untreated	Variable (can be fatal)	25–30% (historical); 5–10% (current)	High if untreated	>70% if untreated
Genetic predisposition	No	No	No	YES , RYR1 gene mutations; autosomal dominant

TABLE 02

Newer Antidepressant Mechanisms: Side-by-Side

FEATURE	VORTIOXETINE	VILAZODONE	ESKETAMINE	BREXANOLONE	ZURANOLONE	AUVELITY (DXM-BUP)	GEPIRONE
Class	SMS (Serotonin modulator and stimulator)	SPARI	NMDA antagonist	Neuroactive steroid	Neuroactive steroid	NMDA antagonist + NDRI	5-HT1A partial agonist (azapirone)
Primary mechanism	SERT inhibition + 5-HT2A/3/7 antagonist + 5-HT1A/1B partial agonist	SERT + 5-HT1A partial agonist	S-enantiomer NMDA open-channel block	GABA-A PAM (synaptic + extrasynaptic δ)	GABA-A PAM (extrasynaptic δ)	DXM: NMDA antagonism; BUP: CYP2D6 inhibitor + NDRI	Selective 5-HT1A partial agonist
FDA indication	MDD	MDD	TRD; MDD with acute suicidality (MDSI)	Postpartum depression	MDD; Postpartum depression	MDD	MDD
Year approved	2013	2011	2019	2019	2023	2022	2023
Route	Oral	Oral	Intranasal	IV infusion	Oral	Oral	Oral (XR)
Onset of antidepressant effect	2–4 weeks	2–4 weeks	Hours–days	24–48 hours	3–7 days	1 week	2–4 weeks
Cognitive benefit	YES (processing speed, executive function)	Minimal	Unclear	Not studied (PPD focus)	Not studied	Not studied	No
Sexual dysfunction risk	Very low	Low	Not applicable	Not applicable	Low	Low	Very low
Weight gain	Minimal	Minimal	Not applicable	Not applicable	Minimal	Minimal	Minimal
REMS required	No	No	YES	YES	No	No	No
Discontinuation syndrome	Minimal (long T1/2)	Yes (moderate)	Not applicable	Not applicable	Minimal	Not studied	Minimal

FEATURE	VORTIOXETINE	VILAZODONE	ESKETAMINE	BREXANOLONE	ZURANOLONE	AUVELITY (DXM-BUP)	GEPIRONE
Key drug interaction	CYP2D6 inhibitors (reduce dose)	CYP3A4 inhibitors; must take WITH FOOD	CYP3A4 interactions	None significant	CYP3A4	CYP2D6 (bupropion is the inhibitor here)	CYP3A4
Unique feature	5-HT3 antagonism → better cognition + GI tolerability	Must be taken with food; SPARI class	Rapid onset; REMS; IV S-ketamine	IV only; first PPD-specific drug	Oral; 14-day course; no REMS	BUP inhibits its own partner DXM's metabolism	No sexual dysfunction; no discontinuation syndrome

TABLE 03

Long-Acting Injectable Antipsychotics: Comprehensive Comparison

WIDE COMPARISON · LANDSCAPE

FEATURE	HALOPERIDOL DECANOATE	FLUPHENAZINE DECANOATE	RISPERIDONE MICROSPHERES (CONSTA)	PALIPERIDONE PALMITATE 1-MONTH	PALIPERIDONE PALMITATE 3-MONTH	ARIPIPRAZOLE MONOHYDRATE (MAINTENA)	ARIPIPRAZOLE LAUROXIL (ARISTADA)	OLANZAPINE PAMOATE (ZYPADHERA)
Frequency	Every 4 weeks	Every 2–6 weeks	Every 2 weeks	Monthly	Every 3 months	Monthly	4–8 weeks (dose-dependent)	Every 2–4 weeks
Vehicle	Sesame oil	Sesame oil	Biodegradable microspheres	Aqueous nanocrystal suspension	Aqueous nanocrystal suspension	Aqueous suspension	Aqueous suspension	Aqueous suspension
Loading dose needed	Yes (oral overlap 4 weeks)	Yes (oral overlap)	No (2-week lag, oral overlap required for 3 weeks)	Yes (Day 1 + Day 8 deltoid)	No (after 4+ months on PP1M)	No (oral aripiprazole 14 days)	NCD: Initio 675mg + oral 30mg same day	No
Injection sites	Gluteal	Gluteal	Deltoid or gluteal	Deltoid only for first 2 doses; then deltoid or gluteal	Deltoid or gluteal	Deltoid or gluteal	Deltoid or gluteal	Gluteal (slow, Z-track)
Generation	First (typical)	First (typical)	Second (atypical)	Second (atypical)	Second (atypical)	Third (atypical, partial agonist)	Third (atypical, partial agonist)	Second (atypical)
EPS risk	High	High	Moderate	Moderate	Moderate	Low (akathisia risk)	Low (akathisia risk)	Low
Weight gain	Moderate	Moderate	Moderate	Moderate	Moderate	Low–moderate	Low–moderate	High
Prolactin elevation	High	High	High	High	High	Minimal (partial agonist)	Minimal	Moderate
QTc risk	Moderate	Moderate	Low	Low	Low	Low	Low	Low
Post-injection monitoring	None required	None required	None required	None required	None required	None required	None required	3 hours (PDSS risk)

FEATURE	HALOPERIDOL DECANOATE	FLUPHENAZIN E DECANOATE	RISPERIDONE MICROSPHERE S (CONSTA)	PALIPERIDONE PALMITATE 1- MONTH	PALIPERIDONE PALMITATE 3- MONTH	ARIPIRAZOLE MONOHYDRA TE (MAINTENA)	ARIPIRAZOLE LAUROXIL (ARISTADA)	OLANZAPINE PAMOATE (ZYPADHERA)
PDSS risk	No	No	No	No	No	No	No	YES, post-injection delirium/sedation syndrome
Available in India	Yes (widely)	Yes	Limited	Limited (Sustenna)	Rare/unavailable	Limited	Not available	Not available
Key distinguishing feature	Oldest, most data	Shortest of older depots	Requires 3-week oral overlap	First aqueous AP depot; del-toid-first protocol	3-monthly; requires 4 months PP1M first	Partial agonist properties preserved	NCD initiation protocol; multiple interval options	Monitoring requirement due to PDSS

TABLE 04

Orexin Receptor Antagonists (DORAs): Full Comparison

FEATURE	SUVOREXANT (BELSOMRA)	LEMBOREXANT (DAYVIGO)	DARIDOREXANT (QUVIVIQ)
FDA approval year	2014	2019	2022
Doses	5, 10, 15, 20 mg	5, 10 mg	25, 50 mg
Recommended dose	10–20 mg	5–10 mg	25–50 mg
Half-life	~12 hours	~17–27 hours	~8 hours
Schedule	IV (controlled)	IV (controlled)	IV (controlled)
OX1R affinity	High	High	Moderate
OX2R affinity	High	Higher selectivity	Moderate
Mechanism selectivity	Dual OX1R + OX2R	Dual; higher OX2R bias	Dual OX1R + OX2R
Key clinical trials	SUNRISE-1, SUNRISE-2	SUNRISE-1, SUNRISE-2; vs zolpidem	ESADA-1, ESADA-2 (daytime functioning co-primary)
vs Zolpidem evidence	Not directly compared in pivotal trials	Lemborexant 5 mg better than zolpidem ER 6.25 mg on subjective sleep at 1 month	Not directly compared
Sleep onset benefit	Yes	Yes	Yes
Sleep maintenance benefit	Yes	Yes (strong)	Yes
Next-day impairment	Moderate concern	Greater concern (long T1/2)	Least concern
Daytime functioning endpoint	Not primary	Not primary	Co-primary endpoint, validated in trials
CYP3A4 interaction	Significant, reduce to 5 mg with strong inhibitors	Significant	Less clinically significant at approved doses
Use in elderly	Approved; caution	Preferred (sleep maintenance data in elderly; SUNRISE-2)	Approved; best next-day profile
Rebound insomnia	Minimal	Minimal	Minimal

FEATURE	SUVOREXANT (BELSOMRA)	LEMBOREXANT (DAYVIGO)	DARIDOREXANT (QUVIVIQ)
Tolerance development	Minimal (vs BZDs)	Minimal	Minimal
Complex sleep behaviour BBW	Yes	Yes	Yes
Best suited for	General insomnia; onset + maintenance	Elderly; sleep maintenance prominent	When patient's day-time performance is critical

TABLE 05

CYP450 Drug Interaction Matrix: Psychiatry High-Yield

DRUG	CYP1A2	CYP2D6	CYP2C19	CYP3A4	NET CLINICAL CONCERN
Fluvoxamine	Strong inhibitor	Moderate inhibitor	Strong inhibitor	Moderate inhibitor	Raises clozapine levels dramatically (CYP1A2); raises diazepam, TCA levels
Fluoxetine	Weak	Strong inhibitor	Moderate inhibitor	Moderate inhibitor	Raises risperidone, aripiprazole, TCA levels; pheno-conversion of EMs to functional PMs
Paroxetine	Weak	Strong inhibitor	Moderate inhibitor	Weak	Same as fluoxetine for CYP2D6; clinically most potent 2D6 inhibitor of SSRIs
Carbamazepine	Inducer	Inducer	Inducer	Strong inducer	Reduces levels of: clozapine, haloperidol, olanzapine, quetiapine, lamotrigine, valproate, TCAs

DRUG	CYP1A2	CYP2D6	CYP2C19	CYP3A4	NET CLINICAL CONCERN
Valproate			Inhibitor (modest)		Raises lamotrigine levels 2× (UGT inhibition, not CYP); raises clozapine slightly; reduces phenytoin
Rifampicin	Strong inducer	Inducer	Inducer	Strong inducer	Dramatically reduces levels of virtually all psychiatric drugs
Smoking (cigarettes)	Strong inducer				Reduces clozapine and olanzapine levels significantly; stopping smoking = toxicity risk
Ketoconazole				Strong inhibitor	Raises quetiapine, buspirone, haloperidol levels
Bupropion	Weak	Strong inhibitor			Raises TCA levels; the therapeutic basis of Auvelity (DXM-BUP)
Clozapine	Substrate	Substrate	Substrate	Substrate	Victim of multiple interactions; CYP1A2 induction by smoking most clinically significant
Olanzapine	Substrate	Minor substrate		Minor	CYP1A2 induction (smoking) reduces levels 40–50%

DRUG	CYP1A2	CYP2D6	CYP2C19	CYP3A4	NET CLINICAL CONCERN
Haloperidol	Substrate	Substrate + weak inhibitor		Substrate	CYP2D6 PMs get higher haloperidol levels → EPS risk
Quetiapine				Substrate	Levels rise with CYP3A4 inhibitors (ketoconazole); fall with inducers (carbamazepine)
Aripiprazole		Substrate		Substrate	CYP2D6 PMs get higher levels; reduce aripiprazole dose by 50% with strong 2D6 inhibitors

Key rule: Substrates are victims; inhibitors/inducers are perpetrators. Most psychiatric drugs are substrates, they are affected by co-prescribed inhibitors/inducers.

TABLE 06

Ketamine vs Esketamine: Clinical Comparison

FEATURE	RACEMIC KETAMINE (IV)	ESKETAMINE INTRANASAL (SPRAVATO)
Composition	50:50 mixture of R- and S-enantiomers	S-enantiomer only
Route	IV infusion (most common); IM; oral (compounded)	Intranasal
FDA approval	NOT approved for depression (off-label)	Approved: TRD (2019); MDSI (2020)
REMS	No	Yes , REMS programme required
Setting	Ketamine infusion clinics; anaesthesia settings	Certified healthcare settings only
NMDA receptor potency	R-ketamine: moderate; S-ketamine: higher	Higher (3–4× more potent than R-ketamine at NMDA)

FEATURE	RACEMIC KETAMINE (IV)	ESKETAMINE INTRANASAL (SPRAVATO)
Bioavailability	~100% (IV)	~48% intranasal
Dose	0.5 mg/kg over 40 min (typical)	56 mg or 84 mg per session
Dose standardisation	Variable across clinics	Standardised
Induction protocol	Typically 6 infusions over 2–3 weeks	2×/week × 4 weeks
Dissociation	Yes, common	Yes, very common (>50%)
Duration of effect	Days to 2 weeks per infusion series	Days to weeks per session
Regulatory oversight	Limited; no registry	REMS certification + monitoring
Evidence base	Extensive (meta-analyses, multiple RCTs, decades of data)	Phase III RCTs available (TRANSFORM series)
Cost	~\$400–800 per infusion (often not insured)	~\$800–900 per session (insurance coverage varies)
Insurance coverage	Rarely covered	Better coverage in US (FDA-approved)
Concomitant antidepressant	Not standardised	Yes, must be combined with oral AD
Antidepressant without concurrent AD?	Sometimes used alone	No, esketamine is adjunctive
Abuse/diversion risk	Higher (Schedule III; IV access)	Lower (REMS controls dispensing)
Monitoring post-dose	Clinic-dependent (usually 1–2h)	Mandatory 2 hours
Key advantage	Flexibility; longer evidence base; lower cost	FDA approval; standardised; REMS accountability; intranasal route
Key disadvantage	No regulatory approval; variable protocols	REMS burden; cost; short duration effect

TABLE 07

Newer Antipsychotics: Mechanism and Side Effect Profile

WIDE COMPARISON · LANDSCAPE

DRUG	KEY RECEPTOR PROFILE	EPS RISK	WEIGHT GAIN	METABOLIC RISK	PROLACTIN	QTC	SEDATION	UNIQUE FEATURE
Lumateperone	D1 agonist + D2 pre-agonist/post-antagonist + 5-HT2A + SERT	Very low	Minimal	Minimal	Minimal	Low	Low	D1 agonism; approved bipolar I + II depression
Pimavanserin	5-HT2A inverse agonist; NO D2 binding	None	Minimal	Minimal	None	Moderate	Low	Only for Parkinson's psychosis; no D2 binding
Cariprazine	D2/D3 partial agonist; D3 high affinity	Moderate (akathisia)	Moderate	Moderate	Low	Low	Low	D3 selectivity; best negative symptom evidence
Brexpiprazole	D2 partial agonist (low intrinsic) + 5-HT1A + 5-HT2A antagonist	Low	Moderate	Moderate	Low	Low	Low	Approved: schizophrenia + MDD augment + AD agitation
Aripiprazole	D2/D3 partial agonist + 5-HT1A partial agonist	Low	Low	Low	Very low	Low	Low	Partial agonist; akathisia at higher doses
Quetiapine	H1 >> 5-HT2A > D2; M1 at low doses	Very low	High	High	Very low	Low–moderate	High	Sedation used therapeutically; off-label for anxiety / insomnia

DRUG	KEY RECEPTOR PROFILE	EPS RISK	WEIGHT GAIN	METABOLIC RISK	PROLACTIN	QTC	SEDATION	UNIQUE FEATURE
Olanzapine	H1 > M1 > 5-HT2A > D2	Low	Very high	Very high	Moderate	Low	High	Most effective typical-range AP; worst metabolic profile
Clozapine	D4 > 5-HT2A > H1 > M > α	None	Very high	Very high	Very low	Moderate	Very high	Gold standard for TRS; agranulocytosis risk; seizures
Risperidone	D2 + 5-HT2A	Moderate-high	Moderate	Moderate	Very high	Low	Low	Highest prolactin of all SGAs; galactorrhoea, amenorrhoea
Amisulpride	D2/D3 selective antagonist	Moderate	Minimal	Minimal	High	High	Minimal	Selective D2/D3; highest QTc risk among SGAs

TABLE 08**Lithium Monitoring: Baseline, Ongoing, Specific Situations**

PARAMETER	BASELINE	ONGOING (STABLE)	PREGNANCY	TOXICITY WORKUP
Serum lithium		Every 3–6 months (12h post-dose)	Every 2 weeks in 3rd trimester	Immediately
Renal function (eGFR, Cr, BUN)	Yes	Every 6–12 months	Monthly	Yes
Thyroid (TSH, FT4)	Yes	Annually	Quarterly	Only if symptomatic
Serum calcium	Yes	Annually	Quarterly	If symptomatic
ECG	Yes (>50 years or cardiac history)	As clinically indicated	Yes	If QTc concern
Pregnancy test	Yes (reproductive-age women)	As appropriate		
Urinalysis + urine osmolality	Yes (baseline renal tubular function)	If polyuria develops	Yes	Yes (myoglobinuria check)
FBC	Not routine	Not routine	Not routine	If infection
Weight / BMI	Yes	Every 3 months	Monthly	
Target level		0.6–0.8 mmol/L (maintenance)	0.6–0.8 mmol/L (same)	If >1.5: toxicity management

Special monitoring situations:

- Patient starting NSAID: recheck level in 3–5 days
- Patient febrile/vomiting: advise holding lithium + recheck level on recovery
- Surgery: discuss with surgeon; hold morning dose; restart when eating/drinking
- Stopping smoking: recheck clozapine level (not lithium, this is for CYP1A2)

TABLE 09**Antidepressant Augmentation: Evidence and Practical Guide**

AUGMENTATION STRATEGY	EVIDENCE LEVEL	FDA STATUS	TIME TO EFFECT	DOSE	KEY ADVERSE EFFECTS	BEST FOR
Aripiprazole + AD	Level I	FDA approved (ad-junctive MDD)	2–4 weeks	2–15 mg/day	Akathisia, weight gain	Good tolerability; low metabolic risk
Quetiapine XR + AD	Level I	FDA approved (ad-junctive MDD)	1–2 weeks	50–300 mg/day	Sedation, weight gain, metabolic	Insomnia comorbid; rapid anxiolysis
Brexpiprazole + AD	Level I	FDA approved (ad-junctive MDD)	2–4 weeks	1–3 mg/day	Low akathisia; weight gain	When aripiprazole not tolerated
Lithium + AD	Level I	Off-label (not FDA for this)	2–4 weeks	0.5–0.8 mmol/L	Tremor, polyuria, hypothyroidism	Bipolar spectrum; classic evidence
T3 (liothyronine) + AD	Level II	Off-label	2–4 weeks	25–50 mcg/day	Tachycardia, anxiety, osteoporosis	TCA augmentation; thyroid function normal
Mirtazapine + SSRI/SNRI	Level II	Off-label	2–4 weeks	15–45 mg/day	Sedation, weight gain	Insomnia; appetite loss
Buspirone + SSRI	Level II	Off-label	4–6 weeks	20–60 mg/day	Dizziness, nausea	Anxiety-predominant MDD
Esketamine + oral AD	Level I	FDA approved (TRD)	Hours–days	56–84 mg per session	Dissociation, sedation, BP rise	TRD with urgent response needed
Pramipexole + AD	Level II	Off-label	3–4 weeks	0.5–2 mg/day	Nausea, hypotension, impulse control	Anhedonia; bipolar II depression
Lamotrigine + AD	Level II	Off-label	6–8 weeks	50–200 mg/day	Rash (must titrate slowly)	Bipolar spectrum features; TRD
Olanzapine + fluoxetine (OFC)	Level I	FDA approved (bipolar depression)	1–2 weeks	6/25–12/50 mg	Weight gain, sedation, metabolic	Bipolar depression; TRD with psychotic features

TABLE 10

High-Risk Drug Combinations: Summary Reference

COMBINATION	MECHANISM	RISK LEVEL	CLINICAL CONSEQUENCE	MANAGEMENT
MAOI + SSRI	Excess serotonin	FATAL	Severe serotonin syndrome; potentially lethal	Absolute contraindication; strict washout (5 weeks fluoxetine → MAOI)
MAOI + tramadol	Excess serotonin (tramadol = weak SERT inhibitor + opioid)	FATAL	Serotonin syndrome	Contraindicated
MAOI + meperidine (pethidine)	Excess serotonin + NE	FATAL	Hyperpyrexia crisis, serotonin syndrome	Contraindicated; use morphine instead for pain
Clozapine + carbamazepine	Additive agranulocytosis + CYP1A2 induction	Absolute contraindication	Agranulocytosis + sub-therapeutic clozapine levels	NEVER combine; use valproate instead
Clozapine + IM benzodiazepine	Additive CNS + respiratory depression	High	Respiratory collapse; death reported	Avoid IM BZD within hours of clozapine; oral BZD with caution
Lithium + NSAIDs	NSAIDs reduce renal Li clearance	High	Lithium toxicity (50–100% level rise)	Avoid; if necessary reduce Li dose 25%, monitor in 3–5 days
Lithium + ACE inhibitors	Reduced GFR → Li retention	High	Lithium toxicity	Avoid; if necessary reduce dose + monitor
Lithium + thiazide diuretics	Na depletion → Li retention (competitive)	High	Lithium toxicity	Use loop diuretic instead (less risk); monitor levels
Haloperidol + pimozide	Additive QTc prolongation	High	Torsades de pointes	Avoid combination; ECG monitoring if necessary

COMBINATION	MECHANISM	RISK LEVEL	CLINICAL CONSEQUENCE	MANAGEMENT
Fluvoxamine + clozapine	Fluvoxamine inhibits CYP1A2 → clozapine ↑2–10×	High (unintentional)	Clozapine toxicity (sedation, seizures)	Avoid inadvertent prescription; intentional use requires dose reduction and level monitoring
Valproate + lamotrigine	Valproate inhibits UGT (glucuronidation) → lamotrigine ↑2×	Moderate (manageable)	Lamotrigine toxicity (rash, dizziness), also additive anti-epileptic benefit	Halve lamotrigine dose when adding valproate; slow titration
SSRIs + warfarin	SSRIs inhibit platelet 5-HT uptake + may inhibit CYP2C9	Moderate	Increased bleeding risk; raised INR	Monitor INR; consider gastroprotection
Carbamazepine + oral contraceptives	CYP3A4 induction → OCP levels fall	Moderate	Contraceptive failure	Use higher-dose OCP or barrier method
Smoking + clozapine/olanzapine	Smoking induces CYP1A2 → drug levels fall	Moderate–high	Subtherapeutic levels → relapse	Monitor levels with changes in smoking; adjust dose when smoking changes

PYQ Frequency Analysis

Previous Year Question Analysis

SECTION A: HIGH-FREQUENCY TOPIC MAP

The following topics have appeared repeatedly across Indian PG psychiatry exit examinations (PG exams, Exam pattern). Frequency ratings are based on pattern analysis across 17+ years of available question data.

TOPIC	ESTIMATED FREQUENCY	TYPICAL MARKS	EXAM FORMAT
Clozapine, indications, monitoring, adverse effects	★★★★★ Very High	10–15 marks	Long essay or short note
Serotonin syndrome vs NMS	★★★★★ Very High	10 marks	Compare/contrast or short note
Lithium, pharmacology, toxicity, monitoring	★★★★★ Very High	10–15 marks	Long essay
Drug interactions in psychiatry	★★★★☆ High	8–10 marks	Short note or part of long essay
Treatment-resistant depression, augmentation	★★★★☆ High	8–10 marks	Short note
Long-acting injectable antipsychotics	★★★★☆ High	8–10 marks	Short note
Newer antidepressants (general)	★★★☆☆ Moderate	5–8 marks	Short note
Esketamine / ketamine in depression	★★★☆☆ Moderate	5–8 marks	Short note
NMS, management	★★★★☆ High	8–10 marks	Short note or part of diff dx
Benzodiazepine withdrawal	★★★☆☆ Moderate	5–8 marks	Short note
Pharmacogenomics in psychiatry	★★★☆☆ Moderate	5–8 marks	Short note

TOPIC	ESTIMATED FREQUENCY	TYPICAL MARKS	EXAM FORMAT
Antipsychotic switching	★★★☆☆ Moderate	5–8 marks	Short note
Polypharmacy and deprescribing	★★☆☆☆ Emerging	5 marks	Short note
Psychedelics in psychiatry	★★☆☆☆ Emerging	5 marks	Short note
Brexanolone / post-partum depression	★★☆☆☆ Emerging	5 marks	Short note
Orexin antagonists (insomnia)	★★☆☆☆ Emerging	5 marks	Short note

SECTION B: RECONSTRUCTED PYQ BANK

Category 1: Long Essays (15 marks): Most Likely Patterns

Q1.1

Discuss the pharmacology, indications, adverse effects, and monitoring of clozapine. How would you manage a patient who develops agranulocytosis while on clozapine?

KEY INSIGHT

Ra's Answer Blueprint: - Pharmacology: receptor profile (D4, D2 fast-off, 5-HT_{2A}, H₁, M), pharmacokinetics (CYP1A2), no protein binding - Indications: TRS (TRRIP criteria), suicidality, PD psychosis, refractory bipolar - Adverse effects: haematological (agranulocytosis), cardiovascular (myocarditis), metabolic (weight, DM), neurological (seizures, sedation), autonomic (sialorrhea, constipation) - Monitoring: ANC protocol (weekly × 26 weeks → fortnightly → monthly), cardiac monitoring - Agranulocytosis management: stop clozapine, admit, reverse barrier nursing, G-CSF, haematology consult, permanent registration **Tip:** This question has appeared in some form every 2–3 years. Always include the ANC threshold table and the re-challenge contraindication.

Q1.2

What is treatment-resistant depression? Discuss the various pharmacological augmentation strategies with evidence for each. Which strategy has the strongest evidence base?

KEY INSIGHT

Ra's Answer Blueprint: - Define TRD (2+ adequate trials of different class ADs at adequate dose × adequate duration) - Augmentation vs switching distinction - Tier 1: AP augmentation (aripiprazole, quetiapine, brexpiprazole, FDA approved) + lithium augmentation (Level I, NNT ~5) - Tier 2: T3 augmentation, mirtazapine + SSRI, buspirone - Tier 3: Esketamine (rapid onset, REMS), lamotrigine, pramipexole - Strongest evidence: lithium (decades of RCTs) and AP augmentation (multiple Phase III RCTs, FDA approved) **Tip:** Always include a structured table of evidence levels. Examiners reward systematic organisation.

Q1.3

Describe the pharmacology, therapeutic drug monitoring, long-term effects, and use in pregnancy of lithium. How would you manage lithium toxicity?

KEY INSIGHT

Ra's Answer Blueprint: - Mechanisms: inositol depletion, GSK-3 β inhibition, serotonin potentiation, BDNF - PK: complete absorption, no protein binding, no hepatic metabolism, renal excretion competes with Na⁺ - TDM: 12h post-dose; target levels by indication; monitoring frequency - Long-term: NDI (polyuria), hypothyroidism, chronic kidney disease, hyperparathyroidism - Pregnancy: revised Ebstein anomaly risk (0.6/1000 → 2.1/1000), peripartum management, breastfeeding - Toxicity: precipitants (NSAIDs, ACEi, thiazides, dehydration), features by level, management (IV NS, haemodialysis criteria) **Tip:** The pregnancy section is frequently asked as a standalone short note. Know the NEJM 2017 revised figures.

Category 2: Short Notes (8–10 marks): High-Frequency

Q2.1

Write a short note on serotonin syndrome. How does it differ from NMS?

EXAM PEARL

Key points required: - Pathophysiology (5-HT_{1A} and 5-HT_{2A} excess) - Clinical triad: cognitive + autonomic + neuromuscular - Hunter criteria (5 diagnostic patterns, all involve clonus or hyperreflexia) - Causative drugs (MAOIs, SSRIs, tramadol, linezolid, DXM) - Management: stop drug, cyproheptadine, benzodiazepines, cooling - SS vs NMS table: clonus vs rigidity; hyperreflexia vs normal reflexes; CK normal vs very elevated; onset rapid vs slow **Most commonly lost marks:** Forgetting to state Hunter criteria specifically; confusing SS rigidity with NMS lead-pipe rigidity.

Q2.2

Discuss the pharmacology and clinical uses of newer antipsychotics, cariprazine, lumateperone, and brexpiprazole.

EXAM PEARL

Key points required: - Cariprazine: D3 high-affinity partial agonism; D3 selectivity clinical significance; evidence for negative symptoms; bipolar depression at low doses; long active metabolite half-life - Lumateperone: D1 agonism (novel); dual D2 activity; SERT inhibition; approved bipolar I + II depression; weight-neutral - Brexpiprazole: SDAM; low intrinsic D2 activity; approved for AD agitation (2023, first drug); MDD augmentation; schizophrenia **Tip:** Examiners expect you to distinguish these from earlier SGAs mechanistically, not just list them. The D3 selectivity of cariprazine and the D1 agonism of lumateperone are the examinable novelties.

Q2.3

Write a note on pharmacogenomics in psychiatry. What is the significance of CYP2D6 polymorphisms?

EXAM PEARL

Key points required: - Definition and rationale for pharmacogenomics - CYP2D6 phenotypes: PM, IM, EM, UM; frequencies by ethnicity - Clinical substrates: TCAs, risperidone, aripiprazole, haloperidol - PM risk: toxicity at standard doses; UM risk: treatment failure - Phenoconversion: paroxetine/fluoxetine as inhibitors → functional PM - CYP2C19: Asians 15–20% PM; citalopram/escitalopram QTc risk - HLA-B*1502: carbamazepine + Asian ancestry + SJS/TEN; mandatory testing; FDA label - Limitations of clinical pharmacogenomic testing (PRIME Care trial negative)

Q2.4

Discuss the management of NMS. How does it differ from malignant catatonia?

EXAM PEARL

Key points required: - NMS: stop antipsychotic, IV fluids, cooling, dantrolene, bromocriptine, ICU - Re-challenge protocol: 2-week wait, low-potency atypical, slow titration, informed consent - Malignant catatonia vs NMS: MC features (mutism, posturing, waxy flexibility); MC treatment is ECT (not dantrolene); NMS has no posturing; differentiation important because antipsychotics worsen MC but are causative in NMS - Differential: also include SS (clonus, onset rapid, cyproheptadine) and malignant hyperthermia (intraoperative, RYR1 mutation, dantrolene)

Q2.5

Write a short note on long-acting injectable antipsychotics. What are their advantages and disadvantages?

EXAM PEARL

Key points required: - Rationale: non-adherence as #1 cause of relapse; 50–70% non-adherent within 1 year - Types: first-generation depots (oil-based) vs second-generation (aqueous nanocrystals, microspheres) - Key examples: paliperidone palmitate (monthly, 3-monthly, 6-monthly); aripiprazole lauroxil (NCD initiation); olanzapine pamoate (PDSS monitoring) - Advantages: eliminates covert non-adherence; stable levels; early warning signal; reduced relapse - Disadvantages: PDSS (olanzapine pamoate); cannot rapidly stop; pain; need for clinic attendance; cost - PP3M specific: prerequisites (4+ months PP1M at stable dose); dose calculation (3.5× PP1M dose)

Q2.6

Discuss esketamine nasal spray, mechanism of action, indications, REMS requirements, and place in therapy.

EXAM PEARL

Key points required: - S-enantiomer of ketamine; NMDA antagonist - Mechanism pathway: NMDA block → AMPA disinhibition → BDNF → mTOR → synaptogenesis - Indications: TRD (2019); MDD with acute suicidal ideation (2020) - REMS: certified settings only; 2-hour post-dose monitoring; no driving on dosing day; BP + dissociation monitoring - Protocol: induction 2×/week × 4 weeks; maintenance - Comparison with IV ketamine: FDA-approved vs off-label; standardised vs variable; intranasal vs IV - Limitations: REMS burden; short duration of effect; cost; not monotherapy

Q2.7

Write a short note on benzodiazepine withdrawal syndrome, pathophysiology, clinical features, and management.

EXAM PEARL

Key points required: - Pathophysiology: GABA-A receptor downregulation + NMDA upregulation → CNS excitability rebound - Features: mild (anxiety, insomnia, tremor) → moderate (tachycardia, perceptual disturbances) → severe (seizures, delirium) - Life-threatening potential (unlike most drug withdrawals) - Timeline by half-life (short-acting onset 12–24h; long-acting 3–4 days) - Management: substitution with diazepam; Ashton Protocol (10% taper every 1–2 weeks); adjuncts (carbamazepine, valproate, propranolol) - Protracted withdrawal syndrome: months of residual anxiety and cognitive fog

Q2.8

Discuss drug interactions in psychiatry. Which combinations are potentially fatal?

EXAM PEARL

Key points required: - Classification: pharmacokinetic (CYP450 enzyme inhibition/induction, P-gp) vs pharmacodynamic (additive/synergistic/antagonistic) - Fatal combinations: MAOI + SSRI (SS); MAOI + tramadol/meperidine; clozapine + carbamazepine (absolute contraindication) - High-risk: lithium + NSAIDs; clozapine + IM benzodiazepine; haloperidol + QTc-prolonging drugs - CYP1A2 and smoking: clozapine and olanzapine levels reduced by 40–50%; stopping smoking = toxicity risk - Fluvoxamine + clozapine: raises clozapine 2–10× (clinical use in augmentation but requires dose reduction) - Carbamazepine + most psychotropics: potent CYP3A4/1A2 inducer

Category 3: Short Notes (5 marks): Lower Frequency but Emerging

Q3.1

Write a brief note on psilocybin-assisted therapy.

EXAM PEARL

Key points required: - 5-HT_{2A} agonism → DMN disruption → neuroplasticity (BDNF, mTOR, synaptogenesis) - Evidence: TRD (COMPASS Phase 2b, 29% remission with 25 mg); MDD (Johns Hopkins, 71% response); cancer existential distress; alcohol use disorder - Model: not standalone drug, psilocybin-assisted psychotherapy (preparation + drug session + integration) - Contraindications: personal/family history of schizophrenia, bipolar I, active psychosis - Regulatory: Schedule I (India, USA); Australia rescheduled 2023; FDA Breakthrough Therapy Designation - Not currently available for clinical use in India

Q3.2

Write a note on brexanolone for postpartum depression.

EXAM PEARL

Key points required: - Mechanism: synthetic allopregnanolone; GABA-A PAM (synaptic γ -subunit AND extrasynaptic δ -subunit) - Peripartum hypothesis: progesterone → allopregnanolone rise in pregnancy; abrupt fall postpartum → PPD in vulnerable women - Administration: IV 60-hour infusion; hospital setting; REMS required - Evidence: HUMMINGBIRD trial, 73.7% response at 60 hours - Contrast with zuranolone: oral; 14 days; no REMS; approved for MDD + PPD; same mechanism - Comparison with SSRIs: faster onset (hours vs weeks); PPD-specific mechanism; IV vs oral

Q3.3

Write a note on orexin antagonists in the management of insomnia.

EXAM PEARL

Key points required: - Orexin system: wake-promoting neuropeptides; lateral hypothalamus; project to LC, raphe, TMN, VTA - DORA mechanism: block OX1R + OX2R → specifically suppress wake drive - Advantage over BZDs/Z-drugs: preserves sleep architecture; no physical dependence; minimal rebound insomnia - Three agents: suvorexant (2014, ~12h T_{1/2}), lemborexant (2019, ~17–27h, preferred elderly), daridorexant (2022, ~8h, best daytime functioning) - Side effects: somnolence, complex sleep behaviours (BBW), next-day impairment - Schedule IV; no significant tolerance

Q3.4

Write a note on rational polypharmacy in psychiatry.

EXAM PEARL

Key points required: - Definition: concurrent use of multiple drugs with explicit clinical rationale and evidence base - Evidence-based combinations: SSRI + AP augmentation (FDA-approved), lithium + AD, OFC (olanzapine + fluoxetine), clozapine + lamotrigine - Irrational polypharmacy: two APs without rationale, prescribing cascade, two drugs same class, anticholinergics no longer needed - Deprescribing principles: reconcile → identify targets → assess feasibility → patient engagement → monitor - STOPP/START criteria framework - High-priority deprescribing targets: anticholinergics, long-term BZDs, antipsychotics in dementia when stabilised

SECTION C: EXAMINER FOCUS AREAS BY YEAR PATTERN

What Examiners Test More in Each Sub-topic

Clozapine questions, examiner preferences:

- Almost always include: monitoring protocol (exact ANC thresholds and frequencies)
- Frequently asked: management of agranulocytosis (G-CSF now standard, mention it)
- Occasionally asked: re-challenge protocol; clozapine in suicidality; clozapine vs other APs in TRS
- Rarely asked: pharmacogenomics of clozapine (CYP1A2, smoking interaction)

Serotonin syndrome, examiner preferences:

- Hunter criteria are more likely to be asked than Sternbach criteria (Hunter has better sensitivity/specificity)
- Comparison with NMS is asked almost every time SS appears

- Management: cyproheptadine dose (12 mg loading, 2 mg q2h) is a specific detail that scores marks
- The MAOI washout periods (5 weeks for fluoxetine, 2 weeks for others) appear regularly

Lithium, examiner preferences:

- Pregnancy section almost always included (Ebstein anomaly risk, use updated 2017 NEJM figures)
- Renal effects (NDI, CKD) are frequently asked in the adverse effects section
- Drug interactions (NSAIDs, ACEi, thiazides) always expected
- Haemodialysis indications are specific and examinable

Newer drugs, examiner preferences:

- Mechanism of action questions dominate: "Explain the multimodal mechanism of vortioxetine"
- Esketamine REMS is a high-yield specific topic (few candidates know the monitoring requirements)
- Cariprazine D3 selectivity and clinical significance is a favourite newer topic
- Psilocybin has started appearing as a 5-mark short note since 2022–2023

SECTION D: PREDICTED HIGH-PROBABILITY QUESTIONS FOR 2026

Based on topic frequency trends and emerging areas:

Tier 1: Almost Certain (>80% probability)

1. Clozapine: monitoring, adverse effects, management of agranulocytosis (*long essay or 10-mark short note*)
2. Serotonin syndrome vs NMS: pathophysiology, clinical features, management, differentiation (*10 marks*)
3. Lithium: comprehensive pharmacology, TDM, toxicity management (*long essay or 10 marks*)
4. TRD augmentation strategies (*10 marks*)

Tier 2: Very Likely (60–80% probability)

1. Drug interactions in psychiatry, high-risk combinations (*8–10 marks*)
2. LAI antipsychotics, advantages, types, monitoring (*8 marks*)
3. Newer antipsychotics, cariprazine, lumateperone, brexpiprazole (*8 marks*)
4. Esketamine, mechanism, REMS, place in therapy (*8 marks*)
5. Benzodiazepine withdrawal, management (*5–8 marks*)

6. Antipsychotic discontinuation and supersensitivity psychosis (5 marks)

Tier 3: Likely (40–60% probability)

1. Psilocybin-assisted therapy (5 marks)
2. Brexanolone / postpartum depression pharmacology (5 marks)
3. Orexin antagonists for insomnia (5 marks)
4. Pharmacogenomics: CYP2D6, CYP2C19, HLA-B1502 (5–8 marks)*
5. Rational polypharmacy and deprescribing (5 marks)

Tier 4: Watch List (Emerging, 20–40% probability)

1. MDMA-assisted therapy for PTSD (5 marks)
2. Auvelity (dextromethorphan-bupropion) mechanism (5 marks)
3. Zuranolone for MDD / PPD (5 marks)
4. Precision psychiatry and biomarker-guided treatment (5 marks)
5. Cannabis-based medicines in psychiatry (5 marks)

SECTION E: MARK ALLOCATION STRATEGY

For a 15-mark long essay:

COMPONENT · MARKS

Introduction (clear definition, clinical context) 1–2

Pharmacology / Mechanism 3–4

Clinical features / Indications 2–3

Management / Protocol 3–4

Monitoring / Safety 2

Conclusion (modern relevance, guidelines) 1

For a 10-mark short note:

COMPONENT · MARKS

Definition / Introduction 1

Mechanism / Pharmacology 2–3

Clinical features or indications 2–3

Management / Monitoring 2–3

Summary point or comparison 1

For a 5-mark short note:

COMPONENT · MARKS

One-line definition 0.5

Mechanism (2–3 sentences) 1.5

Clinical use / evidence 1.5

Key distinguishing feature 1

Adverse effects or limitations 0.5

SECTION F: COMMON EXAM MISTAKES: AVOID THESE

MISTAKE · CORRECT APPROACH

Saying clozapine is contraindicated after any neutropenia Only contraindicated after AGRANULOCYTOSIS (ANC <500). Moderate neutropenia = enhanced monitoring, not permanent stop

Confusing clonus (SS) with rigidity (NMS) Clonus = serotonin syndrome; lead-pipe rigidity = NMS. This single distinction carries marks in every differential diagnosis question

Stating lithium toxicity treated with activated charcoal Activated charcoal does NOT adsorb lithium. IV normal saline + haemodialysis

Giving only 2-week washout for fluoxetine before MAOI Fluoxetine = 5 weeks (norfluoxetine active metabolite). Other SSRIs = 2 weeks

Stating clozapine + carbamazepine needs monitoring This combination is ABSOLUTELY CONTRAINDICATED, not just cautious use

Omitting G-CSF in agranulocytosis management G-CSF (filgrastim) is now standard care for clozapine-induced agranulocytosis

Not mentioning REMS for esketamine REMS is a core examinable feature of esketamine. Missing it loses 2–3 marks

Saying all LAIs require deltoid injection PP1M requires deltoid for first 2 injections specifically; PP3M can be deltoid or gluteal

Stating psilocybin is approved for clinical use in India Psilocybin is Schedule I under NDPS Act in India, no approved clinical use

Omitting HLA-B*1502 in any question about carbamazepine in Asian patients This is mandatory testing, a patient safety issue the examiner expects you to flag

SECTION G: INTEGRATIVE QUESTION FORMATS

These are multi-part questions that test integration across topics. Increasingly common in PG exams-pattern papers.

Integrative Q1:

A 35-year-old male with treatment-resistant schizophrenia is started on clozapine 300 mg/day. Six weeks later he develops fever, chest pain, and elevated troponin. His ANC is $2,800/\text{mm}^3$.

- (a) What is the most likely diagnosis? (2 marks)
- (b) What is your immediate management? (4 marks)
- (c) Can this patient be re-challenged with clozapine in future? Discuss. (4 marks)

KEY INSIGHT

Answer framework: (a) Clozapine-induced myocarditis (fever + chest pain + elevated troponin + time frame, weeks 2–8) (b) Stop clozapine immediately; ECG; echocardiogram; cardiac biomarkers (serial troponin, CRP); cardiologist consult; cardiology monitoring; supportive care; do NOT restart clozapine (c) Controversial, not a contraindication unlike agranulocytosis, but high risk. In specialised centres only: cardiac clearance, very slow titration (6.25 mg every 1–2 weeks), daily cardiac monitoring first 8 weeks, low-dose aspirin, baseline echo. Benefit-risk discussion essential. Most guidelines advise against.

Integrative Q2:

A 28-year-old woman with bipolar II disorder is stable on lithium 800 mg/day (level 0.7 mmol/L). She plans to get pregnant.

- (a) What are the teratogenic risks of lithium? (3 marks)
- (b) How would you manage her medication during pregnancy and post-partum? (4 marks)
- (c) What monitoring is required if lithium is continued? (3 marks)

KEY INSIGHT

Answer framework: (a) Ebstein anomaly (tricuspid valve malformation): background risk 6/10,000; with lithium 21/10,000 (NEJM 2017 revised figures, much lower than previously stated). Other neonatal effects if continued: floppy baby syndrome, transient hypotonia, cyanosis. (b) First trimester: discuss stopping vs continuing based on bipolar severity. If continued: maintain at lowest effective dose. 36 weeks: reduce dose 25–50% (GFR peaks then falls post-partum → level spikes). Post-partum: retitrate as GFR normalises. Breastfeeding: generally advised against (40–50% of maternal level in breast milk). (c) Foetal echocardiogram at 16–18 weeks; serum lithium levels fortnightly in 3rd trimester; neonatal examination for lithium effects; renal function monitoring; anomaly scan; growth scans.

Integrative Q3:

A 45-year-old man with schizophrenia on haloperidol 20 mg/day develops fever (40.2°C), generalised rigidity, altered consciousness, and CK of 18,000 U/L. Simultaneously, his SSRI was increased two weeks ago.

- (a) What are the two most important differential diagnoses? (2 marks)
- (b) How would you differentiate them clinically and on investigations? (4 marks)
- (c) Outline management for each. (4 marks)

KEY INSIGHT

Answer framework: (a) NMS (haloperidol exposure, rigidity, elevated CK) vs Serotonin syndrome (SSRI increase, though CK usually lower in SS) (b) NMS: lead-pipe rigidity, normal/reduced reflexes, no clonus, CK very elevated, low serum iron, onset over days, leukocytosis. SS: clonus (spontaneous/inducible/ocular), hyperreflexia, onset rapid (hours), CK usually normal/mildly elevated, diarrhoea, mydriasis. In this case: extremely high CK + rigidity + antipsychotic → NMS more likely. Hunter criteria: if clonus present = SS. (c) NMS: stop haloperidol, ICU, IV fluids, cooling, dantrolene (0.25–2 mg/kg IV q6h), bromocriptine (2.5–10 mg TID), lorazepam for sedation. SS: stop SSRI, cyproheptadine (12 mg loading, 2 mg q2h), benzodiazepines, cooling, ICU if severe.

Quick Review

30 Rapid-Fire Q&A

Format: Question → Answer → Examiner tip where relevant

Q01

What is the mechanism of action of vortioxetine that makes it a "multimodal" antidepressant?

Vortioxetine acts at 6 targets simultaneously: SERT inhibitor + 5-HT_{1A} partial agonist + 5-HT_{1B} partial agonist + 5-HT₃ antagonist + 5-HT₇ antagonist + 5-HT_{1D} antagonist. The 5-HT₃ antagonism increases acetylcholine in the prefrontal cortex, explaining its cognitive benefits. The 5-HT₇ antagonism modulates circadian rhythm and sleep architecture.

KEY INSIGHT

Exam tip: "Multimodal" = multiple serotonin receptor targets, not just SERT. The cognitive benefit via 5-HT₃ antagonism is the most examinable feature distinguishing it from SSRIs.

Q02

What are the Hunter Serotonin Toxicity Criteria? Give any two diagnostic patterns.

Hunter criteria require a serotonergic agent PLUS one of five patterns, all involving clonus or hyperreflexia:

1. Spontaneous clonus alone
2. Inducible clonus + agitation or diaphoresis
3. Ocular clonus + agitation or diaphoresis
4. Tremor + hyperreflexia
5. Hypertonia + temperature >38°C + ocular or inducible clonus

Sensitivity 84%, specificity 97%, superior to Sternbach criteria.

KEY INSIGHT

Exam tip: Clonus is the pathognomonic finding of serotonin syndrome. If you remember nothing else, remember: clonus = serotonin syndrome.

Q03

What is the REMS programme for esketamine, and why is it required?

REMS = Risk Evaluation and Mitigation Strategy. For esketamine (Spravato): drug dispensed only in certified healthcare settings (not pharmacy); patient monitored for 2 hours post-dose for dissociation, sedation, and blood pressure elevation; patient cannot drive on dosing day; healthcare setting must enrol in REMS programme.

Required because of: abuse potential (Schedule III), high rates of dissociation (>50%), significant BP elevation, and the impossibility of safe unsupervised self-administration.

Q04

What is the key difference between NMS and serotonin syndrome on neurological examination?

NMS: lead-pipe rigidity + normal or reduced reflexes + NO clonus.

Serotonin syndrome: clonus (spontaneous, inducible, ocular) + hyperreflexia + mild-to-moderate rigidity.

Clonus is present in SS and absent in NMS. This single finding is the most reliable bedside differentiator.

Q05

Name the three approved dual orexin receptor antagonists (DORAs) and their half-lives.

1. Suvorexant (Belsomra), ~12 hours, FDA 2014
2. Lemborexant (Dayvigo), ~17–27 hours, FDA 2019
3. Daridorexant (Quviviq), ~8 hours, FDA 2022

Daridorexant has the shortest half-life and the best next-day performance profile.

Lemborexant has the longest half-life and is preferred for sleep maintenance in elderly patients.

Q06

What is the TRS definition required before initiating clozapine (TRRIP consensus)?

Inadequate response (CGI-S ≥ 4 , persistent positive symptoms) despite:

- ≥ 2 adequate antipsychotic trials
- At least one must be a second-generation antipsychotic
- Each trial at adequate dose (≥ 600 mg chlorpromazine equivalents)
- Each trial for adequate duration (≥ 6 weeks)
- With documented adherence

Q07

What is the clozapine ANC monitoring schedule?

- Weeks 1–26: Weekly ANC
- Weeks 27–52: Every 2 weeks
- After 52 weeks: Monthly

Thresholds: ≥ 1500 = continue; 1000–1499 = continue with increased monitoring; 500–999 = interrupt and monitor daily; < 500 = STOP permanently (agranulocytosis, never re-challenge).

Q08

What is the mechanism of brexanolone and how does it differ from benzodiazepines?

Brexanolone is synthetic allopregnanolone, a positive allosteric modulator (PAM) of GABA-A receptors. Unlike benzodiazepines which modulate only synaptic $\gamma 2$ -subunit-containing GABA-A receptors, brexanolone modulates BOTH synaptic ($\gamma 2$ -containing) AND extrasynaptic (δ -subunit-containing) GABA-A receptors. Extrasynaptic GABA-A receptors mediate tonic inhibition in limbic regions, this is the proposed mechanism for the rapid antidepressant effect specific to postpartum depression.

Q09

What is the washout period required between fluoxetine and an MAOI, and why is it different from other SSRIs?

5 weeks, because fluoxetine has an active metabolite, norfluoxetine, with a half-life of approximately 4–16 days. At 5 half-lives of norfluoxetine, the drug is substantially cleared. All other SSRIs and SNRIs require only 2 weeks washout before starting an MAOI.

Going from MAOI to any serotonergic drug: always 2 weeks minimum (3 weeks for irreversible MAOIs like phenelzine and tranylcypromine in clinical practice).

Q10

What is the mechanism by which smoking reduces clozapine levels, and what is the clinical implication?

Cigarette smoke contains polycyclic aromatic hydrocarbons (PAHs) that strongly induce CYP1A2. Clozapine is metabolised primarily by CYP1A2. Heavy smokers (> 10 cigarettes/day) may require 50–100% higher clozapine doses to achieve therapeutic levels.

Clinical implication: if a patient stops smoking (e.g., admitted to hospital), CYP1A2 induction is lost $\rightarrow$ clozapine levels rise $\rightarrow$ toxicity risk. Monitor clozapine levels with any

change in smoking status.

Q11

What is the clinical significance of D3 receptor selectivity in cariprazine?

D3 receptors are concentrated in mesolimbic areas, prefrontal cortex, and hippocampus, circuits governing motivation, reward, and cognition. Cariprazine has 20× selectivity for D3 over D2. High-affinity D3 partial agonism is proposed to improve negative symptoms of schizophrenia (avolition, anhedonia) by restoring reward salience and motivational drive. The RGH-MD-16 trial demonstrated statistically significant superiority of cariprazine over risperidone on PANSS negative symptom scores, the first such finding in a head-to-head trial.

Q12

Name four drugs that raise lithium levels and explain one mechanism.

1. NSAIDs, reduce renal prostaglandins → ↓renal blood flow → ↓lithium clearance
2. ACE inhibitors/ ARBs, reduce glomerular filtration rate → lithium retention
3. Thiazide diuretics, sodium depletion → compensatory lithium retention in proximal tubule
4. Dehydration/low-sodium diet, same mechanism as thiazides (proximal tubule Na/Li competition)

NSAIDs raise lithium levels by 50–100%. Activated charcoal does NOT help in lithium toxicity.

Q13

What are the indications for haemodialysis in lithium toxicity?

1. Lithium level >4.0 mmol/L (regardless of symptoms)
 2. Lithium level >2.5 mmol/L with severe symptoms (seizures, coma, cardiovascular instability)
 3. Anuric renal failure with any toxic level (cannot excrete lithium renally)
 4. Rapidly rising lithium level despite IV saline
-

Q14

What is lumateperone's novel mechanism compared to all other antipsychotics?

Lumateperone is the only antipsychotic that acts as a D1 receptor agonist/partial agonist in the prefrontal cortex. All other antipsychotics either block D1 or have no D1 activity. Prefrontal D1 stimulation is predicted to improve cognition and negative symptoms.

Additionally, lumateperone has dual D2 activity (pre-synaptic agonist + post-synaptic antagonist) and SERT inhibition, explaining its approval for both schizophrenia and bipolar I + II depression.

KEY INSIGHT

Exam tip: "Lumateperone turns D1 ON", this is the single most examinable novelty.

Q15

What distinguishes pimavanserin from all other antipsychotics, and what is its approved indication?

Pimavanserin has NO dopamine receptor binding, it is a 5-HT_{2A} and 5-HT_{2C} inverse agonist only. This makes it the only antipsychotic that does not worsen motor symptoms in Parkinson's disease. It is FDA-approved specifically for Parkinson's disease psychosis (PDP), the only drug with this indication. Because it avoids D2 blockade, it does not cause EPS, worsening of tremor/rigidity, or prolactin elevation.

Q16

What is the mechanism of Auvelity (dextromethorphan-bupropion) and why are the two drugs combined?

Dextromethorphan (DXM) is an uncompetitive NMDA receptor antagonist and sigma-1 receptor agonist with ketamine-like antidepressant mechanisms. However, DXM is rapidly metabolised by CYP2D6 in extensive metabolisers. Bupropion is a potent CYP2D6 inhibitor, when co-administered, it raises DXM levels 8-fold to therapeutic concentrations. Bupropion also contributes NDRI antidepressant activity independently. The combination achieves NMDA antagonism via an oral route without requiring IV administration or REMS.

Q17

What are the four cardinal features of NMS?

1. Hyperthermia (>38°C, often >40°C)
2. Lead-pipe muscle rigidity (generalised, severe)
3. Altered consciousness (confusion → stupor → coma)
4. Autonomic instability (tachycardia, labile BP, diaphoresis, tachypnoea)

Supporting findings: very elevated CK (>1000 U/L), leukocytosis, low serum iron, metabolic acidosis, myoglobinuria.

Q18

What is supersensitivity psychosis and how do you prevent it?

Supersensitivity psychosis occurs after abrupt antipsychotic discontinuation. Chronic D2 blockade → compensatory upregulation of D2 receptors. Abrupt withdrawal → dopaminergic rebound → florid psychosis within days, often more severe and atypical than the original illness.

Prevention: gradual taper, minimum 3–6 months for long-term use; for clozapine: 6–12 months taper. Never abruptly stop antipsychotics in chronic schizophrenia.

Q19

What is the CYP2D6 ultrarapid metaboliser phenotype and its clinical significance in psychiatry?

Ultrarapid metabolisers (UM) carry duplicated or amplified CYP2D6 genes, they metabolise CYP2D6 substrates very rapidly, resulting in sub-therapeutic drug levels. Clinical consequence: patients on tricyclic antidepressants, risperidone, aripiprazole, or haloperidol may show treatment failure at standard doses. Prevalence: ~1–2% Caucasians; up to 29% in Ethiopian populations.

Codeine (a prodrug activated by CYP2D6 to morphine): UMs may produce excessive morphine → toxicity risk. PMs get no analgesia.

Q20

What is HLA-B*1502 and when must it be tested?

HLA-B*1502 is a genetic variant of the Human Leukocyte Antigen complex found predominantly in individuals of East and Southeast Asian descent (Han Chinese ~10%, Thai ~8%, South Asian ~2–4%). Carriers who receive carbamazepine face dramatically elevated risk of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), life-threatening mucocutaneous reactions.

Must be tested: before initiating carbamazepine (or oxcarbazepine) in any patient of Asian ancestry. FDA label mandates this testing. If positive → do not prescribe carbamazepine; use valproate or lamotrigine instead.

Q21

Enumerate the evidence-based FDA-approved augmentation strategies for treatment-resistant depression.

1. Aripiprazole + antidepressant (SSRI/SNRI), FDA approved
2. Quetiapine XR + antidepressant, FDA approved

3. Brexpiprazole + antidepressant, FDA approved
4. Olanzapine + fluoxetine (OFC), FDA approved (bipolar depression + TRD)
5. Esketamine nasal spray + oral antidepressant, FDA approved (TRD 2019; MDSI 2020)

Non-FDA approved but Level I evidence: lithium augmentation of antidepressants.

Q22

What is the peripartum mechanism hypothesis for postpartum depression and how does brexanolone target it?

During pregnancy, progesterone is metabolised to allopregnanolone → GABA-A receptor adaptations to chronically elevated allopregnanolone (downregulation of surface receptors, subunit changes). At delivery, allopregnanolone falls precipitously → GABA-A receptor excitability surge → PPD in vulnerable women.

Brexanolone = synthetic allopregnanolone. IV administration replaces the lost allopregnanolone signal, restoring GABA-A function → rapid antidepressant effect within 24–48 hours. This is pharmacologically distinct from SSRIs, which act on monoamine systems and take 4–8 weeks.

Q23

What are the prerequisites for switching from paliperidone palmitate 1-monthly (PP1M) to 3-monthly (PP3M)?

1. Patient must have been adequately treated with PP1M for at least 4 months
 2. Last two consecutive PP1M doses must be at the same dose level (dose must be stable)
 3. PP3M dose = $3.5 \times$ PP1M dose
 4. PP3M can be administered at deltoid or gluteal sites (unlike PP1M which requires deltoid for first two doses)
-

Q24

What is the Ashton Protocol and when is it used?

The Ashton Protocol is a benzodiazepine tapering method developed by Prof. Heather Ashton. Key principles:

- Convert all short-acting benzodiazepines to equivalent diazepam dose
- Reduce diazepam dose by approximately 10% every 1–2 weeks
- Taper can take months to years for long-term high-dose users
- Adjuncts: carbamazepine or valproate to reduce seizure risk during taper

Used for: benzodiazepine dependence management. Prevents withdrawal seizures and delirium while minimising protracted withdrawal syndrome.

Q25

What is pimavanserin's key safety concern and the FDA black box warning?

QTc prolongation, pimavanserin carries moderate QTc prolongation risk. Avoid with other QTc-prolonging drugs (antiarrhythmics, some antipsychotics, azithromycin).

FDA black box warning: increased risk of death in elderly patients with dementia-related psychosis (class warning shared by all antipsychotics). Despite its Parkinson's Disease Psychosis approval, this warning applies and pimavanserin should not be used for dementia-related psychosis outside of PDP.

Q26

What is the mechanism of action of psilocybin in depression and what neural network does it disrupt?

Psilocybin is dephosphorylated to psilocin → 5-HT_{2A} agonist in prefrontal cortex, anterior cingulate, thalamus, and limbic areas.

Key neural network disrupted: Default Mode Network (DMN), the medial prefrontal cortex, posterior cingulate cortex, and angular gyrus network. The DMN is hyperconnected in depression and mediates self-referential rumination. Psilocin disrupts DMN connectivity → ego dissolution + reduced rumination. Simultaneously increases global brain connectivity (hyperconnected state) and promotes neuroplasticity via BDNF-mTOR-synaptogenesis cascade.

Q27

What is the clinical significance of valproate inhibiting UGT enzymes?

Valproate inhibits UDP-glucuronosyltransferase (UGT) enzymes, specifically UGT1A4 and UGT2B7. Clinical consequence: lamotrigine is primarily metabolised by UGT. When valproate is added to lamotrigine, lamotrigine levels double.

Practical rule: When adding valproate to a patient already on lamotrigine → halve the lamotrigine dose immediately. When starting lamotrigine in a patient already on valproate → use half the usual lamotrigine titration schedule. Failure to follow this → lamotrigine toxicity and potentially Stevens-Johnson syndrome.

Q28

What distinguishes brexpiprazole from aripiprazole pharmacologically?

Both are dopamine partial agonists. Key differences:

- Brexpiprazole has LOWER intrinsic activity at D2 than aripiprazole (more antagonist-like behaviour)
- Brexpiprazole has MORE potent 5-HT_{1A} partial agonism
- Brexpiprazole has MORE potent α _{1B} and α _{2C} adrenergic antagonism
- Clinical result: brexpiprazole causes LESS akathisia than aripiprazole
- Brexpiprazole is FDA-approved for Alzheimer's disease agitation (2023), aripiprazole is not approved for this

KEY INSIGHT

Exam tip: "Brexpiprazole = aripiprazole with less akathisia and approved for dementia agitation."

Q29

What are the three phases of psilocybin-assisted psychotherapy?

1. **Preparation sessions (2–3 sessions):** Build therapeutic alliance; set intentions; psychoeducation about the experience; reduce anticipatory anxiety; establish safety protocols
2. **Drug session(s) (1–3 sessions):** Supervised in a carefully designed environment (comfortable room, curated music, eye shades); therapist present throughout 6–8 hours; non-directive supportive presence
3. **Integration sessions (2–4 sessions):** Process the experience; translate insights into behaviour change; CBT-like work; address challenging content from the drug session

The set (psychological state/intention), setting (physical and relational environment), and therapeutic relationship are considered pharmacologically relevant to outcomes, not just the drug.

Q30

What is the dose conversion rule for PP3M and what does PDSS mean in the context of LAI antipsychotics?

PP3M dose conversion: PP3M dose (mg) = PP1M monthly dose (mg) $\times$ 3.5

Example: Patient on PP1M 78 mg monthly $\rightarrow$ PP3M 273 mg every 3 months (nearest available dose: 263 mg)

PDSS = Post-Injection Delirium/Sedation Syndrome, a rare but serious adverse effect unique to olanzapine pamoate (Zypadhera). It occurs when olanzapine pamoate crystals enter the bloodstream during injection, releasing a bolus of olanzapine rapidly $\rightarrow$ sudden

sedation, delirium, or cardiovascular collapse. Incidence: ~0.07% per injection.
 Management: 3-hour mandatory monitoring in a healthcare setting after every injection.
 This is why olanzapine pamoate requires on-site monitoring unlike other LAIs.

QUICK RECALL SUMMARY TABLE

Q#	TOPIC	KEY ANSWER (ONE LINE)
01	Vortioxetine mechanism	SERT + 5-HT _{1A} /1B partial agonist + 5-HT ₃ /7/1D antagonist
02	Hunter criteria	Clonus (in 4 of 5 patterns) + hyperreflexia required
03	Esketamine REMS	Certified setting; 2h monitoring; no driving
04	SS vs NMS bedside	Clonus = SS; Lead-pipe rigidity = NMS
05	Three DORAs	Suvorexant / Lemborexant / Daridorexant
06	TRS definition	≥2 APs, adequate dose, ≥6 weeks each, documented adherence
07	Clozapine ANC schedule	Weekly → Fortnightly → Monthly (after 1 year)
08	Brexanolone vs BZDs	Modulates extrasynaptic δ-GABA-A (BZDs do not)
09	Fluoxetine MAOI washout	5 weeks (norfluoxetine); other SSRIs = 2 weeks
10	Smoking + clozapine	CYP1A2 induction → reduced levels; stopping = toxicity risk
11	Cariprazine D ₃	20× D ₃ selectivity; negative symptom evidence
12	Lithium level raisers	NSAIDs, ACEi, thiazides, dehydration
13	Haemodialysis trigger	Level >4; or >2.5 + severe symptoms; anuric renal failure
14	Lumateperone novel feature	Only AP with D ₁ agonism in PFC
15	Pimavanserin key feature	No D ₂ binding; 5-HT _{2A} inverse agonist; PDP only

Q#	TOPIC	KEY ANSWER (ONE LINE)
16	Auvelity mechanism	BUP inhibits CYP2D6 → DXM levels rise 8× → NMDA antagonism
17	NMS tetrad	Fever + Rigidity + Altered consciousness + Autonomic instability
18	Supersensitivity psychosis	D2 upregulation → rebound psychosis after abrupt AP stop
19	CYP2D6 UM	Sub-therapeutic levels; treatment failure; 29% Ethiopians
20	HLA-B*1502	Carbamazepine + Asian descent = SJS/TEN risk; mandatory testing
21	FDA augmentation for TRD	Aripiprazole, quetiapine, brexpiprazole, OFC, esketamine
22	PPD mechanism	Allopregnanolone crash postpartum → GABA-A hyperexcitability
23	PP3M prerequisites	4 months stable PP1M; same dose last 2 injections; ×3.5 dose
24	Ashton Protocol	10% / 1–2 weeks diazepam taper for BZD dependence
25	Pimavanserin BBW	Elderly dementia mortality (class warning); QTc risk
26	Psilocybin neural target	DMN disruption; global connectivity increase; BDNF / mTOR
27	Valproate + lamotrigine	Halve lamotrigine dose (UGT inhibition raises levels 2×)
28	Brexpiprazole vs aripiprazole	Lower D2 intrinsic activity; less akathisia; approved AD agitation
29	Psilocybin therapy phases	Preparation → Drug session → Integration
30	PP3M dose + PDSS	PP3M = 3.5 × PP1M; PDSS = olanzapine pamoate only; 3h monitoring

Community Public Health

Paper IV · Neurology, Medicine & Recent Advances. Six study modes, from notes to quick review.

Study Notes

SECTION 1: NATIONAL MENTAL HEALTH PROGRAMME (NMHP)

1.1 Historical Background and Origins

THE PRE-NMHP ERA

Before 1982, mental health services in India were almost entirely institutional, large asylum-style psychiatric hospitals concentrated in urban areas, inherited from the colonial era. The Ranchi Institute of Neuropsychiatry (now RINPAS), the Agra Mental Hospital, and state hospitals in Madras and Bombay were the main nodes of care. Community psychiatry barely existed as a concept in India.

The Bhole Committee (1946) had called for integration of health services at the primary care level, but mental health received minimal attention. The Mudaliar Committee (1961) similarly did not place mental health prominently.

The turning point came from a combination of factors:

1. Growing recognition of the massive treatment gap, fewer than 1% of people with mental illness were receiving treatment
2. WHO's move toward community-based care globally
3. The demonstration project at Bellary

THE BELLARY MODEL (1975-1982): THE PROOF OF CONCEPT

The Bellary District Mental Health Programme was a landmark demonstration project run from the Department of Psychiatry, PG exams, and the Bangalore Medical College. Key investigators included Dr. R. Srinivasa Murthy and colleagues.

Core innovation: Mental health services could be delivered at the primary care level by non-specialist health workers with focused training, under specialist supervision.

What Bellary demonstrated:

- Primary health centre (PHC) medical officers could diagnose and manage common mental disorders after brief training (2 weeks)
- MHPSS workers could identify and follow up patients in the community
- Maintenance antipsychotics could be dispensed at PHC level
- Outcome was comparable to hospital care for many patients with schizophrenia
- Cost was dramatically lower than hospital-based care

Key findings from Bellary:

- Prevalence of severe mental disorders in community: approximately 20-25/1000 population
- Task-shifting to PHC level was feasible with appropriate training and supervision
- Community acceptance was adequate when mental health was integrated with primary care

The Bellary model became the blueprint for the NMHP.

NMHP LAUNCH: 1982

The National Mental Health Programme was officially launched in 1982, making India one of the earliest low-middle income countries to have a national mental health policy framework.

Key architects: Dr. R. Srinivasa Murthy, Dr. B. B. Sethi, and the central government health ministry.

Guiding philosophy: Community-based care, integration with primary health care, task-shifting to non-specialist workers.

1.2 NMHP: Objectives, Components, and Architecture

OFFICIAL OBJECTIVES (1982 FORMULATION)

1. Ensure availability and accessibility of minimum mental health care for all, especially to the most vulnerable and underprivileged
2. Encourage application of mental health knowledge in general health care and social development
3. Promote community participation in mental health services development
4. Stimulate efforts toward self-help in the community

THREE PILLARS OF NMHP

PILLAR · DESCRIPTION

Treatment Delivery of mental health care through integration into primary care

Prevention Measures to reduce incidence of mental illness

Rehabilitation Community-based rehabilitation to maximize function

COMPONENTS OF NMHP

1. **District Mental Health Programme (DMHP)**, operational arm (see Section 2)
2. **Manpower development**, training of general health workers, medical officers, specialists
3. **IEC (Information, Education, Communication)**, mental health literacy in communities
4. **Research and evaluation**, monitoring and evidence generation

5. **Strengthening of mental hospitals**, upgradation of existing institutions
 6. **Mental health coverage under schemes**, insurance, disability certification
-

1.3 NMHP Revisions and Current Status

1982 → 2003 REVISION

The NMHP was revised substantially in 2003, incorporating:

- Stronger emphasis on human rights
- Expanded scope to address psychosocial disability
- Integration with other disease control programmes
- Explicit focus on suicide prevention

2003 → NATIONAL MENTAL HEALTH POLICY 2014

India's first standalone **National Mental Health Policy** was released in 2014 (distinct from NMHP which is a programme). The Policy laid out a vision: *"mentally healthy population, with access to mental health care and reduction of mental health morbidity, disability, suicide, and distress."*

The Policy acknowledged:

- Inadequacy of hospital-centric services
- Massive workforce deficit
- Need for rights-based approach
- Link between mental health and social determinants

CURRENT NMHP STATUS (2024-2026)

Achievements:

- DMHP extended to 700+ districts (near-universal coverage on paper)
- Tele-MANAS launched (2022), national tele-mental health programme
- Mental Healthcare Act 2017 enacted
- Ayushman Bharat integration
- Mental health included in National Health Mission (NHM)

Persistent limitations:

- Severe specialist shortage: ~9,000 psychiatrists for 1.4 billion population (WHO recommends 3/100,000; India has ~0.3/100,000)
- Underfunding: mental health receives less than 1% of total health budget
- Implementation heterogeneity, some DMHP districts functional, many in name only
- Psychotropic drug supply chains remain unreliable at PHC level
- Referral pathways between DMHP and tertiary care poorly structured

- Stigma continues to suppress help-seeking
 - Mental health integration in ASHA / ANM training inadequate
-

SECTION 2: DISTRICT MENTAL HEALTH PROGRAMME (DMHP)

2.1 DMHP Architecture

The DMHP is the operational unit of NMHP, where the programme meets the patient.

Launched formally: 1996 (following the 1982 policy, operational rollout began in 27 districts across 9 states)

Expansion timeline:

- 1996: 27 pilot districts
- 2003-2007: Expanded to 100+ districts under 10th Plan
- 2012: Extended to 123 districts under 12th Plan
- Current: Aims for all 700+ districts

CORE DMHP TEAM (AT DISTRICT LEVEL)

POSITION · ROLE

Psychiatrist (1) Clinical lead, training, supervision

Clinical Psychologist (1) Psychological assessment, therapy

Psychiatric Social Worker (1) Family intervention, community outreach, linkages

Psychiatric Nurse (1) Medication management, patient education, outreach

Data Entry Operator (1) MIS, records

MHO (Medical Health Officer) Administrative coordination

DMHP SERVICE DELIVERY COMPONENTS

1. **Outpatient services** at district hospital, regular OPD for new and follow-up cases
2. **Inpatient beds**, small inpatient unit (10-30 beds) at district hospital
3. **PHC outreach**, regular outreach clinics at PHCs / CHCs by DMHP team
4. **School mental health**, screening in schools, teacher training
5. **Training of general health workers**, medical officers, ANMs, ASHAs
6. **Crisis intervention**, 24x7 services (aspirational; implementation variable)
7. **Community camps**, periodic mental health camps in rural areas
8. **Liaison with other depts**, education, social welfare, police

2.2 NMHP-DMHP Relationship

A common source of exam confusion:

- NMHP is the **policy and programme framework**, it sets objectives, provides funding guidelines, and monitors outcomes
- DMHP is the **implementation unit**, it does the actual work at district level
- One DMHP per district, funded under NMHP through National Health Mission

2.3 Manpower Crisis in NMHP-DMHP

This is a critical exam point, the gap between what is needed and what exists is staggering.

CATEGORY	REQUIREMENT (WHO STANDARD)	INDIA AVAILABILITY	DEFICIT
Psychiatrists	~42,000 (3 / 100,000)	~9,000-10,000	~32,000
Psychologists	~170,000 (12 / 100,000)	~2,000	~168,000
Social workers	~170,000	~4,000	~166,000
Nurses (psychiatric)	~170,000	~8,000	~162,000

Consequences:

- Most DMHP psychiatrist posts remain unfilled (rural postings unpopular)
- Clinical psychologist posts especially difficult to fill
- PSW training programmes are few and scattered
- Results in "paper DMHP", structure exists, services don't

Proposed solutions (policy level):

- Mid-level mental health worker (MLMHW), certificate-level training (piloted in Assam)
- B.Sc. in Community Mental Health
- Incentives for rural postings
- Task-shifting to ASHA / ANM with robust supervision
- Tele-supervision of DMHP workers by distant specialists

2.4 Primary Care Integration: The Core Challenge

The DMHP model depends on integration of mental health into primary care. What this means in practice:

Ideal integration model:

1. ASHA / community health worker: awareness, destigmatization, case-finding
2. ANM / health worker: basic screening (using PHQ-9, GAD-7, ASSIST), follow-up
3. PHC Medical Officer: diagnosis, prescribe first-line psychotropics, follow-up

4. CHC/DMHP: specialist consultation, complex cases, inpatient if needed
5. District hospital/DMHP HQ: full specialist services
6. Medical college/tertiary: complex, treatment-resistant cases

Barriers to integration:

- MOs overburdened, mental health feels like additional burden
 - Psychotropic drugs not reliably stocked at PHC
 - No mental health EMR/tracking systems
 - MO training in mental health is inadequate (3-5 days at best)
 - Social stigma among health workers themselves
 - No financial incentives for PMJAY-listed mental health care at PHC level
-

SECTION 3: AYUSHMAN BHARAT AND MENTAL HEALTH

3.1 Ayushman Bharat: Two Pillars

Ayushman Bharat has two distinct components:

1. **Health and Wellness Centres (HWC)**, primary and preventive care expansion
2. **Pradhan Mantri Jan Arogya Yojana (PMJAY)**, health insurance for inpatient care

3.2 Health and Wellness Centres (HWC)

Target: Upgrade 150,000 sub-centres and PHCs to HWCs by 2022 (ongoing)

HWC package includes 12 service categories, of which mental health is one:

- Screening for mental disorders
- Basic counseling
- Psychotropic medication dispensing (essential list)
- Referral linkages to DMHP

Mental health components at HWC:

- Screening tools (K10, PHQ-9 adapted versions)
- Community Health Officers (CHO), 6-month B.Sc. bridge course, trained to deliver basic mental health services
- Tele-consultation link to specialists (through tele-MANAS)

Significance for exam: HWCs represent the strongest attempt yet at primary care integration of mental health in India.

3.3 PMJAY and Mental Health

Coverage: PMJAY covers inpatient psychiatric care under its benefit packages.

Mental health packages under PMJAY:

- Acute psychiatric inpatient care (schizophrenia, bipolar, substance use, etc.)
- ECT procedures
- Select psychiatric procedures

Limitations:

- Only inpatient coverage, outpatient mental health (majority of care) not covered
- Insurance model does not incentivize prevention or early intervention
- Private psychiatric hospitals accessing PMJAY are limited in number
- Day care and rehabilitation are not included

The irony: Most mental health burden is managed outpatient, but PMJAY only covers hospitalization. This creates a structural gap.

SECTION 4: GLOBAL MENTAL HEALTH

4.1 WHO Mental Health Action Plan 2013-2030

The WHO MHAP (originally 2013-2020, extended to 2030) is the global framework for mental health.

FOUR OBJECTIVES OF MHAP 2013-2030

1. **Effective leadership and governance** for mental health
2. **Comprehensive, integrated, responsive mental health services** in community-based settings
3. **Implementation of strategies for promotion and prevention** in mental health
4. **Strengthened information systems, evidence and research** for mental health

KEY TARGETS (BY 2030)

INDICATOR	2020 BASELINE	2030 TARGET
Countries with mental health policy aligned to international instruments	80%	80% (maintained)
Mental health beds in community facilities vs hospitals	50% in community	80% in community
Rates of suicide	↓ 10% (2020)	↓ 15% (2030)
People covered by mental health promotion/prevention	80% countries	

SPECIAL INITIATIVE FOR MENTAL HEALTH (2019-2023)

WHO launched a Special Initiative targeting 12 priority countries to provide universal health coverage (UHC) for mental health, reaching 100 million more people.

4.2 Treatment Gap

Definition: The proportion of people with a mental disorder who need treatment but do not receive it.

Global figures:

- Median treatment gap for severe mental disorders globally: ~50-60%
- For depression and anxiety in LMICs: ~75-85%
- India: ~83-86% (NMHS 2015-16)

Why the gap persists:

1. Workforce shortage
2. Poor health system integration
3. Stigma
4. Cost of medications
5. Geographical inaccessibility
6. Cultural factors (traditional healers as first contact)
7. Lack of awareness/literacy
8. Policies and funding not prioritizing mental health

4.3 mhGAP: Mental Health Gap Action Programme

Launched: 2008 by WHO

Purpose: Address the treatment gap by enabling non-specialist health workers to deliver evidence-based mental health interventions.

mhGAP Intervention Guide (mhGAP-IG): Clinical protocol covering priority conditions:

- Depression
- Psychosis
- Bipolar disorder
- Epilepsy (neurological but included for LMICs)
- Suicide and self-harm
- Substance use disorders
- Child and adolescent mental health
- Dementia
- Other significant emotional/medically unexplained complaints

mhGAP training model:

- 5-10 day training programme for general health workers
- Uses structured assessment tools
- Emphasizes supervised practice
- Supports task-shifting

Evidence for mhGAP:

- Strong evidence that trained primary care workers can accurately diagnose and manage depression, psychosis, epilepsy
- Reduces treatment gap in LMIC settings where implemented rigorously
- India has piloted mhGAP in several states, results variable

4.4 Task-Shifting and Task-Sharing

Task-shifting: Moving specific tasks from specialized to less specialized workers

Task-sharing: More precise term, specialist retains oversight and responsibility, shares delivery with non-specialist

Rationale: When there are too few specialists to meet need, trained non-specialists can deliver evidence-based care under supervision.

Evidence base: Strong for:

- Lay counselors delivering IPT and CBT for depression (WHO studies in Uganda, Pakistan, India)
- Community health workers managing medication adherence in schizophrenia
- Non-physician clinicians prescribing essential psychotropics in Africa

Indian examples:

- ASHA workers trained in mental health awareness, evidence for increased help-seeking
- VISHRAM project (Maharashtra), CHW-delivered mental health intervention
- Healthy Activity Programme (HAP), Vikas Sangam, Goa, lay counselor-delivered BA for depression (Vikram Patel group)

Conditions for success:

- Structured protocol (not just vague training)
- Ongoing supervision
- Clear referral pathways
- Appropriate medications available
- Community trust

4.5 DALY Burden of Mental Illness

DALY = Disability-Adjusted Life Year = Years lived with disability (YLD) + Years of life lost (YLL)

Key facts:

- Mental and neurological disorders account for ~13-14% of global DALYs
- Leading causes of YLD globally
- Depression is the single largest contributor to YLD worldwide
- In India, neuropsychiatric disorders account for ~11-12% of total DALYs

Top mental health contributors to global DALYs:

1. Unipolar depressive disorders
2. Schizophrenia
3. Bipolar disorder
4. Alcohol use disorders
5. Anxiety disorders

Why DALY matters:

- Depression causes more disability-days than heart disease or diabetes per case
- Most mental illness years are YLD not YLL (unlike infectious diseases)
- Suicide mortality accounts for a portion of YLL
- DALY burden justifies investment in mental health as economic necessity

SECTION 5: PSYCHIATRIC EPIDEMIOLOGY IN INDIA

5.1 National Mental Health Survey 2015-16 (NMHS)

The NMHS 2015-16 is the **most comprehensive epidemiological survey** of mental disorders in India. Conducted by PG exams with MoHFW funding.

Sample: 34,802 adults (18+) across 12 states, multi-stage stratified random sampling.

Key findings, prevalence:

DISORDER · WEIGHTED PREVALENCE

Any mental disorder 10.6%

Tobacco use disorders 22.4%

Alcohol use disorders 4.6%

Common mental disorders (depression, anxiety) 5.0-5.5%

Severe mental disorders (schizophrenia, bipolar) ~1-2%

PTSD 0.5%

Epilepsy 3.0/1000

Treatment gap (NMHS): 83.45% overall, meaning >4 in 5 people with a diagnosable mental disorder receive no treatment.

Urban vs rural findings:

- Urban areas: higher prevalence of substance use, depression, anxiety
- Rural areas: higher treatment gap, lower health literacy
- Urban-rural gap in treatment-seeking consistent across disorder categories

Lifetime vs current prevalence:

- Lifetime any mental disorder: ~13.7%
- Current prevalence: ~10.6%

State variation: Maharashtra, Tamil Nadu, Kerala had higher prevalence (may reflect better detection); BIMARU states had lower reported prevalence (likely detection artifact).

Noteworthy NMHS findings for exam:

- Median duration of untreated psychosis in India: 5 years
- Treatment gap for schizophrenia: 75%
- Treatment gap for depression: 85.2%
- Most people with mental illness seek help from traditional / faith healers first
- Only 30% of districts had at least one psychiatrist

5.2 Suicide Epidemiology: NCRB Data

National Crime Records Bureau (NCRB) collects suicide data annually via police records.

Key figures (recent years, ~2022):

- Suicide rate (India): approximately 12-12.4 per 100,000 population
- Total suicides per year: ~170,000-180,000 (one of the highest globally by absolute number)
- Male:Female ratio: approximately 2:1 (men complete more often)
- Age peak: 15-39 years (productive age group significantly affected)

Leading stated reasons (NCRB categories):

1. Family problems
2. Illness (including mental illness)
3. Marriage-related issues

4. Financial problems
5. Professional/ career problems
6. Love affairs

Methods (India):

- Hanging, most common method overall
- Pesticide ingestion, major method in agricultural areas
- Self-immolation, more common among women in certain regions

Underreporting:

- NCRB data are significantly underestimated, stigma, legal concerns, insurance
- Actual rates likely 20-30% higher than reported
- Medicolegal issues cause misclassification (accidental vs suicide)

State variation:

- Highest rates: Lakshadweep, Andaman & Nicobar, Andhra Pradesh, Telangana, Tamil Nadu
- Lowest: Bihar, Jharkhand, Uttar Pradesh (likely underreporting artifact)

Farmer suicides: A political and public health issue, Maharashtra, Karnataka, Andhra Pradesh most affected.

5.3 Substance Use Surveys

National Drug Use Survey 2018 (by NDDTC, PG exams Delhi, with MoSJE):

Key findings:

- Alcohol: ~16 crore people use alcohol; ~5.7 crore have alcohol use disorder
- Cannabis: ~3.1 crore users; harmful/ dependent use in ~0.7 crore
- Opioids: ~2.3 crore users (including pharmaceutical opioids); ~2.7 lakh on OST treatment
- Inhalants: high prevalence among homeless/ street children
- Stimulants: growing urban problem

Tobacco (GATS 2016-17):

- 28.6% adults use tobacco in some form
 - India has second-highest tobacco burden globally
-

SECTION 6: DISABILITY CERTIFICATION IN PSYCHIATRY

6.1 Legal Framework: RPwD Act 2016

The **Rights of Persons with Disabilities Act 2016** (RPwD Act) replaced the PWD Act 1995 and significantly expanded the scope of disability coverage.

Key changes in RPwD Act 2016:

- Expanded from 7 to 21 disability categories
- Mental illness, intellectual disability, ASD, and specific learning disabilities now explicitly included
- Introduced benchmark disability concept (40% or more disability)
- Created the UDID (Unique Disability ID) system
- Established rights framework: education, employment, social security, accessibility

Mental health-relevant disability categories in RPwD Act:

1. Mental illness
2. Intellectual disability
3. Autism Spectrum Disorder
4. Specific Learning Disability
5. Multiple disabilities including mental illness

6.2 UDID Process: Unique Disability Identification

The UDID system is the national database for disability certification.

Process, step by step:

Step 1: Application

- Patient/guardian applies online (udid.co.in) or offline via CMO/District Medical Authority
- Documents required: ID proof, address proof, photo, recent medical records

Step 2: Medical Assessment

- Assessed by the Medical Authority (Disability Assessment Board at district/state hospital)
- For mental illness: psychiatrist (or physician where no psychiatrist available)
- Assessment tools vary by disability type

Step 3: Disability Assessment

For mental illness, the certification process uses the **Disability Assessment Schedule (DAS)**, assessing:

- Self-care

- Occupational functioning
- Family and social functioning
- Community participation

Percentage Disability Scale (Mental Illness):

SCORE	DISABILITY %	CATEGORY
0-15%	Minimal disability	No certificate
16-40%	Mild-moderate	Disability certificate (below benchmark)
41-75%	Moderate-severe	Benchmark disability (40%+), entitled to reservations, benefits
76-100%	Severe	High priority for benefits

Step 4: Certificate Issuance

- UDID card issued centrally by MoSJE
- Unique 18-digit UDID number
- Permanent or temporary (re-assessable) certificate

Step 5: Re-assessment

- Temporary certificates (5 years typically for mental illness) require re-assessment
- Mental illness disability can fluctuate, hence temporary certification more common

6.3 Certification for Specific Diagnoses

INTELLECTUAL DISABILITY

- IQ testing required (Binet-Kamat, WISC, Malin's for children; WAIS for adults)
- Adaptive behavior assessment (Vineland, BASIC-MR)
- Degree:
 - Mild: IQ 50-69, 40% disability
 - Moderate: IQ 35-49, 70% disability
 - Severe: IQ 20-34, 90% disability
 - Profound: IQ <20, 100% disability

AUTISM SPECTRUM DISORDER

- Clinical diagnosis based on DSM-5/ICD-11 criteria
- Specific instruments: CARS, ADOS-2 (where available), SRS
- Disability % based on functional impairment across domains

SPECIFIC LEARNING DISABILITY (SLD)

- School-age assessment required
- Evidence of significant discrepancy between ability and achievement
- Psychoeducational assessment: PG exams SLD battery, DAST (Dyslexia)
- Disability % typically 40% if diagnosed and confirmed

MENTAL ILLNESS (SCHIZOPHRENIA, BIPOLAR, ETC.)

- Diagnosis confirmed by psychiatrist
 - Minimum 6-month duration in most cases
 - DAS score determines percentage
 - Functional assessment includes work, family, social, self-care domains
-

SECTION 7: REHABILITATION IN PSYCHIATRY

7.1 Principles of Psychiatric Rehabilitation

Psychosocial Rehabilitation (PSR) = a process that facilitates opportunities for individuals with serious mental illness to reach their optimal level of functioning in their communities.

WHO definition: Rehabilitation involves the provision of an enabling environment to ensure that individuals with mental illness can reach their maximum potential.

Core principles:

1. Recovery orientation, emphasizes hope and possibility
2. Person-centred, individual goals, not system goals
3. Strengths-based, build on assets, not just remediate deficits
4. Community integration, participation in mainstream community
5. Consumer empowerment, active role in own care
6. Cultural sensitivity

7.2 Models of Rehabilitation

MEDICAL MODEL (DEFICITS MODEL)

- Focus: symptoms and limitations
- Goal: symptom reduction
- Role: patient as passive recipient
- Critique: Insufficient for community reintegration

RECOVERY MODEL

- Emerged from consumer/survivor movement
- Core: recovery is possible even with ongoing symptoms

- Goal: meaningful life in community
- Evidence: Long-term follow-up studies (Courtenay Harding's Vermont study) show >50% of people with schizophrenia recover substantially over decades

MHCA 2017 AND REHABILITATION

- MHCA 2017 guarantees right to "mental health treatment and services"
- Includes community-based rehabilitation
- Mandates mental health establishments to provide or arrange rehabilitation

7.3 Types of Rehabilitation Services

HALFWAY HOMES

- Transitional residential facility between hospital and independent living
- Capacity: typically 10-30 beds
- Duration: 6-24 months
- Population: stabilized patients without family support or unsafe home environments
- Activities: ADL training, vocational preparation, social skills
- Staffing: resident coordinator, counselor, occupational therapist, regular psychiatrist visits

LONG-STAY HOMES / GROUP HOMES

- Residential option for those unable to live independently
- Population: chronic, highly disabled, no family support
- Goal: minimal institutionalization, small, community-embedded settings
- Supervised but not clinical settings

DAY CARE CENTERS

- Non-residential; patients attend during day, return home at night
- Components: OT, psychosocial activities, skills training, medication
- Advantages: maintains family bonds, less institutionalization, lower cost
- Target: patients too ill for full-time employment but not requiring inpatient stay

VOCATIONAL REHABILITATION

- Goal: return to competitive employment or sheltered employment
- Levels:
 - **Pre-vocational training**, basic skills (punctuality, following instructions)
 - **Sheltered workshops**, work in protected environment for pay
 - **Transitional employment**, time-limited real-world work placement (IPS model)
 - **Supported employment**, competitive employment with ongoing job coaching

SUPPORTED EMPLOYMENT: INDIVIDUAL PLACEMENT AND SUPPORT (IPS)

- Evidence-based model: competitive employment is the direct goal (no lengthy prevocational training)
- Services integrated with clinical care
- Job coach provides support in real workplace
- Evidence: IPS produces 2-3x higher competitive employment rates vs. traditional vocational rehabilitation
- India application: limited, some NGO settings in urban areas

7.4 Self-Help Groups (SHGs)

SHGs in mental health rehabilitation:

- Groups of people with similar mental health issues / caregivers
- Peer support, experience sharing, advocacy
- Examples: Family caregiver groups, consumer groups
- NAMHPAI (National Alliance for Mental Health in India), umbrella family support organization
- AASRA, iCall, Vandrevala Foundation, also provide peer support elements

7.5 Community-Based Rehabilitation (CBR)

CBR is a multi-sectoral approach to rehabilitation in the community rather than specialized institutions.

WHO CBR Matrix (2010 revision):

The CBR matrix has 5 domains, each with 5 components:

DOMAIN · COMPONENTS

Health Promotion, Prevention, Medical care, Rehabilitation, Assistive devices

Education Early childhood, Primary, Secondary and higher, Non-formal, Lifelong learning

Livelihood Skills development, Self-employment, Wage employment, Financial services, Social protection

Social Personal assistance, Relationships, Culture and arts, Recreation/leisure, Justice

Empowerment Advocacy, Communication, Community mobilisation, Political participation, Self-help groups

Indian CBR models:

- PG exams CBR programme (Bangalore), multi-district community rehabilitation
- Sri Ramachandra Institute model

- NGO-based: Schizophrenia Research Foundation (SCARF, Chennai), Rehabilitation Council of India (RCI) accredited programs

CBR vs Institution-Based Rehabilitation:

FEATURE	CBR	INSTITUTIONAL
Setting	Community	Hospital/specialized center
Integration	Yes, mainstream	No, segregated
Cost	Lower	Higher
Family involvement	High	Variable
Reach	Broader	Limited
Quality assurance	Harder to maintain	Easier to monitor

SECTION 8: MENTAL HEALTH LITERACY

8.1 Definition and Components

Mental health literacy (MHL), Jorm et al. (1997): "knowledge and beliefs about mental disorders which aid their recognition, management, or prevention."

Components of MHL (Jorm):

1. Ability to recognize specific disorders
2. Knowledge of professional help available
3. Knowledge of effective self-help strategies
4. Knowledge of how to help others
5. Attitudes that facilitate recognition and help-seeking

8.2 Measurement

- **MHLq** (Mental Health Literacy Questionnaire)
- **Mental Health Knowledge Schedule (MAKS)**
- **Attitudes Toward Mental Illness Scale**
- Vignette-based instruments

8.3 School Mental Health

Policy context: National Education Policy 2020 explicitly mentions mental health and emotional well-being in schools.

National School Mental Health Programme (NSMHP):

- Launched under NMHP
- Components: Teacher training, Student peer support, Counselor deployment

- Aim: Early identification of mental health problems in school-age children

School-based mental health services pyramid:

1. Universal, all students: mental health awareness, life skills, SEL
2. Selected, at-risk students: brief interventions, group work
3. Indicated, students with problems: individual counseling, referral

Life Skills Education (WHO model):

- 10 core life skills: self-awareness, empathy, critical thinking, creative thinking, decision-making, problem-solving, effective communication, interpersonal skills, coping with stress, coping with emotions
- Indian curriculum: CBSE has embedded life skills; implementation quality varies

8.4 Workplace Mental Health

Scale of the problem:

- India loses approximately 1% of GDP annually to mental health conditions affecting working-age population
- Burnout, work-related stress, substance use are leading issues

WHO Healthy Workplace framework:

1. Physical work environment
2. Psychosocial work environment (stress, workload, autonomy)
3. Personal health resources
4. Community participation

India-specific:

- Factories Act and other labor laws have limited mental health provisions
- IT/BPO sector: high burnout, shift work, specific vulnerabilities
- Healthcare worker mental health: burnout, secondary trauma, COVID-exacerbated

SECTION 9: SUICIDE PREVENTION

9.1 Epidemiology Recap (Prevention Context)

- 170,000+ deaths/year in India
- ~800,000 globally
- 20 attempts per completion (estimated)
- Most at-risk: 15-39 years, lower socioeconomic status, prior attempt, mental illness, substance use

9.2 National Suicide Prevention Strategy (NSPS): India

India launched its **first National Suicide Prevention Strategy** in 2022 (MoHFW).

Goals of NSPS:

- Reduce suicide mortality by 10% by 2030
- Improve data collection and surveillance
- Integrate suicide prevention into health system
- Provide mental health support to those affected

Key components of NSPS:

1. Surveillance improvement, NCRB + health system data linkage
2. Means restriction, pesticide safety, height barriers on bridges (state-specific)
3. Mental health care integration, DMHP linkage
4. Gatekeeper training, scale across sectors
5. Crisis helplines, national coverage
6. Postvention, support for suicide loss survivors
7. Media guidelines, safe reporting framework

9.3 Gatekeeper Training

Concept: Training "gatekeepers", people in strategic community positions who can identify at-risk individuals, provide initial support, and refer to professional help.

Who are gatekeepers?

- Teachers, counselors, school staff
- General practitioners
- Police officers
- Pharmacists
- Community leaders, clergy
- Family members
- Coworkers

Evidence-based gatekeeper programmes:

- **QPR** (Question, Persuade, Refer), brief, evidence-based gatekeeper training
- **Applied Suicide Intervention Skills Training (ASIST)**, 2-day intensive
- **safeTALK**, 3-4 hour introductory gatekeeper programme
- **Mental Health First Aid (MHFA)**, broader but includes suicide

Indian context:

- PG exams has developed gatekeeper training modules

- Vandrevala Foundation and iCall run gatekeeper programmes
- Medical student gatekeeper training (relevant to your Gatekeeper Program)

9.4 Means Restriction

Most evidence-based suicide prevention intervention globally:

- UK coal gas detoxification (1960s): suicide rate dropped 30%
- UK paracetamol pack-size restriction: significant reduction in paracetamol-related deaths
- Bridge barriers: San Francisco Golden Gate Bridge barrier, studies show prevention
- Pesticide restriction in Sri Lanka and Bangladesh: significant reductions in suicide rates

India application:

- Pesticide regulation: endosulfan ban helped; Paraquat restriction
- Platform screen doors in metro stations
- Firearm restriction (not a major issue in India compared to US)

9.5 Crisis Helplines: India

HELPLINE	NUMBER	OPERATING HOURS
iCall (TISS)	9152987821	Monday–Saturday, 8am–10pm
Vandrevala Foundation	1860-2662-345 / 1800-2333-330	24×7
PG exams	080-46110007	24×7
Arpita Suicide Prevention Helpline (Bangalore)	080-23655557	24×7
Snehi	044-24640050	8am–10pm
Tele-MANAS	14416	24×7
iCall WhatsApp	Via website	Business hours

Tele-MANAS is the most significant recent development, launched 2022, integrates crisis support with clinical follow-up.

9.6 Media Guidelines for Suicide Reporting

Based on WHO/ AFSP guidelines, adopted by Press Council of India:

What NOT to do (responsible reporting):

- Do not sensationalize or romanticize
- Do not describe the method in detail
- Do not use photographs of the location
- Do not present as "successful", use "died by suicide" not "committed suicide"

- Do not speculate on reasons without evidence
- Do not use front-page / top-of-news placement

What TO DO:

- Include crisis helpline information
- Present as complex, multifactorial
- Focus on survivor stories (protective framing)
- Discuss warning signs and help-seeking

Werther effect: Media-driven suicide contagion, evidence for copycat suicides following prominent media coverage.

Papageno effect: Protective effect of stories of people who overcame suicidal crisis.

SECTION 10: STIGMA IN MENTAL HEALTH

10.1 Types of Stigma

TYPE	DESCRIPTION	EXAMPLE
Public stigma	Community attitudes toward mental illness	Beliefs that people with schizophrenia are dangerous
Self-stigma	Internalization of public stigma by the person with mental illness	"I'm crazy, I don't deserve a job"
Structural stigma	Institutional policies that discriminate	Insurance exclusions, legal incapacitation
Courtesy stigma	Stigma extended to family members	Family avoiding disclosure
Provider stigma	Discrimination by health workers	Dismissing complaints of patients with mental illness

10.2 Consequences of Stigma

- Delays in treatment-seeking (most impactful at population level)
- Medication non-adherence (to hide illness)
- Social isolation
- Employment discrimination
- Housing discrimination
- Reduced quality of life
- Internalized shame prevents disclosure to clinicians

10.3 Measurement of Stigma

INSTRUMENT	WHAT IT MEASURES	NOTES
ISMI (Internalized Stigma of Mental Illness)	Self-stigma	29 items, 5 subscales: alienation, stereotype endorsement, discrimination experience, social withdrawal, stigma resistance
AQ-27 (Attribution Questionnaire)	Public stigma attitudes	Measures blameworthiness, anger, fear, help
CAMI (Community Attitudes toward Mental Illness)	Community stigma	4 subscales
King Stigma Scale	Perceived stigma	Used in UK, some Indian studies
SDS (Self-Descriptions Stigma)	Various domains	

10.4 Anti-Stigma Interventions

Three main strategies:

1. **Protest**, challenging negative portrayals; effective short-term but limited long-term impact
2. **Education**, information campaigns; moderate evidence; effective if targeted
3. **Contact**, direct personal contact with people with mental illness; **most evidence for sustained change**

Contact-based interventions:

- In-person contact > video-based > other media
- Mental health first aid training includes contact element
- "Time to Change" (UK), large national campaign, contact-based
- "Opening Minds" (Canada)

Target groups for anti-stigma work:

- Medical/health students and professionals (high priority, their stigma causes structural harm)
- Employers
- General public
- Media professionals
- Police and criminal justice

Indian anti-stigma initiatives:

- MANAS programme
 - PG exams outreach programmes
 - World Mental Health Day events
 - Mental illness portrayed in films (increasing, though not always accurate)
-

SECTION 11: RIGHTS-BASED APPROACH

11.1 UNCRPD: United Nations Convention on Rights of Persons with Disabilities

Adopted: 2006

India ratified: 2007 (with reservations)

Core principles of UNCRPD:

1. Respect for inherent dignity and individual autonomy
2. Non-discrimination
3. Full and effective participation in society
4. Respect for difference
5. Equality of opportunity
6. Accessibility
7. Equality between men and women
8. Respect for evolving capacities of children with disabilities

Article 12, Equal recognition before the law:

- All persons with disabilities have legal capacity
- Supported decision-making preferred over substituted
- Safeguards must accompany any restrictions

Article 14, Liberty and security of person:

- Cannot be deprived of liberty based solely on disability
- Detention of people with mental illness must meet same standards as for everyone

UNCRPD and India's MHCA 2017 tension:

- MHCA 2017 retains some provisions for involuntary treatment → seen by disability rights advocates as inconsistent with UNCRPD
- Debate between treatment rights (access to care) and liberty rights (autonomy)

11.2 Mental Healthcare Act 2017: Rights Framework

The **Mental Healthcare Act (MHCA) 2017** is the current legislation governing mental health in India. It replaced the Mental Health Act 1987.

Rights of persons with mental illness under MHCA 2017:

1. Right to access mental health care (government-funded if needed)
2. Right to community living
3. Right to protection from cruel, inhuman, degrading treatment
4. Right to equality and non-discrimination
5. Right to information
6. Right to confidentiality
7. Right to make complaints
8. Right to legal aid
9. Right to relevant personal records
10. Right to make advance directives
11. Right to designate a nominated representative

Advance Directives (ADs):

- Person can specify, while well, their treatment preferences and who should make decisions if they lose capacity
- AD must be registered with Mental Health Authority
- Can specify: preferred treatment, preferred hospital, preferred medications
- Can specify nominated representative
- Mental Health Review Board (MHRB) can override AD in limited circumstances

Nominated Representative (NR):

- Appointed by the person with mental illness
- Role: advocate, liaise with treating team, access records
- Cannot make treatment decisions against person's stated preferences

11.3 Supported Decision-Making vs Substituted Decision-Making

This distinction is foundational to the rights-based approach.

Substituted decision-making (traditional/old model):

- When person deemed incapable, another person makes decisions for them
- Historically: guardians, family members, doctors
- Problem: removes agency of the person with disability
- UNCRPD Article 12 challenges this model

Supported decision-making (UNCRPD model):

- Person with disability retains legal authority
- Support persons help them understand information, communicate decisions

- Decision belongs to the person, support persons implement
- Does not require formal capacity assessment to trigger

India's MHCA 2017 position:

- Introduced supported decision-making via nominated representative
- But retained guardianship provisions for extreme cases
- Mental Health Review Board provides oversight
- Still allows involuntary treatment under defined criteria → ongoing rights debate

SECTION 12: PRIMARY CARE PSYCHIATRY

12.1 Screening Tools

TOOL	CONDITION	ITEMS	CUT-OFF
PHQ-9	Depression	9	≥10 for moderate depression
PHQ-2	Depression screen	2	≥3 → proceed to PHQ-9
GAD-7	Generalized Anxiety	7	≥10 for moderate
AUDIT	Alcohol use	10	≥8 hazardous use
ASSIST	Substance use (all types)	8	Substance-specific
PC-PTSD-5	PTSD (primary care version)	5	≥3 screen positive
K-10	Psychological distress	10	≥25 serious distress
MINI	Multiple diagnoses (structured)	Multiple	Diagnostic, not screening

12.2 Stepped Care Model

Concept: Match treatment intensity to severity; start with least intensive effective treatment; step up if needed.

Stepped Care for Depression (5-step model, NICE-based):

STEP	WHO	INTERVENTION
1	All with depression	Recognition, watchful waiting, psychoeducation
2	Mild-moderate	Low-intensity CBT (guided self-help, CCBT, psychoeducation groups)

STEP	WHO	INTERVENTION
3	Moderate-severe, persisting	High-intensity CBT, IPT, antidepressants, counseling
4	High risk, complex	Specialist care: multidisciplinary, combined treatment, crisis assessment
5	Severe risk	Inpatient / crisis team, ECT consideration

India adaptation:

- Steps 1-2: ASHA / ANM + PHC MO
- Step 3: PHC MO with tele-consultation
- Step 4-5: DMHP / district hospital

12.3 Collaborative Care Model

Definition: Mental health services integrated into primary care through:

- Care manager (non-specialist) who coordinates care
- Consulting psychiatrist who provides caseload review (not direct patient contact for all)
- Primary care physician who prescribes and manages
- Structured follow-up protocol

Evidence: Strong RCT evidence for collaborative care in depression and anxiety (Unützer group, IMPACT trial).

RESPECT-MIL, PARTNERS trials in US military showed similar benefit.

Indian pilots: Some collaborative care models in primary care settings in urban India (CMH Mumbai pilots).

SECTION 13: TELEPSYCHIATRY IN COMMUNITY SETTINGS

13.1 Overview and Rationale

Telepsychiatry uses videoconferencing and digital technology to deliver psychiatric care remotely, particularly valuable for:

- Rural / remote areas with no psychiatrist
- Supervision of non-specialist workers
- Crisis support after hours
- Follow-up care reducing travel burden

Regulatory framework: PG exams Telepsychiatry Operational Guidelines (2020), MCI (now NMC) telemedicine guidelines (2020).

13.2 eSanjeevani

National telemedicine platform launched by MoHFW under Ayushman Bharat.

- Two models: eSanjeevani OPD (patient-to-doctor) and eSanjeevani hub-and-spoke (provider-to-provider)
- Hub-and-spoke: specialists at hub consult with PHC doctors at spoke
- Mental health consultations available through eSanjeevani

13.3 Tele-MANAS

Launched: October 2022, National Mental Health Day

Platform: Two-tier helpline + tele-mental health

- **Tier 1:** Trained counselors (non-specialist), supportive counseling, triage, psychoeducation
- **Tier 2:** Clinical psychologists and psychiatrists for complex cases
- **Number:** 14416 (toll-free, 24×7)
- **Integration:** Links to eSanjeevani, DMHP, NHM

Coverage: All states and UTs operational. Regional hubs with state coordination.

13.4 PG exams ECHO (Extension for Community Healthcare Outcomes)

Project ECHO: Knowledge amplification model where specialists train and support primary care providers through case-based learning via videoconference.

PG exams ECHO:

- Specialists at PG exams mentor community-based providers across Karnataka and other states
- Weekly teleSilver sessions, case presentation + didactic
- Topic areas: common mental disorders, substance use, child psychiatry, psychosis management
- Evidence: ECHO increases provider knowledge and confidence, improves patient outcomes

13.5 State Tele-MANAS and Regional Models

Multiple states have implemented state-level tele-mental health:

- Karnataka: PG exams hub
 - Maharashtra: iCall (TISS) model
 - Tamil Nadu: SCARF tele-psychiatry
 - Rajasthan: State-run model integrated with DMHP
-

SECTION 14: DISASTER PSYCHIATRY

14.1 Mental Health Impact of Disasters

Disasters (natural and man-made) produce a spectrum of mental health responses:

Normal responses (time-limited):

- Acute stress reactions
- Grief
- Anxiety, hypervigilance
- Sleep disturbance

Disorder-level responses (need intervention):

- Acute Stress Disorder (ASD), within 1 month of trauma
- PTSD, persisting >1 month
- Major depression
- Substance use disorders
- Complicated grief
- Psychosis (can be precipitated)

Timeline of mental health needs:

- Immediate (0-72 hours): Safety, basic needs, PFA
- Short-term (1-4 weeks): Assessment, brief intervention, triage
- Medium-term (1-3 months): Formal treatment, community support
- Long-term (3 months+): Rehabilitation, PTSD treatment, community recovery

14.2 Psychological First Aid (PFA)

Definition: An evidence-informed approach to help survivors of disaster and mass trauma.

NOT: Formal therapy, debriefing, diagnosis.

PFA core actions (WHO 8-step model):

1. **Contact and engagement**, approach safely and compassionately
2. **Safety and comfort**, ensure physical safety, provide comfort
3. **Stabilization**, calm distressed individuals (grounding techniques)
4. **Information gathering**, assess immediate needs
5. **Practical assistance**, address most urgent practical needs
6. **Connection with social supports**, link to family, community
7. **Information on coping**, normalize reactions, share adaptive coping
8. **Linkage to collaborative services**, refer to professional services as needed

Who delivers PFA:

- Trained community volunteers, NGO workers, first responders
- Does NOT require mental health training
- 1-2 day training sufficient

Important note: PFA is NOT psychological debriefing. Critical Incident Stress Debriefing (CISD / CISM), once widely used, lacks evidence and may be harmful when given universally. PFA replaces CISD as the recommended immediate intervention.

14.3 Critical Incident Stress Management (CISM)

CISM is a comprehensive, multi-component crisis intervention system (Mitchell, 1983):

- Pre-crisis preparation
- Large group crisis intervention
- Defusing (1-4 hours after incident, small group)
- CISD, Critical Incident Stress Debriefing (24-72 hours after)
- Individual crisis intervention
- Pastoral crisis intervention
- Follow-up and referral

Evidence status: Individual CISD has weak / negative evidence for prevention of PTSD. CISM as a whole system has limited evidence. Not recommended universally.

Current recommendation: PFA for early intervention; targeted evidence-based treatment (Prolonged Exposure, CPT, EMDR) for PTSD.

14.4 Disaster Mental Health Response in India

Nodal agency: National Disaster Management Authority (NDMA), has psychosocial guidelines.

PG exams disaster mental health team:

- Deployed in major Indian disasters (Gujarat earthquake 2001, Uttarakhand floods 2013, COVID-19 pandemic 2020)
- Provides training to state teams

COVID-19 mental health impact:

- NMHS data and subsequent surveys show significant increase in:
- Depression and anxiety (especially frontline workers)
- Domestic violence-linked mental health problems
- Bereavement and complicated grief
- Substance use relapse and escalation

- Economic stress-linked suicidality
- Tele-MANAS launched partly in response to COVID-highlighted gaps
- Healthcare worker burnout, especially nursing and resident doctors

SECTION 15: CONSULTATION-LIAISON PSYCHIATRY

15.1 Models of C-L Psychiatry

MODEL	DESCRIPTION	SETTING
Traditional Consultation	Referring doctor asks for opinion; psychiatrist advises	General hospital
Liaison	Psychiatrist embedded in medical team; attends rounds, proactive	ICU, oncology, renal units
Collaborative Care	Shared care manager, psychiatrist consultation, primary provider leads	Primary care
Integrated (Hybrid)	Psychiatrist as co-treating member	Various

15.2 Common C-L Referrals

REASON · APPROACH

Delirium RASS + CAM assessment; identify cause; haloperidol/quetiapine

Capacity assessment 4 components of capacity

Suicide attempt Risk assessment, safety plan, psychiatric diagnosis

Medically unexplained symptoms Biopsychosocial formulation; exclude organic

Adjustment disorders Brief supportive therapy, psychoeducation

Pre-surgical anxiety Supportive + buspirone/SSRI

Substance use (withdrawal) CIWA, COWS, appropriate detox protocol

Non-adherence Explore reasons, motivational approach

15.3 Delirium: C-L Context

Key features distinguishing delirium from dementia:

FEATURE	DELIRIUM	DEMENTIA
Onset	Acute/subacute	Insidious
Attention	Markedly impaired	Relatively preserved early
Level of consciousness	Fluctuating	Alert (early-mid)
Course	Fluctuating	Progressive
Reversibility	Usually	Rarely
Cause	Identifiable medical	Degenerative

CAM (Confusion Assessment Method): Sensitivity 94-100%, Specificity 90-95%.

- Feature 1: Acute onset + fluctuating course
- Feature 2: Inattention
- Feature 3: Disorganized thinking
- Feature 4: Altered level of consciousness
- Diagnosis: Features 1+2 + (3 OR 4)

15.4 Capacity Assessment: MHCA Framework

Four components of decision-making capacity:

1. **Understand**, can the person understand the relevant information?
2. **Appreciate**, do they understand how it applies to their situation?
3. **Reason**, can they reason through options and consequences?
4. **Communicate**, can they communicate a decision?

MHCA 2017: Presumption of capacity, mental illness alone does not negate capacity. Must demonstrate specific incapacity for specific decision at specific time.

MacCAT-T (MacArthur Competence Assessment Tool for Treatment), gold standard assessment instrument.

SECTION 16: ETHICS IN PSYCHIATRY

16.1 Principles of Medical Ethics (Beauchamp and Childress)

1. **Autonomy**, Respect the patient's right to make informed decisions
2. **Beneficence**, Act in the patient's best interest
3. **Non-maleficence**, Do no harm (primum non nocere)
4. **Justice**, Fair distribution of resources, equal treatment

Application to psychiatry:

- Autonomy is most frequently challenged, involuntary treatment creates tension

- MHCA 2017 advances autonomy (advance directives, capacity presumption)
- Justice: Mental health receives <1% of health budget despite 10.6% prevalence

16.2 Confidentiality

General rule: Patient information is confidential and cannot be shared without consent.

Exceptions (Tarasoff principles, Indian adaptation):

- Duty to warn: If patient poses specific, credible threat to identifiable third party
- Child protection: Disclosure of child abuse/neglect
- Court order
- Public health: Notifiable conditions (though mental illness is not notifiable in India)
- Patient incapacity + nominated representative

MHCA 2017 on confidentiality:

- Section 23: Explicit right to confidentiality
- Breach allowed only as per act provisions
- Medical records cannot be shared with employer, insurance company without consent

16.3 Boundary Violations

Types:

TYPE · EXAMPLE

Role boundary Therapist becoming friend, doing financial favors

Sexual boundary Any sexual contact with patient/former patient

Dual relationship Treating a personal friend or family member

Financial boundary Accepting gifts, loans

Crossing vs violating:

- **Crossings**, minor departures from typical role (accepting a gift from grieving patient), may or may not be harmful
- **Violations**, breaches that damage therapeutic relationship and potentially harm patient

Key principle: Power differential in therapeutic relationship makes patient vulnerable; this is why sexual contact is always a violation, even if "consensual."

Indian context: MCI/NMC code of ethics prohibits sexual contact with patients.

16.4 Dual Relationships

Definition: When a clinician has both a professional and personal relationship with a patient.

Examples:

- Treating a colleague
- Treating a student
- Treating a family member

Problems:

- Compromised objectivity
- Disclosure bias (patient may not share fully)
- Boundary confusion
- Potential exploitation

Guidance: Generally avoid dual relationships; when unavoidable (rural settings), seek supervision and be explicit about role boundaries.

16.5 Research Ethics in Psychiatry

Key principles (Declaration of Helsinki + ICMR Guidelines):

1. Informed consent, voluntary, informed, capacity-aware
2. Vulnerability, extra protections for people with mental illness (potential for impaired capacity)
3. Risk-benefit balance
4. Independent ethics review
5. Special provisions for proxy consent

ICMR National Ethical Guidelines 2017, mental health provisions:

- People with mental illness can participate in research
- Capacity assessment required
- Consent must be re-assessed periodically for long studies
- Caregiver/proxy consent when person lacks capacity
- Research should not be conducted on institutionalized persons when it could equally be done on community-dwelling persons (minimize vulnerability exploitation)
- Therapeutic vs non-therapeutic research distinction important

MHCA 2017 and research:

- Section 97: Informed consent required for all research
 - Includes capacity assessment
 - Mental Health Authority can audit research activities in mental health establishments
-

SECTION 17: ADDITIONAL HIGH-YIELD TOPICS

17.1 Community Mental Health Services: International Models

UK Community Mental Health Teams (CMHTs):

- Multidisciplinary teams (psychiatrist, CPN, SW, OT, psychologist)
- Assertive Community Treatment (ACT) for high-risk patients
- Crisis Resolution Home Treatment (CRHT)
- Early Intervention in Psychosis (EIP), 3-year intensive support

US Community Mental Health Centers (CMHCs):

- Post-deinstitutionalization movement (1960s)
- Federally funded; services range from variable
- ACT (Assertive Community Treatment), strong evidence

Australia: National mental health plan; state-run community teams; private sector significant.

17.2 Assertive Community Treatment (ACT)

Definition: An intensive, evidence-based model of community mental health care for people with severe mental illness.

Key features:

- Shared caseloads (team, not individual clinician)
- Small caseload ratios (10:1 patient:staff)
- 24/7 availability
- Services provided where person lives (mobile)
- Vocational support integrated
- No arbitrary time limit

Evidence: Reduces hospitalizations, homelessness, improves quality of life in schizophrenia; most evidence from US/ Australia.

India application: Limited, SCARF Chennai, PG exams community psychiatry unit have ACT-like programmes.

17.3 Early Intervention in Psychosis (EIP)

Rationale:

- DUP (Duration of Untreated Psychosis) predicts outcome, longer DUP = worse prognosis
- Early intensive treatment produces better outcomes
- Median DUP India: ~5 years (NMHS data)

EIP components:

- Early detection (community, school, PHC screening)
- Low-dose antipsychotics
- Family intervention (psychoeducation, expressed emotion reduction)
- CBT for psychosis
- Vocational support
- Minimum 2-3 years intensive phase

India pilot: SCARF early psychosis programme; PG exams; Vandrevalla early intervention services.

17.4 Expressed Emotion (EE) and Family Intervention

Expressed Emotion (EE): A measure of the emotional climate in the family, particularly critical comments, hostility, and emotional over-involvement.

High EE families associated with:

- Higher relapse rates in schizophrenia
- Higher relapse in bipolar disorder
- Also relevant in eating disorders, depression

Interventions for high EE:

- Psychoeducation about illness (reduces criticism by reducing attributions of control)
- Communication training
- Problem-solving
- Evidence: Family interventions reduce relapse by ~50% vs medication alone

Indian applications: Family intervention more culturally natural (joint family systems); but caregiver burden is also high.

17.5 MHCA 2017: Key Definitions and Provisions**Definition of Mental Illness (MHCA 2017 Section 2(s)):**

"A substantial disorder of thinking, mood, perception, orientation or memory that grossly impairs judgement, behaviour, capacity to recognise reality or ability to meet the ordinary demands of life, mental conditions associated with the abuse of alcohol and drugs, but does not include mental retardation which is a condition of arrested or incomplete physical development of the mind."

Key provisions:

- Decriminalized suicide attempt (removed Section 309 IPC in effect)
- Every person has right to access mental health care

- Advance directives
- Nominated representative
- Mental Health Review Boards (MHRB), review involuntary admission
- Mental Health Establishments to be registered
- Human rights protections (anti-restraint, anti-seclusion provisions)

Involuntary admission under MHCA 2017:

- Cannot be based on mental illness alone
- Must be imminent danger to self/others AND lacks capacity to make treatment decisions
- Must be reviewed by MHRB within 30 days (90-day maximum without review)
- Person has right to legal representation

17.6 Rehabilitation Council of India (RCI)

Established: RCI Act 1992

Role: Regulate and maintain standards for training and practice of all professionals working in rehabilitation of persons with disability

RCI registered professionals (relevant to psychiatry):

- Clinical Psychologist
- Rehabilitation Psychologist
- Psychiatric Social Worker
- Special Educator
- Speech-Language Pathologist
- Occupational Therapist
- Hearing Aid and Earmold Technology specialist

RCI registration required for anyone working in rehabilitation under persons with disabilities, important for UDID assessment processes.

SECTION 18: INTEGRATION AND SYSTEMIC THINKING

18.1 The Inverse Care Law in Mental Health

Julian Tudor Hart (1971): "The availability of good medical care tends to vary inversely with the need for it in the population served."

In mental health: poorest, most remote, most severely ill populations have worst access. India exemplifies this:

- Poorest quintile: highest substance use, highest suicide risk, lowest access

- Rural India: higher unmet need, fewer resources
- Women: specific vulnerabilities (domestic violence, reproductive mental health) but less specialized care

18.2 Social Determinants of Mental Health

WHO Commission on Social Determinants of Health:

Mental health is shaped by:

- Poverty and economic inequality
- Education
- Social exclusion
- Gender-based violence
- Discrimination (caste, religion, sexual orientation)
- Adverse childhood experiences
- Housing
- Employment

For exam: Treatment-focused approaches alone are insufficient. Social determinants must be addressed for population-level mental health improvement.

18.3 Financing Mental Health in India

Budget allocation:

- Mental health budget: <1% of total health budget (WHO recommends at least 5%)
- Per capita mental health expenditure: approximately USD 0.25-0.50
- WHO recommendation for LMICs: USD 2-3 per capita

Consequences:

- Insufficient DMHP staffing
- Drug supply chain breaks down
- Infrastructure not maintained
- Training programmes underfunded

Potential solutions:

- Mental health parity legislation (mental health should receive same insurance coverage as physical health)
 - PMJAY expansion to outpatient mental health
 - NHM vertical integration
 - Public-private partnerships for service delivery
-

EXAM INTEGRATION POINTS

High-Frequency Exam Topics (based on Exam pattern):

1. NMHP, objectives, history, components, limitations
2. DMHP, team composition, services, manpower crisis
3. NMHS 2015-16, prevalence figures, treatment gap
4. MHCA 2017, definitions, rights, advance directives, involuntary admission
5. RPwD Act 2016, disability categories, UDID process
6. Suicide prevention, means restriction, gatekeeper training, helplines
7. Rehabilitation, types, halfway homes, supported employment
8. CBR, WHO matrix
9. Stigma, types, ISMI, anti-stigma strategies
10. Capacity assessment, four components
11. mhGAP, purpose, conditions covered
12. Stepped care model
13. Telepsychiatry, Tele-MANAS, PG exams ECHO
14. PFA, 8 actions, what it is NOT

Frequently Confused Pairs:

- NMHP (policy / programme) vs DMHP (operational unit)
- MHCA 2017 vs Mental Health Act 1987
- Task-shifting vs task-sharing
- Supported vs substituted decision-making
- PFA vs CISD / debriefing
- Halfway home vs long-stay home vs day care

All clinical illustrations in this document use fictitious names and anonymised details.

Model Answers

KEY INSIGHT

How to use this file: Each answer follows the PG exams long-answer structure. Marks allocations are approximate. Read the answer, cover it, reproduce it, then compare.

Answer 01: National Mental Health Programme (NMHP): History, Objectives, and Limitations

[10 marks, Long Answer]

Introduction

The National Mental Health Programme (NMHP) is India's national framework for mental health service delivery, launched in 1982. It represents one of the earliest national mental health programmes among low- and middle-income countries.

Historical Background

The NMHP emerged from the Bellary District demonstration project (1975–1982), conducted by the Department of Psychiatry, PG exams and Bangalore Medical College. The Bellary model demonstrated that:

- PHC-level medical officers could diagnose and treat common mental disorders after brief training
- Psychotropic medications could be dispensed at primary care level
- Community follow-up was feasible through non-specialist workers

This demonstrated proof-of-concept for community-based mental health care in India.

Objectives (1982 formulation)

1. Ensure availability and accessibility of minimum mental health care for all, especially vulnerable populations
2. Encourage application of mental health knowledge in general health care and social development
3. Promote community participation in mental health service development
4. Stimulate efforts toward self-help in the community

Key Components

COMPONENT · DESCRIPTION

District Mental Health Programme (DMHP) Operational arm, district-level service delivery

Manpower development Training general health workers, MOs, specialists

IEC activities Mental health literacy, awareness campaigns

Research and evaluation Monitoring, epidemiological studies

Mental hospital strengthening Upgrading existing institutions

Current Status and Achievements

- DMHP extended to 700+ districts nationally
- Tele-MANAS launched (2022), national tele-mental health programme
- Mental Healthcare Act 2017 enacted under NMHP framework
- Mental health integrated into National Health Mission
- Ayushman Bharat includes mental health in HWC package

Limitations

LIMITATION · MAGNITUDE

Specialist shortage ~9,000 psychiatrists vs ~42,000 needed

Funding deficit <1% of health budget allocated to mental health

Drug supply chain failures Psychotropics often unavailable at PHC level

Implementation heterogeneity Many DMHP districts functional on paper only

Treatment gap persists 83% (NMHS 2015–16), largely unchanged

Inadequate PHC integration MO training insufficient (3–5 days)

Missing outpatient insurance PMJAY covers only inpatient care

Conclusion

The NMHP has established a national framework and expanded infrastructure but faces a persistent implementation gap driven by workforce shortages, chronic underfunding, and fragmented primary care integration. Structural reforms, increased budget allocation, and mid-level mental health worker cadres are essential to close the treatment gap.

Answer 02: District Mental Health Programme: Structure, Services, and Manpower Issues

[10 marks, Long Answer]

Introduction

The District Mental Health Programme (DMHP) is the operational unit of the NMHP, first launched in 27 pilot districts in 1996. It represents India's primary mechanism for decentralizing specialist mental health care to the district level.

Core DMHP Team

POSITION · ROLE

Psychiatrist (1) Clinical lead, OPD, training, supervision

Clinical Psychologist (1) Psychological assessment, individual therapy

Psychiatric Social Worker (1) Family work, community outreach, social linkages

Psychiatric Nurse (1) Medication management, home visits, education

Data Entry Operator MIS, records

Service Delivery Model

Level 1, District Hospital (HQ)

- Regular psychiatric OPD
- Inpatient unit (10–30 beds)
- Emergency psychiatric services

Level 2, Outreach to CHC/PHC

- Scheduled outreach clinics (monthly or fortnightly)
- DMHP team visits PHCs for case detection and follow-up
- Supervision of PHC medical officers

Level 3, Community

- Mental health camps in rural areas
- School mental health screening
- Training of frontline workers (ASHA, ANM)
- Collaboration with other government departments

NMHP-DMHP Relationship

Manpower Crisis

CATEGORY	REQUIREMENT	AVAILABLE	DEFICIT
Psychiatrists	~42,000	~9,000–10,000	~32,000
Clinical Psychologists	~170,000	~2,000	~168,000
Psychiatric Social Workers	~170,000	~4,000	~166,000
Psychiatric Nurses	~170,000	~8,000	~162,000

Consequences: Rural DMHP posts remain vacant; clinical psychology posts especially difficult to fill; service quality highly variable.

Proposed Solutions

1. Mid-level mental health worker (MLMHW) cadre, certificate training
2. B.Sc. Community Mental Health (new course)
3. Rural posting incentives
4. Task-shifting to ASHA / ANM with specialist tele-supervision
5. ECHO model, specialist knowledge amplification without full deployment

Conclusion

The DMHP framework is sound but chronically under-resourced. A functional DMHP requires not just creation of posts but active filling of posts, which demands incentivized rural postings and innovative workforce models.

Answer 03: Treatment Gap in Mental Health: Definition, Magnitude, and Strategies to Reduce It

[8 marks]

Definition

The **treatment gap** is the proportion of people with a mental disorder who need treatment but do not receive any form of evidence-based care.

Formula: $\text{Treatment Gap} = \frac{(\text{People needing treatment} - \text{People receiving treatment})}{\text{People needing treatment}} \times 100$

Magnitude

SOURCE · TREATMENT GAP

WHO global (severe disorders) ~50–60%

LMIC (depression/anxiety) ~75–85%

India, NMHS 2015–16 (overall) 83.45%

India, Depression ~85.2%

India, Schizophrenia ~75%

India, Bipolar disorder ~70%

Determinants of the Treatment Gap

Supply-side factors:

- Specialist workforce deficit (0.3 psychiatrists / 100,000 vs 3 needed)
- Geographic inaccessibility of services
- Absence of psychotropics at PHC level
- Inadequate insurance coverage for mental health

Demand-side factors:

- Stigma, reduces help-seeking at all levels
- Low mental health literacy
- First contact through traditional / faith healers
- Cost of care (transport, lost wages)
- Cultural illness models (mental illness as spiritual problem)

Health system factors:

- Fragmented primary care integration
- Absent mental health in NHM priority targets
- Underfunding (<1% of health budget)

Strategies to Reduce Treatment Gap

STRATEGY	MECHANISM	EVIDENCE
mhGAP training	Task-shifting to primary care	Strong
Tele-MANAS	Remote access to specialists	Emerging
Anti-stigma campaigns	Increases demand	Moderate
Community health worker training	Identification and referral	Good
PMJAY outpatient expansion	Removes financial barrier	Policy level

STRATEGY	MECHANISM	EVIDENCE
School mental health	Early detection	Moderate
Increasing psychiatric training seats	Supply-side	Long-term

Conclusion

The 83% treatment gap is India's most striking mental health system failure. Closing it requires simultaneous demand-side (literacy, stigma) and supply-side (workforce, primary care integration, financing) interventions, no single strategy is sufficient.

Answer 04: Mental Healthcare Act 2017: Key Provisions and Rights Framework

[10 marks]

Introduction

The Mental Healthcare Act (MHCA) 2017 replaced the Mental Health Act 1987, bringing India's mental health legislation in line with UNCRPD principles. It came into force on May 29, 2018.

Key Definitional Changes

- **Mental illness** redefined: "A substantial disorder of thinking, mood, perception, orientation or memory that grossly impairs judgement, behaviour, capacity to recognise reality..."
- Mental illness explicitly excludes: mental retardation, personality variations, ordinary distress
- **Mental health establishment** broadly defined, includes all private and public facilities providing mental health care

Rights Under MHCA 2017

RIGHT · PROVISION

Access to mental health care Government must ensure availability, affordability

Community living Right to live in community, not just institutions

Protection from cruel treatment Prohibition of ECT without anesthesia, seclusion, restraints (unless emergency)

Equality and non-discrimination No discrimination in workplace, insurance, education

Confidentiality Section 23, information cannot be shared without consent

Advance Directives Can specify treatment preferences while well

Nominated Representative Can designate person to advocate on their behalf

Free legal aid In all proceedings under the Act

Complaints Right to complain to MHRB

Advance Directives

- Specifies preferred treatment, preferred establishment, refusals
- Can specify nominated representative
- Must be registered with Mental Health Authority
- MHRB can override only in defined circumstances

Involuntary Admission Criteria

Must meet BOTH:

1. Person has mental illness AND poses imminent danger to self / others
2. Person lacks capacity to make treatment decisions

Review by Mental Health Review Board (MHRB) mandatory within 30 days.

Decriminalization of Suicide Attempt

- Section 115: Creates a rebuttable presumption of severe stress, person presumed to be under stress, must receive care rather than prosecution
- Does not fully repeal Section 309 IPC but creates a protective provision

Key Bodies Created

- **Mental Health Authority (MHA)**, state-level regulatory body
- **Mental Health Review Board (MHRB)**, review involuntary admissions, advance directives
- **Central Mental Health Authority (CMHA)**, national level

Limitations of MHCA 2017

- Involuntary treatment provisions, tension with UNCRPD Article 12 and 14
 - Implementation incomplete, MHAs and MHRBs not fully functional in all states
 - Insurance equality not yet operational
 - Government establishments mandate not fully funded
-

Answer 05: Disability Certification in Mental Illness: RPwD Act 2016 and UDID Process

[8 marks]

Introduction

The Rights of Persons with Disabilities Act 2016 (RPwD Act) expanded disability categories from 7 to 21, explicitly including mental illness, intellectual disability, ASD, and specific learning disability. The UDID (Unique Disability Identification) system operationalizes certification.

Disability Categories Relevant to Psychiatry (RPwD Act 2016)

1. Mental illness
2. Intellectual disability (including specific learning disability)
3. Autism Spectrum Disorder
4. Multiple disabilities including mental illness

UDID Process

Step 1, Application

- Online via udid.co.in or offline at District Medical Authority / CMO office
- Documents: ID proof, address proof, photograph, medical records

Step 2, Medical Assessment

- At Disability Assessment Board (district / state hospital)
- For mental illness: assessed by psychiatrist
- Disability Assessment Schedule (DAS) used, evaluates self-care, occupational function, family / social functioning, community participation

Step 3, Percentage Disability

SCORE	DISABILITY %	IMPLICATIONS
0–15%	Minimal	No certificate
16–40%	Mild-moderate	Certificate issued, limited benefits
41–75%	Moderate-severe	Benchmark disability ($\geq 40\%$), reservations, welfare benefits
76–100%	Severe	Maximum benefits

Step 4, UDID Card

- 18-digit unique ID

- Issued by Ministry of Social Justice & Empowerment (MoSJE)
- Temporary (typically 5 years for mental illness, due to fluctuating course) or permanent

Step 5, Re-assessment

- Temporary certificates require reassessment at expiry
- Mental illness often temporary due to episodic nature

Certification for Specific Conditions

CONDITION · KEY ASSESSMENT TOOLS

Intellectual Disability IQ testing (Binet-Kamat, WISC/WAIS) + adaptive behavior (Vineland)

ASD Clinical diagnosis + CARS, ADOS-2 (if available)

SLD PG exams SLD battery, psychoeducational assessment

Mental illness Psychiatrist diagnosis + DAS functional assessment

Benefits of Certification

- Education: reservations in schools/colleges
- Employment: 4% reservation in government jobs (RPwD Act)
- Social protection: disability pension, free transport
- Legal protection: rights enforcement under RPwD Act
- UDID card, pan-India portability of benefits

Answer 06: Stigma in Mental Illness: Types, Measurement, and Interventions

[8 marks]

Introduction

Stigma is a major driver of the mental health treatment gap globally. It operates at multiple levels, societal, institutional, and individual, reducing help-seeking and worsening outcomes.

Types of Stigma

TYPE	DEFINITION	IMPACT
Public stigma	Community negative attitudes (stereotypes, prejudice, discrimination)	Reduces community acceptance, employment discrimination

TYPE	DEFINITION	IMPACT
Self-stigma	Internalization of negative social attitudes by the person with mental illness	Reduces self-esteem, delays help-seeking ("why try?")
Structural stigma	Institutional policies that restrict opportunities	Insurance exclusions, legal deprivation of rights, inadequate mental health funding
Courtesy stigma	Stigma experienced by family members and caregivers	Family isolation, shame-based concealment
Provider stigma	Discriminatory attitudes among healthcare workers	Diagnostic overshadowing, dismissive care

Measurement

INSTRUMENT	TYPE OF STIGMA	ITEMS	KEY SUBSCALES
ISMI (Internalized Stigma of Mental Illness)	Self-stigma	29	Alienation, stereotype endorsement, discrimination experience, social withdrawal, stigma resistance
AQ-27 (Attribution Questionnaire)	Public attitudes	27	Blameworthiness, anger, fear, help
CAMI (Community Attitudes to Mental Illness)	Community	40	Authoritarianism, benevolence, social restrictiveness, community mental health ideology
SDS (Social Distance Scale)	Discrimination	7	Willingness to interact

Anti-Stigma Strategies

APPROACH	MECHANISM	EVIDENCE
Protest	Challenge negative media portrayals	Limited, suppresses expression without changing attitudes
Education	Information campaigns about mental illness	Moderate, short-term attitude change
Contact	Direct interaction with people with mental illness	Strongest evidence , sustained attitude change

Contact-based programmes:

- "Time to Change" (UK), largest national programme

- "Opening Minds" (Canada)
- Mental Health First Aid, includes contact element
- In-person > video > social media contact

Target populations for anti-stigma work:

- Health professionals and students (structural impact)
- Employers (occupational discrimination)
- General public (social distance)
- Media professionals (portrayal)
- Police and criminal justice

Conclusion

Self-stigma is measured by ISMI; public stigma by AQ-27 and CAMI. Contact-based interventions have the strongest evidence for change. Structural stigma (funding gaps, legal exclusions) requires policy-level intervention beyond attitudes work.

Answer 07: Psychosocial Rehabilitation: Components and Models

[8 marks]

Definition

Psychosocial Rehabilitation (PSR) facilitates opportunities for persons with serious mental illness to reach their optimal level of functioning in community settings. It is distinct from clinical treatment, focused on function and participation, not only symptom reduction.

Recovery Model

The philosophical underpinning of modern PSR, recovery is defined as living a meaningful, satisfying life with or without ongoing symptoms. Courtenay Harding's Vermont Longitudinal Study showed >50% of people with schizophrenia recover substantially over 20–32 years.

Types of Rehabilitation Services

SERVICE	SETTING	POPULATION	DURATION	KEY ACTIVITIES
Halfway Home	Transitional residential	Stabilized, no family support	6–24 months	ADL, vocational prep, social skills
Long-stay Home	Permanent residential	Severely disabled, no family	Indefinite	Supervised community living
Day Care Center	Non-residential (daytime)	Semi-independent	Variable	OT, skills training, medication

SERVICE	SETTING	POPULATION	DURATION	KEY ACTIVITIES
Sheltered Workshop	Supervised work	Low-functioning	Variable	Protected work environment with pay
Supported Employment (IPS)	Real workplace	Ready for competitive work	Ongoing	Job placement + job coaching

Individual Placement and Support (IPS): Evidence-Based Model

Key features:

- Direct competitive employment (not prevocational training)
- Integrated with clinical care
- Zero exclusion (anyone who wants to work is eligible)
- Rapid job search
- Ongoing support in real workplace

Evidence: IPS produces competitive employment rates 2–3x higher than traditional vocational rehabilitation. Cochrane review confirms superiority.

Community-Based Rehabilitation (CBR): WHO Matrix

Five domains, five components each:

- **Health** (promotion, prevention, medical care, rehabilitation, assistive devices)
- **Education** (early childhood through lifelong learning)
- **Livelihood** (skills, employment, financial services, social protection)
- **Social** (personal assistance, relationships, arts, recreation, justice)
- **Empowerment** (advocacy, communication, community mobilisation, SHGs)

Indian Models

- PG exams community psychiatry programme
- SCARF (Chennai), rehabilitation services + research
- Ashadeep, Aasra, Vandrevala Foundation rehabilitation wings
- RCI-registered rehabilitation centers

Answer 08: Psychological First Aid: Principles, Components, and Distinction from Debriefing

[6 marks]

Definition

Psychological First Aid (PFA) is an evidence-informed approach to assist survivors of disaster and mass trauma by reducing initial distress, meeting immediate basic needs, and connecting people with support.

What PFA Is NOT

- Not formal psychotherapy
- Not psychological debriefing (CISD)
- Not a diagnostic procedure
- Not forcing people to talk about their trauma

WHO 8-Step PFA Model

STEP · ACTION

1 Contact and engagement, approach safely and compassionately

2 Safety and comfort, ensure physical safety, create calm

3 Stabilization, ground acutely distressed individuals

4 Information gathering, identify immediate needs and concerns

5 Practical assistance, address most pressing needs

6 Connection with social supports, link to family / community

7 Information on coping, normalize reactions, adaptive coping

8 Linkage to collaborative services, referral to professional help

Who Delivers PFA

- Trained community volunteers, NGO workers, first responders, teachers
- Does NOT require mental health training, 1-2 day course sufficient

PFA vs Critical Incident Stress Debriefing (CISD)

FEATURE	PFA	CISD
Timing	Immediate (0–72 hours)	24–72 hours post-event
Who delivers	Community workers	Trained debriefers
Approach	Needs-based, flexible	Structured group protocol
Evidence	Supported	Weak; possible harm if universal

FEATURE	PFA	CISD
Current status	Recommended	Not universally recommended
Forces disclosure	No	Group sharing expected

Key point for exam: Universal psychological debriefing (CISD) applied to all trauma survivors has no evidence of preventing PTSD and may increase PTSD risk by premature forced processing. PFA does not push people to recount trauma.

Answer 09: Suicide Prevention: National Strategy, Gatekeeper Training, and Means Restriction

[10 marks]

Epidemiology Recap

- India: ~170,000–180,000 suicides/year; rate ~12–12.4/100,000
- Most at risk: 15–39 years, males (2:1 ratio)
- Leading methods: hanging, pesticide ingestion
- NCRB data likely underestimated by 20–30%

National Suicide Prevention Strategy (NSPS) 2022

India's first NSPS, launched 2022 by MoHFW.

Goals:

- Reduce suicide mortality by 10% by 2030
- Improve surveillance (NCRB + health system linkage)
- Health system integration (DMHP linkage)
- National gatekeeper training programme
- Crisis helpline coverage
- Postvention support

Five pillars of NSPS:

1. Surveillance and data improvement
2. Means restriction and environmental modification
3. Mental health services integration
4. Community awareness and gatekeeper training
5. Media guidelines implementation

Gatekeeper Training

Definition: Training non-clinicians in strategic community positions to identify at-risk individuals and connect them to care.

Evidence-based programmes:

PROGRAMME	DURATION	SETTING
QPR (Question, Persuade, Refer)	1–2 hours	Community, online
safeTALK	3–4 hours	Community, broad
ASIST	2 days	Professionals, depth
Mental Health First Aid	1 day	Broad community

QPR steps:

- Q, Question: Ask directly about suicidal ideation
- P, Persuade: Offer support, listen non-judgmentally
- R, Refer: Connect to professional resources

Evidence: Gatekeeper training increases knowledge, confidence, and appropriate referrals. Effect on suicide rates harder to demonstrate directly but supported by modelling.

Indian context: PG exams, iCall (TISS), Vandrevalla Foundation run gatekeeper programmes. Medical student training is a priority given patient contact volume.

Means Restriction

Strongest evidence-based intervention in suicide prevention:

INTERVENTION · EVIDENCE

UK coal gas detoxification (1960s) ~30% suicide rate reduction

Paracetamol pack-size restriction (UK) Significant reduction in paracetamol deaths

Bridge barriers (Golden Gate, UK bridges) Prevention at site + minimal substitution

Pesticide restriction (Sri Lanka, Bangladesh) Significant reduction in rural suicides

Firearm restriction (Australia) Mass shooting prevention; firearm suicide reduction

India-specific:

- Paraquat and endosulfan bans contributed to reduction in rural pesticide suicides
- Metro platform screen doors (Delhi Metro), height / rail access restriction
- Buffer zones around known suicide sites (bridges, buildings)

Crisis Helplines in India

HELPLINE	NUMBER	HOURS
Tele-MANAS	14416	24×7
Vandrevala Foundation	1860-2662-345	24×7
iCall (TISS)	9152987821	Mon–Sat, 8am–10pm
PG exams	080-46110007	24×7

Answer 10: mhGAP: Purpose, Conditions, and Application in India

[6 marks]

Introduction

The WHO **Mental Health Gap Action Programme (mhGAP)**, launched 2008, addresses the treatment gap in LMICs by enabling non-specialist health workers to deliver evidence-based mental health care.

Purpose

- Bridge the treatment gap through task-shifting
- Provide evidence-based clinical protocols for priority conditions
- Enable primary care and non-specialist workers to manage common mental disorders

mhGAP Priority Conditions

CONDITION · INCLUDED

Depression Yes

Psychosis Yes

Bipolar disorder Yes

Epilepsy Yes (neurological, included for LMICs)

Suicide/self-harm Yes

Alcohol and substance use disorders Yes

Child and adolescent mental health Yes

Dementia Yes

Medically unexplained symptoms Yes

Other significant emotional complaints Yes

mhGAP-IG (Intervention Guide)

- Structured clinical decision-making flowcharts
- Assessment modules for each priority condition
- Management algorithms including medication and psychosocial interventions
- Available in multiple Indian languages

Training Model

- 5–10 day intensive training
- Uses case-based vignettes
- Supervised practice component
- Booster training sessions recommended

Evidence

Strong RCT evidence that mhGAP-trained workers:

- Accurately identify depression, psychosis, epilepsy
- Provide appropriate treatment
- Reduce DUP and time to treatment
- Improve outcomes comparable to specialist care for non-complex cases

India Application

- Piloted in several states under DMHP framework
- Results variable, where supervision is maintained, outcomes are good
- Integration with ASHA/ANM training ongoing but incomplete
- Recommended by NMHP guidelines as primary training approach

Answer 11: Telepsychiatry in India: Models, Platforms, and Evidence

[6 marks]

Rationale

India's psychiatrist shortage (0.3/100,000 vs WHO recommendation 3/100,000) makes telepsychiatry essential for expanding access, particularly in rural/underserved areas.

Regulatory Framework

- NMC Telemedicine Practice Guidelines 2020, permits telemedicine including psychiatry across India

- PG exams Telepsychiatry Operational Guidelines 2020, specific protocols for psychiatry
- Prescribing: Schedule H drugs (including psychotropics) can be prescribed via telemedicine

Key Platforms

PLATFORM	TYPE	PURPOSE
Tele-MANAS	National helpline + tele-consultation	Crisis + clinical follow-up; 24x7; 14416
eSanjeevani	Government telehealth (hub-and-spoke)	PHC-to-specialist consultation
PG exams ECHO	Knowledge amplification	Specialist mentoring of primary care providers

Tele-MANAS (Detail)

- Tier 1: Trained counselors, supportive counseling, triage
- Tier 2: Clinical psychologists and psychiatrists, complex cases
- Integrates with DMHP for referral
- Available in multiple Indian languages
- Launched October 2022

Project ECHO

- Extension for Community Healthcare Outcomes, developed at University of New Mexico
- PG exams ECHO: specialists mentor community providers via weekly video cases
- Topics: depression, psychosis, substance use, child psychiatry
- Evidence: Increases provider confidence and knowledge; improves patient outcomes
- Model of "moving knowledge not patients"

Evidence for Telepsychiatry

- Meta-analyses: No significant difference in diagnostic accuracy, patient satisfaction, or treatment outcomes compared to in-person care
- Specific evidence for: depression screening, medication management, CBT delivery
- Limitations: Requires internet access, device literacy; physical examination limited; rapport-building may be slower

Answer 12: Community-Based Rehabilitation: WHO Matrix and Indian Models

[6 marks]

Definition

CBR is a multi-sectoral strategy for rehabilitation, equalization of opportunities, and social inclusion of all children and adults with disabilities. It focuses on community empowerment rather than institutional services.

WHO CBR Matrix (2010)

The matrix comprises 5 domains × 5 components each:

DOMAIN · COMPONENTS

Health Promotion, Prevention, Medical care, Rehabilitation, Assistive devices

Education Early childhood, Primary, Secondary and higher, Non-formal, Lifelong learning

Livelihood Skills development, Self-employment, Wage employment, Financial services, Social protection

Social Personal assistance, Relationships, Culture and arts, Recreation/leisure, Justice

Empowerment Advocacy, Communication, Community mobilisation, Political participation, Self-help groups

CBR vs Institutional Rehabilitation

FEATURE	CBR	INSTITUTIONAL
Setting	Community	Hospital/center
Integration	Mainstream	Segregated
Family involvement	High	Variable
Cost	Lower	Higher
Reach	Broader population	Limited catchment
Quality assurance	Harder to standardize	Easier to monitor

Indian CBR Models

1. PG exams CBR Programme, multi-district community mental health and rehabilitation
2. SCARF (Schizophrenia Research Foundation, Chennai), CBR with family training, employment support
3. Saarthak, Delhi, urban CBR for mental illness

4. **RCI-accredited community rehabilitation workers**, standardized training
5. **NGO-based models**, Ashadeep, Vandrevale, Fellowship of Mentally Ill

Role of Family in CBR

Family is the primary rehabilitation unit in India (joint family system). Family interventions (psychoeducation, EE reduction, problem-solving) are cost-effective and culturally congruent. High caregiver burden, however, must be addressed to sustain family-based CBR.

Answer 13: Supported vs Substituted Decision-Making: Ethical and Legal Framework

[6 marks]

Context

The shift from substituted to supported decision-making represents the most significant conceptual shift in contemporary psychiatric ethics, driven by UNCRPD Article 12 and reflected in MHCA 2017.

Substituted Decision-Making (Traditional Model)

Basis Person deemed to lack decision-making capacity

Mechanism Another person (guardian, relative, doctor) makes decisions for them

Standard "Best interests" or "substituted judgment"

Problem Removes agency entirely; capacity is treated as all-or-nothing

Historical use Guardianship in mental illness; parents for adults with ID

Supported Decision-Making (UNCRPD Model)

Basis All persons retain legal capacity regardless of disability

Mechanism Support persons help individual understand information and communicate decisions

Standard Person's own will and preferences, not "best interests"

Benefit Preserves autonomy, dignity, self-determination

Safeguards Supporter cannot override the person's decision

UNCRPD Article 12

"Persons with disabilities enjoy legal capacity on an equal basis with others in all aspects of life."

Support measures must:

- Respect rights, will, and preferences of the person
- Be free of conflicts of interest
- Be subject to regular review
- Be proportional to needs

India's Position: MHCA 2017

- Advance directives: closest to supported decision-making (person's own prior decisions govern care)
- Nominated representative: advocacy role, not decision-maker
- Emergency provisions still allow involuntary treatment → tension with UNCRPD
- Disability rights advocates argue MHCA 2017 falls short of full UNCRPD compliance

Clinical Implications

- Always presume capacity (MHCA Section 89)
- Capacity is specific (for a specific decision at a specific time) not global
- Even in involuntary admission, person's stated preferences must be documented and considered
- Supported decision-making is achievable in many cases with adequate explanation and communication support

Answer 14: Principles of Ethics in Psychiatry: Autonomy, Confidentiality, and Boundary Violations

[8 marks]

Four Principles (Beauchamp and Childress)

PRINCIPLE	DEFINITION	PSYCHIATRY APPLICATION
Autonomy	Respect patient's right to make informed decisions	Central tension, involuntary treatment may override autonomy for beneficence
Beneficence	Act in patient's best interest	Treatment decisions when patient cannot decide
Non-maleficence	Avoid harm	Medication side effects, ECT risks, hospitalization trauma

PRINCIPLE	DEFINITION	PSYCHIATRY APPLICATION
Justice	Fair distribution of resources; equal treatment	Mental health receives <1% of health budget despite 10.6% disease burden

Confidentiality

Core rule: Patient information cannot be shared without informed consent.

Legal basis in India:

- MHCA 2017 Section 23, explicit right to confidentiality
- Records cannot be shared with employers or insurers without consent

Exceptions:

1. Duty to warn, specific credible threat to identifiable third party (Tarasoff principle)
2. Child protection, mandatory reporting of abuse/neglect
3. Court order (legitimate judicial process)
4. Patient incapacity, share with nominated representative
5. Public health emergency (limited; mental illness not notifiable)

Practical scenarios:

- Employer asking about an employee's psychiatric diagnosis → cannot disclose without consent
- Spouse asking about medication prescribed → requires patient consent

Boundary Violations

CATEGORY · EXAMPLES

Role boundaries Becoming friend/confidant, doing favors outside clinical role

Sexual boundaries Any sexual contact, always a violation, never acceptable

Financial boundaries Accepting large gifts, loans, financial favors

Dual relationships Treating a colleague, student, or family member

Crossing vs violation distinction:

- Crossing = minor departure (accepting a small gift at discharge), may or may not harm
- Violation = exploitation of therapeutic relationship causing harm

Why sexual contact is always wrong:

Power differential in therapeutic relationship persists even after termination. "Transference" may persist years later. Any sexual contact represents exploitation of this power imbalance.

Research Ethics: Key Provisions

- Informed consent required; capacity must be assessed
 - Vulnerable population provisions (ICMR 2017), extra protections
 - Institutional ethics committee review mandatory
 - No coercion; voluntary participation
 - Right to withdraw without consequence
-

Answer 15: National Mental Health Survey 2015-16: Key Findings and Implications

[6 marks]

Background

The NMHS 2015–16, conducted by PG exams with MoHFW funding, is the largest and most rigorous psychiatric epidemiological study in India. Sample: 34,802 adults across 12 states.

Key Prevalence Findings

DISORDER · WEIGHTED PREVALENCE

Any mental disorder 10.6%

Tobacco use disorder 22.4%

Alcohol use disorder 4.6%

Depression (current) ~2.7%

Anxiety disorders ~3.3%

Schizophrenia spectrum ~0.6%

Bipolar disorder ~0.5%

PTSD 0.5%

Lifetime any mental disorder: ~13.7%

Estimated absolute number: ~150 million people

Treatment Gap

- Overall treatment gap: **83.45%** (>4 in 5 people with diagnosable disorder receive no treatment)
- Depression: 85.2%

- Schizophrenia: 75%
- Alcohol use disorder: 86.3%
- Bipolar disorder: ~70%

Other Significant Findings

FINDING · VALUE

Median DUP (psychosis) ~5 years

First contact for mental illness Traditional / faith healer in majority

Districts with ≥ 1 psychiatrist <30%

Urban prevalence > rural for Depression, anxiety, substance use

Caregiver burden High; ZARIT score elevated in most families

Implications

1. **Scale of need** confirms NMHP underfunding is catastrophic
 2. **Treatment gap** requires combined supply and demand interventions
 3. **Faith healer as first contact**, opportunity for collaborative care / referral partnerships
 4. **DUP of 5 years**, mandate for Early Intervention in Psychosis programmes
 5. **Urban-rural gradient**, targeted rural resource allocation needed
 6. **NMHS as baseline**, next national survey needed to track NSPS and Tele-MANAS impact
-

All names and case identifiers in this document are fictitious.

Mnemonics & Memory Tricks

KEY INSIGHT

How to use: Learn the device first. Then reconstruct what each letter means without looking. Test again 24 hours later.

MNEMONIC 01: NMHP Objectives: "EASE"

- E, Ensure availability and accessibility of minimum mental health care
- A, Apply mental health knowledge in general health care and social development
- S, Stimulate self-help in the community
- E, Encourage community participation in mental health service development

KEY INSIGHT

Memory hook: NMHP wants to EASE the treatment gap. Four objectives, four letters.

MNEMONIC 02: DMHP Core Team: "P-CPN + D"

- P, Psychiatrist
- C, Clinical Psychologist
- P, Psychiatric Social Worker (PSW)
- N, Nurse (Psychiatric)
- +D, Data Entry Operator

KEY INSIGHT

Memory hook: DMHP = P-CPN + D. The team that runs a DMHP has a doctor (P), a thinker (C), a connector (PSW), a nurse (N), and a data person (D).

MNEMONIC 03: RPwD Act 2016: Mental Health Disability Categories, "MIAS"

- M, Mental Illness
- I, Intellectual Disability

A, Autism Spectrum Disorder

S, Specific Learning Disability

KEY INSIGHT

Memory hook: MIAS, "My IAS prep got a disability certificate." The four psychiatric categories in RPwD Act 2016.

MNEMONIC 04: UDID Certification Steps: "AACP-R"

A, Application (online / offline)

A, Assessment (Disability Assessment Board)

C, Calculate percentage (DAS score → disability %)

P, Print / issue UDID card

R, Re-assessment (for temporary certificates)

KEY INSIGHT

Memory hook: AACP-R. "Apply, Assess, Calculate, Print, Revisit." You AACP-R your disability certificate.

MNEMONIC 05: ISMI Subscales: "ASSESS"

A, Alienation

S, Stereotype endorsement

S, Social withdrawal

E, Experience of discrimination

S, Stigma resistance (fifth subscale)

S, Self (overall, it's a self-stigma scale)

KEY INSIGHT

Memory hook: To ASSESS self-stigma, use ISMI. Five subscales, remember ASSES (first 5 letters) + resistance is the 5th.

KEY INSIGHT

Precise subscales: Alienation, Stereotype Endorsement, Discrimination Experience, Social Withdrawal, Stigma Resistance. Alternative mnemonic: "All Students Deserve Social Recognition" → A, S, D, S, R.

MNEMONIC 06: Capacity Assessment Components: "UARC"

U, Understand the relevant information

A, Appreciate how it applies to their situation

R, Reason through options and consequences

C, Communicate a decision

KEY INSIGHT

Memory hook: You need UARC to have capacity. "Understanding And Reasoning, then Communicate." All four must be present.

MNEMONIC 07: PFA Core Actions (WHO 8 Steps): "CESSI-CPL"

C, Contact and engagement

E, Ensure safety and comfort

S, Stabilization

S, Survey / gather information

I, Immediate practical assistance

C, Connect with social supports

P, Provide coping information

L, Link to services

KEY INSIGHT

Memory hook: CESSI-CPL, "CESSI, Connect, Provide, Link." Eight steps of PFA. The middle four (S, S, I, C) are the core action steps.

KEY INSIGHT

Alternate hook: "Can Every Scared Soul In Crisis Please Live?", Contact, Ensure safety, Stabilize, Survey, Immediate help, Connect, Provide coping, Link.

MNEMONIC 08: Anti-Stigma Strategies: "PEC" (in order of evidence)

P, Protest (weakest, short-term)

E, Education (moderate)

C, Contact (strongest, most sustained)

KEY INSIGHT

Memory hook: PEC, "Protest first, Educate better, Contact best." As you go P→E→C, evidence gets stronger.

KEY INSIGHT

Extended: In-person contact > Video contact > Social media contact. "PERSON beats VIDEO beats TWITTER."

MNEMONIC 09: MHCA 2017 Rights: "FACE-CLARN"

F, Free legal aid

A, Access to mental health care

C, Community living

E, Equality and non-discrimination

C, Confidentiality

L, Legal aid and complaint mechanisms

A, Advance directives

R, Records (right to personal records)

N, Nominated representative

KEY INSIGHT

Memory hook: FACE-CLARN, your rights under MHCA 2017 FACE the CLARN of past oppression. Not pretty, but memorable.

KEY INSIGHT

Simpler version: "MHCA gives you the right to FACE CLAN": Free legal aid, Access to care, Confidentiality, Equality, Community living, Legal aid, Advance directive, Nominated rep.

MNEMONIC 10: WHO CBR Matrix Domains: "HELSE"

H, Health

E, Education

L, Livelihood

S, Social

E, Empowerment

KEY INSIGHT

Memory hook: HELSE, Norwegian/Danish for "health." Appropriate since the CBR matrix is WHO's framework for health-inclusive rehabilitation globally. Five domains: HELSE.

MNEMONIC 11: Rehabilitation Service Types: "HLDS-D"

H, Halfway Home (transitional residential)

L, Long-stay Home (permanent residential)

D, Day Care Center (non-residential)

S, Sheltered Workshop (supervised work)

D, Dedicated Supported Employment / IPS (competitive work)

KEY INSIGHT

Memory hook: HLDSD, "He Lives Daily in Supported Dwellings." From most residential (H) to most independent (IPS/D).

MNEMONIC 12: Stepped Care Levels (Depression): "RWSH-C"

R, Recognize and watchful waiting (Step 1)

W, Watch and low-intensity CBT (Step 2)

S, Specialist therapy + antidepressants (Step 3)

H, High-risk multidisciplinary (Step 4)

C, Crisis/inpatient/ECT (Step 5)

KEY INSIGHT

Memory hook: "Recognise, Watch, Specialise, Handle, Crisis", RWSHC. As letters ascend, so does intensity.

MNEMONIC 13: mhGAP Priority Conditions: "DEP-BEAS-CDM"

D, Depression

E, Epilepsy

P, Psychosis

B, Bipolar disorder

E, Emotional/medically unexplained symptoms

A, Alcohol and substance use
S, Suicide/self-harm
C, Child and adolescent mental health
D, Dementia
M, (Other significant) Mental complaints

KEY INSIGHT

Memory hook: DEP-BEAS-CDM, "Depression, Epilepsy, Psychosis: these are the BIG EASY cases for DEMentia too." 10 priority conditions in mhGAP-IG.

MNEMONIC 14: Suicide Prevention Means Restriction Evidence: "COBRA"

C, Coal gas detoxification (UK 1960s, 30% rate reduction)
O, Over-the-counter paracetamol pack-size restriction
B, Bridge barriers (Golden Gate; UK railway overheads)
R, Rifles/firearm legislation (Australia)
A, Agrochemical/pesticide restriction (Sri Lanka, Bangladesh, India)

KEY INSIGHT

Memory hook: COBRA strikes lethally, COBRA also kills suicide rates when each method is restricted. The five big means restriction wins.

MNEMONIC 15: Types of Stigma: "PSSC-P"

P, Public stigma (community attitudes)
S, Self-stigma (internalized)
S, Structural stigma (institutional policies)
C, Courtesy stigma (family/caregivers)
P, Provider stigma (health workers)

KEY INSIGHT

Memory hook: PSSC-P, "Psychiatry Still Struggles Changing Perceptions." Five levels, five letters. Public, Self, Structural, Courtesy, Provider.

MNEMONIC 16: NMHS 2015-16 Key Numbers: "10-83-5"

10, 10.6% overall prevalence of mental disorders

83, 83% treatment gap

5, 5-year median Duration of Untreated Psychosis

KEY INSIGHT

Memory hook: 10-83-5. "Ten percent ill, eighty-three percent untreated, five years before psychosis gets help." India's three most cited NMHS figures.

MNEMONIC 17: CAM Criteria for Delirium: "AFDC"

A, Acute onset + Fluctuating course (Feature 1, required)

F, (same Feature 1, Fluctuating)

D, Disorganized thinking (Feature 3)

C, Consciousness altered (Feature 4)

+ **Feature 2:** Inattention (also required)

KEY INSIGHT

CAM diagnosis requires: Feature 1 (acute + fluctuating) + Feature 2 (inattention) + Feature 3 OR Feature 4.

KEY INSIGHT

Memory hook: "Attention Always First and Definitely Counts", Acute onset, Always fluctuates (F1), Feature 2 = inAttention (required), Disorganized (F3), Consciousness (F4). You need F1 + F2 + (F3 or F4).

MNEMONIC 18: Bellary Model Key Contributions: "D-T-C-O"

D, Diagnosis possible at PHC level (by trained MO)

T, Treatment (psychotropics) dispensable at primary care

C, Community follow-up feasible by non-specialist workers

O, Outcomes comparable to hospital-based care

KEY INSIGHT

Memory hook: D-T-C-O, "Diagnosis, Treatment, Community, Outcomes." What Bellary proved before NMHP was launched.

MNEMONIC 19: Supported Employment IPS Principles: "ZERO RAPID"

- Z, Zero exclusion (anyone who wants to work)
- E, Employment in competitive settings (not sheltered)
- R, Rapid job search (direct, not lengthy pre-vocational training)
- O, On the job support (job coach in workplace)
- R, Recovery-oriented (employment supports recovery)
- A, According to consumer preferences
- P, Personalized benefits counseling
- I, Integration with clinical care
- D, Duration unlimited (ongoing support)

KEY INSIGHT

Memory hook: ZERO RAPID, IPS moves at ZERO delay with RAPID placement. Not just a mnemonic, it reflects the core philosophy: get people working fast, support them while they work.

MNEMONIC 20: UNCRPD Core Principles: "RIDE-FACE"

- R, Respect for inherent dignity and individual autonomy
- I, Individual autonomy (freedom to make own choices)
- D, Difference respected (disability as part of human diversity)
- E, Equality of opportunity
- F, Full participation and inclusion in society
- A, Accessibility
- C, Capacity of children with disabilities (evolving)
- E, Equality between men and women

KEY INSIGHT

Memory hook: RIDE-FACE, "RIDE with dignity, FACE equality." Eight UNCRPD principles. Most exams test Article 12 (legal capacity) and Article 14 (liberty), know these specifically.

All names and case references fictitious. Mnemonics are memory aids, always verify with primary source.

High-Yield Comparisons

KEY INSIGHT

How to use: Cover the right column(s). Reconstruct from memory. These tables are optimised for high-yield exam points, every row is a potential MCQ or short-answer fact.

TABLE 01: NMHP vs DMHP: Conceptual Distinction

FEATURE	NMHP	DMHP
Full form	National Mental Health Programme	District Mental Health Programme
Nature	Policy and programme framework	Operational implementation unit
Level	National	District
Year of origin	1982	1996 (pilot, 27 districts)
Function	Sets objectives, provides funding, monitors outcomes	Delivers services, trains staff, conducts outreach
Who manages	Ministry of Health & Family Welfare	District health administration + state NHM
Funding channel	Central → State → District (NHM route)	NHM funds to district
Key document	National Mental Health Policy 2014	DMHP operational guidelines
Relationship	NMHP is the parent programme	DMHP is the operational arm of NMHP
Analogy	Constitution	Municipal corporation (implements the law)

TABLE 02: Supported vs Substituted Decision-Making

FEATURE	SUPPORTED DECISION-MAKING	SUBSTITUTED DECISION-MAKING
Philosophical basis	UNCRPD Article 12, legal capacity for all	Functional incapacity removes legal capacity

FEATURE	SUPPORTED DECISION-MAKING	SUBSTITUTED DECISION-MAKING
Who decides	The person with disability (with support)	Guardian, family member, or clinician
Standard applied	Person's own will and preferences	"Best interests" or "substituted judgment"
Role of supporter	Help understand, communicate, implement decision	Make the decision on behalf of person
Capacity assessment	Not required to trigger support	Required to justify substitution
India's MHCA 2017	Advance directives + nominated representative approach	Emergency powers for involuntary treatment retained
UNCRPD compliance	Full compliance	Partial, rights activists argue substitution violates UNCRPD
Safeguards	Supporter cannot override person's decision	MHRB review, time-limited
Example	Nominated representative attending consent discussions	Guardian signing consent for ECT
Trend	Global move toward this model	Being phased out in progressive frameworks

TABLE 03: NMHS 2015-16 Key Findings Summary

CATEGORY · FINDING

Sample size 34,802 adults across 12 states

Overall prevalence (any disorder) 10.6% (current); 13.7% (lifetime)

Tobacco use disorder 22.4%

Alcohol use disorder 4.6%

Depression (current) ~2.7%

Anxiety disorders ~3.3%

Schizophrenia spectrum ~0.6%

Bipolar disorder ~0.5%

PTSD 0.5%

Overall treatment gap 83.45%

Depression treatment gap 85.2%

Schizophrenia treatment gap 75%

Alcohol use disorder treatment gap 86.3%

Median DUP (psychosis) ~5 years

First contact Traditional / faith healer in majority

Districts with ≥ 1 psychiatrist <30%

Estimated absolute numbers ~150 million affected

Urban vs rural Urban: higher depression, anxiety, substance use; Rural: higher treatment gap

TABLE 04: Disability Certification Process (Mental Illness)

STAGE	STEPS	DETAILS
Application	Step 1	Online (udid.co.in) or offline at CMO/DMA
Documents required	Step 1	ID proof, address, photo, medical records
Assessment body	Step 2	Disability Assessment Board at district / state hospital
Assessing clinician	Step 2	Psychiatrist (physician where unavailable)
Assessment tool	Step 2	Disability Assessment Schedule (DAS), 4 domains
DAS domains	Step 2	Self-care, occupational function, family / social function, community participation
Disability %: 0–15%	Step 3	Minimal, no certificate
Disability %: 16–40%	Step 3	Mild-moderate, certificate, limited benefits
Disability %: 41–75%	Step 3	Benchmark disability ($\geq 40\%$), reservations, welfare
Disability %: 76–100%	Step 3	Severe, maximum priority
Certificate type	Step 4	Temporary (5 years, mental illness) or permanent

STAGE	STEPS	DETAILS
ID issued	Step 4	UDID card, 18-digit unique ID, MoSJE
Re-assessment	Step 5	Required at expiry of temporary certificate

TABLE 05: CBR vs Institutional Rehabilitation

FEATURE	COMMUNITY-BASED REHABILITATION (CBR)	INSTITUTIONAL REHABILITATION
Setting	Community, person's own environment	Hospital, residential center, workshop
Integration	Mainstreamed with community life	Segregated from general community
Family involvement	Central, family is primary unit	Variable; often reduced
Cost	Generally lower	Higher (infrastructure, staffing)
Geographical reach	Broader, can serve remote areas	Limited to facility catchment
Sustainability	Community-driven; culturally embedded	Dependent on institutional funding
Quality assurance	Harder to standardize, monitor	Easier to monitor and audit
Empowerment	High, person remains in community	Risk of learned helplessness, dependency
Evidence	Strong for social outcomes, inclusion	Strong for symptom control, safety
WHO recommendation	Preferred for most disabilities	Reserved for acute/severe episodes
Indian context	NGO-driven; SCARF, PG exams models	Government psychiatric hospitals, long-stay units
RPwD Act 2016	Explicitly supports community living	Residual role
MHCA 2017	Right to community living guaranteed	Inpatient only when necessary

TABLE 06: Stepped Care Levels for Depression

STEP	SEVERITY	WHO PROVIDES	INTERVENTION
Step 1	All depression presentations	GP / PHC MO / ASHA	Recognition, psychoeducation, watchful waiting
Step 2	Mild to moderate	PHC / Low-intensity worker	Guided self-help, low-intensity CBT, psychoeducation groups, exercise
Step 3	Moderate to severe / step 2 failure	Specialist / trained MO	High-intensity CBT, IPT, antidepressants, structured problem-solving
Step 4	Complex / risk / treatment-resistant	Multidisciplinary team	Combined therapy + medication, crisis assessment, specialist referral
Step 5	Severe risk / acute	Inpatient / crisis team	ECT consideration, intensive inpatient care, acute risk management
India mapping		Steps 1–2: ASHA / ANM + PHC	Steps 3–5: DMHP → district hospital → tertiary
Key principle		Step up if no response in 6–8 weeks	Step down when stable, least intensive effective treatment

TABLE 07: Telepsychiatry Models in India

PLATFORM	TYPE	TIER	USERS	HOURS	MENTAL HEALTH ROLE
Tele-MANAS	National helpline + tele-consultation	Two-tier (counselors → specialists)	General public	24×7	Crisis + clinical MH; 14416
eSanjeevani (hub-spoke)	Government teleconsultation	Provider-to-provider	PHC doctors consulting specialists	Day hours	MH specialist consultations for PHC MOs
eSanjeevani OPD	Patient-to-doctor	Direct	Patients	Day hours	Psychiatry OPD remotely

PLATFORM	TYPE	TIER	USERS	HOURS	MENTAL HEALTH ROLE
PG exams ECHO	Knowledge amplification	Specialist-to-provider	Community health workers, MOs	Weekly sessions	Case-based learning, supervision
State tele-MH models	State-specific	Variable	State PHC workers, patients	Variable	Karnataka (PG exams hub), TN (SCARF)
iCall (TISS)	Helpline + counselling	Single-tier (counselors)	General public	Mon–Sat, 8am–10pm	Crisis support, referral

TABLE 08: PFA vs CISD (Critical Incident Stress Debriefing)

FEATURE	PFA	CISD
Full name	Psychological First Aid	Critical Incident Stress Debriefing
Origin	WHO; multiple contributors	Jeffrey Mitchell, 1983
Timing	Immediate (0–72 hours)	24–72 hours post-incident
Setting	Any post-disaster/ trauma context	Group setting, structured
Deliverer	Trained community workers (1–2 day training)	Trained debriefers
Approach	Flexible, needs-based, non-intrusive	Structured group protocol with phases
Forces disclosure	No, follows person's lead	Group sharing expected; structured recall
Requires mental health training	No	Yes (CISD training)
Evidence status	Evidence-informed; recommended	No RCT evidence of benefit; possible harm if universal
Risk	Minimal	Universal CISD may increase PTSD risk
Goal	Stabilize, connect, refer	Process trauma in group
Current WHO status	Recommended first response	Not recommended as universal intervention
India context	Used in NDMA guidelines	Historically used; being replaced by PFA

TABLE 09: Types of Stigma: Comparison

TYPE	DEFINITION	LEVEL	KEY MEASUREMENT	KEY INTERVENTION
Public stigma	Community negative stereotypes, prejudice, discrimination toward mentally ill	Societal	AQ-27, CAMI	Contact-based anti-stigma campaigns
Self-stigma	Person with mental illness internalizes public stigma	Individual	ISMI (29 items, 5 subscales)	CBT-based self-stigma interventions, peer support
Structural stigma	Institutional policies that restrict opportunities for mentally ill	Systemic	Policy audits, MHCA compliance	Legislation (MHCA 2017), parity laws, budget advocacy
Courtesy stigma	Stigma toward families/care-givers of people with mental illness	Family/social	Family stigma scales	Family psychoeducation, caregiver support groups
Provider stigma	Discriminatory attitudes by health/social workers	Healthcare system	Provider attitude surveys	Undergraduate training, contact-based education for professionals
Effect on treatment gap	All types reduce help-seeking; structural stigma reduces supply		Treatment gap (83%) reflects cumulative stigma	Multi-level interventions required

TABLE 10: Gatekeeper Training Programmes: Comparison

PROGRAMME	DURATION	TARGET	EVIDENCE LEVEL	CORE METHOD
QPR (Question, Persuade, Refer)	1–2 hours	Broad community, online feasible	Good (RCT evidence for knowledge/confidence)	Q: Ask directly; P: Listen and persuade; R: Refer
safeTALK	3–4 hours	Community, any setting	Good, widely disseminated	TALK: Tell, Ask, Listen, KeepSafe
ASIST	2 days	Professionals, community leaders	Strong (RCT; reduces suicidality in trainees)	Applied Suicide Intervention Skills, full safe messaging

PROGRAMME	DURATION	TARGET	EVIDENCE LEVEL	CORE METHOD
Mental Health First Aid (MHFA)	8 hours (1 day)	Community, workplaces	Strong, 37 RCTs across countries	Broad MH first aid including suicide module
PG exams Gatekeeper Module	1 day	Medical students, healthcare workers	Pilot data, KMCRI type settings	Indian-adapted QPR/ASIST principles
Key shared elements		All		Ask directly, non-judgmental listening, connecting to help, no secrecy pact

TABLE 11: Mental Health Acts: 1987 vs 2017 (MHCA)

FEATURE	MENTAL HEALTH ACT 1987	MENTAL HEALTHCARE ACT 2017
Year in force	1987	2018 (May 29)
Rights framework	Minimal rights provisions	Comprehensive rights framework (10 explicit rights)
Definition of mental illness	Narrow, lists conditions	Broad functional definition; excludes mental retardation
Advance directives	Not included	Introduced, can specify treatment preferences
Nominated representative	Not included	Introduced, advocacy role
Capacity presumption	Not explicit	Explicit: all adults presumed to have capacity
Involuntary admission	Family/guardian could admit	Imminent danger + incapacity required; MHRB review
Suicide attempt	Section 309 IPC not addressed	Section 115: Presumption of severe stress; protective
Regulatory body	Licensing Authority	Mental Health Authority (MHA) + MHRB
Research protections	Absent	Section 97: explicit informed consent
Human rights protections	Weak	Strong: prohibits non-anesthetic ECT, solitary confinement, restraints except emergency
Insurance parity	Not mentioned	Mandated equal insurance coverage

FEATURE	MENTAL HEALTH ACT 1987	MENTAL HEALTHCARE ACT 2017
UNCRPD alignment	Pre-UNCRPD	Partially aligned (full compliance debated)

TABLE 12: Halfway Home vs Long-Stay Home vs Day Care Center

FEATURE	HALFWAY HOME	LONG-STAY HOME	DAY CARE CENTER
Nature	Transitional residential	Permanent residential	Non-residential (day-time only)
Duration	6–24 months	Indefinite	Open-ended
Target population	Stabilized, no family support, needs bridging	Severely disabled, no family, cannot live independently	Semi-independent; too ill for full-time work
Clinical oversight	Regular psychiatrist visits	Regular medical input	Daily or near-daily clinical contact
Goal	Transition to independent/family living	Supported long-term living	Maintain function without hospitalization
Activities	ADL training, vocational prep, social skills	Daily living support, social activities	OT, skills training, medication management, peer support
Cost	Moderate	High (long-term)	Lowest
RPwD / MHCA	Supported under MHCA community living rights	Supported; risk of institutional culture if poorly run	MHCA preferred model over hospitalization
Example	Pre-discharge placements in SCARE, PG exams programmes	NGO group homes, state-run long-stay units	Day hospitals attached to district psychiatry departments

All comparisons based on standard guidelines and policy documents. Names fictitious where used.

PYQ Frequency Analysis

EXAM PEARL

Note: Question patterns are synthesised from PG exams MD Psychiatry Paper IV trends, PG theory exams, and PG entrance patterns. Specific years are not cited to keep material institution-neutral and broadly applicable.

SECTION A: FREQUENCY MAP

Topic Frequency by Exam Weight

TOPIC	LONG ANSWER (10M)	SHORT ANSWER (5–6M)	VERY SHORT (2–3M)	MCQ TARGETS	OVERALL PRIORITY
NMHP, history, objectives, limitations	★★★★★	★★★★★	★★★	★★★★★	Tier 1
DMHP, structure, team, manpower	★★★★★	★★★★★	★★★	★★★★★	Tier 1
MHCA 2017, rights, AD, involuntary	★★★★★	★★★★★	★★★	★★★★★	Tier 1
NMHS 2015-16, findings, treatment gap	★★★★★	★★★★★	★★★★★	★★★★★	Tier 1
Stigma, types, measurement, interventions	★★★	★★★★★	★★★	★★★	Tier 1
Rehabilitation, types, IPS, CBR	★★★★★	★★★★★	★★★	★★★	Tier 1
RPwD Act 2016 + UDID	★★★	★★★★★	★★★	★★★	Tier 2

TOPIC	LONG ANSWER (10M)	SHORT ANSWER (5–6M)	VERY SHORT (2–3M)	MCQ TARGETS	OVERALL PRIORITY
Suicide prevention, strategy, means restriction	★★★	★★★★★	★★★	★★★	Tier 2
mhGAP, purpose, conditions, task-shifting	★★★	★★★★	★★★	★★★	Tier 2
PFA vs CIRD	★★	★★★★★	★★★	★★★	Tier 2
CBR, WHO matrix	★★	★★★★	★★★	★★★	Tier 2
Telepsychiatry, Tele-MANAS, ECHO	★★	★★★★	★★★	★★★	Tier 2
Capacity assessment	★★	★★★★	★★★	★★★	Tier 2
Stepped care model	★★	★★★★	★★	★★★	Tier 3
DALY and global burden	★	★★	★★★	★★★	Tier 3
C-L psychiatry models	★★	★★	★★	★★	Tier 3
Disaster psychiatry	★★	★★★★	★★	★★	Tier 3
Ethics, confidentiality, boundaries	★★	★★★★	★★	★★	Tier 3

SECTION B: CATEGORISED QUESTION BANK

CATEGORY 1: NMHP and DMHP (Highest Frequency)

Long Answer Questions (10 marks)

1. Describe the National Mental Health Programme. Discuss its objectives, history, and current limitations. (10 marks)

2. Write a comprehensive account of the District Mental Health Programme, its structure, team composition, service delivery model, and manpower challenges. (10 marks)
3. Describe the evolution of community psychiatry in India with special reference to NMHP and DMHP. (10 marks)
4. Critically evaluate the implementation of NMHP in India. What are the barriers to achieving its objectives? (10 marks)

Short Answer Questions (5–6 marks)

1. What is the Bellary model and how did it influence Indian mental health policy? (5 marks)
2. Enumerate the DMHP team composition and the role of each member. (5 marks)
3. What is the relationship between NMHP and DMHP? (5 marks)
4. Discuss the manpower crisis in Indian psychiatry and proposed solutions. (6 marks)
5. What is mhGAP? How does it address the treatment gap? (5 marks)
6. Write a note on task-shifting in mental health care. (5 marks)

Very Short / MCQ-type

1. Year NMHP was launched. (Answer: 1982)
 2. Year DMHP was first piloted. (Answer: 1996)
 3. Number of pilot districts in DMHP. (Answer: 27)
 4. India's psychiatrist density per 100,000. (Answer: ~0.3)
 5. WHO recommended psychiatrist density per 100,000. (Answer: 3)
-

CATEGORY 2: Mental Healthcare Act 2017

Long Answer Questions

1. Describe the rights of persons with mental illness under the Mental Healthcare Act 2017. (10 marks)
2. Compare the Mental Health Act 1987 with the Mental Healthcare Act 2017. (10 marks)
3. Discuss advance directives and the nominated representative system under MHCA 2017. (8 marks)
4. Write a note on the involuntary admission criteria under MHCA 2017. How does it differ from the 1987 Act? (8 marks)

Short Answer Questions

1. What is a Mental Health Review Board? What is its role? (5 marks)
2. Describe the statutory definition of mental illness under MHCA 2017. (5 marks)
3. How does MHCA 2017 protect persons with mental illness from inhumane treatment? (5 marks)

4. Discuss the MHCA 2017 provisions regarding suicide attempt. (5 marks)
5. What is the role of the Central Mental Health Authority? (4 marks)

Very Short

1. Year MHCA 2017 came into force. (Answer: May 29, 2018)
 2. Section of MHCA 2017 dealing with confidentiality. (Answer: Section 23)
 3. MHCA 2017, which section deals with advance directives? (Answer: Sections 5–14)
-

CATEGORY 3: Psychiatric Epidemiology and Burden

Long Answer Questions

1. Discuss the findings of the National Mental Health Survey 2015-16 and its implications for mental health policy. (10 marks)
2. Describe the burden of mental illness in India. Discuss the treatment gap and strategies to bridge it. (10 marks)
3. Write a comprehensive note on psychiatric epidemiology in India with reference to prevalence, treatment gap, and service gaps. (10 marks)

Short Answer Questions

1. Define treatment gap. What are the factors contributing to the treatment gap in India? (6 marks)
2. Describe the DALY concept and the global burden of mental illness. (5 marks)
3. Write a note on suicide epidemiology in India with reference to NCRB data. (5 marks)
4. Describe the findings of the National Drug Use Survey 2018. (5 marks)

Very Short / MCQ-type

1. NMHS 2015-16 overall prevalence. (Answer: 10.6%)
 2. NMHS 2015-16 treatment gap. (Answer: 83.45%)
 3. Median DUP for psychosis in India. (Answer: ~5 years)
 4. India's suicide rate per 100,000. (Answer: ~12–12.4)
 5. India's annual suicides (approximate). (Answer: ~170,000–180,000)
-

CATEGORY 4: Stigma

Long Answer Questions

1. Discuss the types of stigma in mental health, their measurement, and evidence-based interventions. (10 marks)
2. Define self-stigma. Describe the ISMI and anti-stigma strategies. (8 marks)

Short Answer Questions

1. What is structural stigma? How does it affect mental health care delivery? (5 marks)
2. Discuss contact-based anti-stigma interventions with evidence. (5 marks)
3. Describe the AQ-27. What does it measure? (4 marks)
4. What is courtesy stigma? (3 marks)

Very Short / MCQ-type

1. ISMI, number of items and subscales. (Answer: 29 items, 5 subscales)
 2. Most evidence-based anti-stigma strategy. (Answer: Contact-based intervention)
 3. Anti-stigma strategy with weakest long-term evidence. (Answer: Protest)
-

CATEGORY 5: Rehabilitation

Long Answer Questions

1. Describe the types of rehabilitation services for persons with severe mental illness. (10 marks)
2. Write a note on the principles and models of psychosocial rehabilitation. Include supported employment. (8 marks)
3. Describe community-based rehabilitation and the WHO CBR matrix. (8 marks)

Short Answer Questions

1. What is a halfway home? How does it differ from a long-stay home? (5 marks)
2. Describe the Individual Placement and Support (IPS) model. (5 marks)
3. What is the WHO CBR matrix? Name its five domains. (5 marks)
4. Describe the recovery model in psychiatric rehabilitation. (5 marks)
5. Write a note on day care centers in psychiatric rehabilitation. (4 marks)

Very Short / MCQ-type

1. Domains of WHO CBR matrix (5). (Answer: Health, Education, Livelihood, Social, Empowerment)
 2. IPS, what does it stand for? (Answer: Individual Placement and Support)
 3. Courtenay Harding's study, what did it show? (Answer: >50% of schizophrenia patients recover substantially over 20–32 years)
-

CATEGORY 6: Disability Certification

Long Answer Questions

1. Describe the process of disability certification for mental illness under the RPwD Act 2016 and UDID system. (8 marks)

2. Discuss the Rights of Persons with Disabilities Act 2016, mental health provisions, disability categories, and certification process. (10 marks)

Short Answer Questions

1. What is UDID? Describe the steps for obtaining a UDID certificate. (5 marks)
2. List the mental health-relevant disability categories under RPwD Act 2016. (4 marks)
3. What is benchmark disability? What percentage qualifies? (3 marks)
4. How is disability percentage assessed for intellectual disability? (5 marks)

Very Short / MCQ-type

1. Year RPwD Act was passed. (Answer: 2016)
 2. Number of disability categories in RPwD Act 2016. (Answer: 21)
 3. Benchmark disability threshold. (Answer: 40% or more)
 4. Tool used for mental illness disability assessment. (Answer: Disability Assessment Schedule, DAS)
-

CATEGORY 7: Suicide Prevention

Long Answer Questions

1. Describe the National Suicide Prevention Strategy 2022, its goals, components, and key interventions. (10 marks)
2. Discuss gatekeeper training for suicide prevention, programmes, evidence, and Indian context. (8 marks)
3. Write a comprehensive note on means restriction as a suicide prevention strategy. (6 marks)

Short Answer Questions

1. What is gatekeeper training? Describe the QPR programme. (5 marks)
2. List the crisis helplines available in India for suicide prevention. (4 marks)
3. Discuss media guidelines for suicide reporting. (5 marks)
4. What is the Werther effect? What is the Papageno effect? (4 marks)
5. Describe means restriction with examples from India. (5 marks)

Very Short / MCQ-type

1. Tele-MANAS helpline number. (Answer: 14416)
2. Year National Suicide Prevention Strategy was launched. (Answer: 2022)
3. Most evidence-based suicide prevention intervention globally. (Answer: Means restriction)
4. Most common suicide method in India. (Answer: Hanging)

5. Most common method in agricultural India. (Answer: Pesticide ingestion)

CATEGORY 8: PFA and Disaster Psychiatry

Long Answer Questions

1. Describe Psychological First Aid. How does it differ from psychological debriefing? (8 marks)
2. Discuss the mental health response to disasters, phases, interventions, and Indian models. (8 marks)

Short Answer Questions

1. What are the WHO 8 steps of PFA? (6 marks)
2. Why is universal CISD not recommended after trauma? (5 marks)
3. What is the mental health impact of COVID-19? (5 marks)
4. Write a note on Critical Incident Stress Management (CISM). (5 marks)

Very Short / MCQ-type

1. PFA, who can deliver it? (Answer: Any trained community worker; no mental health training required)
 2. CISD, creator. (Answer: Jeffrey Mitchell, 1983)
 3. What does PFA NOT do? (Answer: Force trauma disclosure; diagnose; provide formal therapy)
-

CATEGORY 9: Community Care Models and Telepsychiatry

Short Answer Questions

1. Describe the stepped care model for depression. (6 marks)
 2. What is telepsychiatry? Describe Tele-MANAS. (5 marks)
 3. Write a note on Project ECHO and PG exams ECHO. (5 marks)
 4. Describe the collaborative care model in primary care psychiatry. (5 marks)
 5. What is Assertive Community Treatment (ACT)? (5 marks)
 6. Describe Early Intervention in Psychosis, rationale and components. (6 marks)
-

CATEGORY 10: Ethics in Psychiatry

Long Answer Questions

1. Discuss the ethical principles applicable to psychiatry. Describe boundary violations. (8 marks)
2. Write a note on confidentiality in psychiatry, principles and exceptions. (6 marks)

Short Answer Questions

1. What are the four components of decision-making capacity? (5 marks)
 2. Discuss the duty to warn in psychiatry. (5 marks)
 3. What is dual relationship? Give examples and discuss implications. (5 marks)
 4. Describe research ethics in psychiatry with reference to ICMR guidelines. (5 marks)
-

SECTION C: QUESTION PATTERN ANALYSIS

Observation 1: NMHP/DMHP: Always Asked

Every paper in the last several years has had at least one question on NMHP or DMHP, either as a long answer or paired short answers. It is never safe to skip this topic.

Predicted forms:

- "Discuss NMHP, objectives, achievements, limitations" (10m)
- "Write a note on DMHP" (5m)
- "NMHP and DMHP, relationship and manpower crisis" (8m)

Observation 2: MHCA 2017: Increasing Frequency

Since 2018 (when the Act came into force), MHCA 2017 appears in almost every paper. Rights framework, advance directives, and involuntary admission criteria are the high-yield sub-topics.

Watch for: Questions that combine MHCA 2017 with UNCRPD or with the 1987 Act comparison.

Observation 3: NMHS Data as Stand-Alone Topic

The NMHS 2015-16 figures are now standard, examiners expect specific numbers (10.6%, 83%, 5 years DUP). Vague answers without statistics score poorly.

Observation 4: Rehabilitation Gets More Long Answers Than Expected

CBR, halfway homes, IPS, examiners treat this as a knowledge-depth test. Simply listing types is insufficient; mechanism, evidence, and Indian context are expected.

Observation 5: Emerging Topics: Telepsychiatry, NSPS

Tele-MANAS (2022) and NSPS (2022) are recent enough that questions have appeared in post-2022 papers and will continue. Know the structure of both.

Observation 6: Ethics Paired with Clinical Context

Ethics questions rarely appear in isolation. Expect: "A patient tells you about plans to harm someone, discuss confidentiality and your obligations" or "Discuss capacity assessment in a patient refusing surgery."

SECTION D: HIGH-RISK MCQ TARGETS

FACT · ANSWER

NMHP launched year 1982

Bellary model institution PG exams + Bangalore Medical College

DMHP pilot year 1996

DMHP pilot districts 27

NMHS sample size 34,802 adults

NMHS overall prevalence 10.6%

NMHS treatment gap 83.45%

India's psychiatrist density ~0.3 / 100,000

WHO recommended psychiatrist density 3 / 100,000

RPwD Act 2016, disability categories 21

Benchmark disability threshold 40%

MHCA 2017 in force May 29, 2018

ISMI items 29

ISMI subscales 5

WHO CBR matrix domains 5 (Health, Education, Livelihood, Social, Empowerment)

mhGAP launched 2008

WHO MHAP launched 2013 (extended to 2030)

Tele-MANAS number 14416

NSPS launched 2022

Most evidence-based anti-stigma Contact-based

Most evidence-based suicide prevention Means restriction

PFA, WHO steps 8

CISD creator Jeffrey Mitchell, 1983

CAM, features required for delirium F1 + F2 + (F3 or F4)

Capacity components 4 (Understand, Appreciate, Reason, Communicate)

IPS, competitive employment rates vs traditional 2–3× higher

Vermont longitudinal study finding >50% schizophrenia recover substantially

DUP median India ~5 years

India suicide rate/100,000 ~12–12.4

SECTION E: ANSWER CONSTRUCTION TIPS

For 10-Mark Long Answers

Structure: Introduction (2 sentences) → Background/History → Core Content (headings + tables) → Current Status → Limitations/Critique → Conclusion.

Target: 800–1000 words, at least 2 tables or structured lists, specific statistics cited.

For 5–6 Mark Short Answers

Structure: Definition → Classification/Components (table or numbered list) → Brief clinical context → One exam pearl.

Target: 400–500 words, 1 table acceptable.

For 3–4 Mark Very Short Answers

Structure: Definition → 3–5 key points → done.

Target: 150–200 words. No padding.

Examiner Red Flags (lose marks)

- NMHP and DMHP conflated as one thing
- NMHS prevalence stated without treatment gap figure
- Disability certification without mentioning DAS or percentage scale
- Stigma answer that only lists types without measurement tools or interventions
- PFA described as "debriefing", opposite meaning, serious error
- Capacity assessment with fewer than 4 components
- MHCA 2017 rights stated without specific section references where known

Examiner Green Flags (gain marks)

- Specific statistics from NMHS
- India-specific examples (Tele-MANAS, PG exams ECHO, SCARF)

- Acknowledging limitations of policy / programmes (shows critical thinking)
 - Mentioning UNCRPD in MHCA / rights questions
 - Evidence base for interventions (IPS over traditional vocational rehab; contact over protest)
 - Distinguishing MHCA 2017 from 1987 Act precisely
-

*PYQ patterns derived from multi-year analysis of Indian MD Psychiatry Paper IV examinations.
All question examples are reconstructions, not verbatim reproductions.*

Quick Review

KEY INSIGHT

How to use: Read the question. Answer out loud or write it down. Then reveal. Do all 30 in one pass, aim for under 20 minutes. Flag anything you hesitated on and return to D1.

Q01

What year was the NMHP launched, and what was its immediate precursor?

The NMHP was launched in **1982**. Its immediate precursor was the **Bellary District demonstration project (1975–1982)**, conducted by PG exams and Bangalore Medical College, which proved that mental health care could be delivered at the PHC level by trained non-specialist workers.

Q02

Name the four official objectives of the NMHP (1982 formulation).

1. Ensure availability and accessibility of minimum mental health care for all, especially vulnerable populations
2. Encourage application of mental health knowledge in general health care and social development
3. Promote community participation in mental health service development
4. Stimulate efforts toward self-help in the community

Mnemonic: **EASE**

Q03

What are the five core positions in a DMHP team?

1. Psychiatrist
2. Clinical Psychologist
3. Psychiatric Social Worker (PSW)
4. Psychiatric Nurse
5. Data Entry Operator

Mnemonic: **P-CPN + D**

Q04

Distinguish NMHP from DMHP in one sentence each.

NMHP = the national policy and programme framework, sets objectives, provides funding through NHM, monitors outcomes.

DMHP = the district-level operational unit, delivers services, trains staff, runs outreach clinics.

One analogy: NMHP is the constitution; DMHP is the municipality that implements it.

Q05

What are India's psychiatrist density figures vs WHO recommendation?

- India: approximately **0.3 psychiatrists per 100,000** population (~9,000–10,000 total)
 - WHO recommendation: **3 per 100,000**
 - Deficit: approximately **32,000 psychiatrists**
-

Q06

State three key findings from the NMHS 2015-16.

1. Overall prevalence of any mental disorder: **10.6%** (current), 13.7% lifetime
2. Treatment gap: **83.45%**, over 4 in 5 people with a diagnosable disorder receive no treatment
3. Median duration of untreated psychosis: **~5 years**

Bonus: First contact for mental illness in most people = traditional / faith healer, not health system.

Q07

Define treatment gap. What is India's overall figure?

Treatment gap = the proportion of people who need evidence-based mental health treatment but do not receive it.

India's overall treatment gap (NMHS 2015-16): **83.45%**

Disorder-specific: Depression 85.2%, Schizophrenia 75%, Alcohol use 86.3%.

Q08

What does mhGAP stand for, when was it launched, and what is its purpose?

mhGAP = Mental Health Gap Action Programme

Launched: 2008, by WHO

Purpose: Address the treatment gap in LMICs by providing structured clinical protocols that enable non-specialist health workers to identify and manage priority mental health conditions.

It uses the **mhGAP Intervention Guide (mhGAP-IG)** covering 10 priority conditions.

Q09

Name the 10 priority conditions covered in mhGAP-IG.

1. Depression
2. Psychosis
3. Bipolar disorder
4. Epilepsy
5. Suicide and self-harm
6. Alcohol and substance use disorders
7. Child and adolescent mental health
8. Dementia
9. Other significant emotional/medically unexplained symptoms
10. (Other significant mental health complaints)

Mnemonic: **DEP-BEAS-CDM**

Q10

Distinguish task-shifting from task-sharing.

Task-shifting: Moving specific tasks from specialized to less specialized workers, the specialist exits the picture for those tasks.

Task-sharing (preferred term): The specialist retains oversight and clinical responsibility; delivery is shared with a non-specialist under supervision. The specialist doesn't disappear, they supervise and mentor.

Most mhGAP and DMHP models are **task-sharing**, not pure task-shifting.

Q11

Name the four psychiatric/neurodevelopmental disability categories under RPwD Act 2016.

1. Mental illness
2. Intellectual disability
3. Autism Spectrum Disorder
4. Specific Learning Disability

Mnemonic: **MIAS**

Q12

What percentage of disability qualifies as "benchmark disability" under RPwD Act 2016, and what does it entitle the person to?

40% or more = benchmark disability.

Entitlements: 4% reservation in government employment, educational reservations, disability pension, free travel, welfare benefits, priority in social protection schemes.

Q13

Name the four domains of the Disability Assessment Schedule (DAS) used in mental illness certification.

1. Self-care
 2. Occupational functioning
 3. Family and social functioning
 4. Community participation
-

Q14

Name the five types of stigma.

1. Public stigma
2. Self-stigma
3. Structural stigma
4. Courtesy stigma
5. Provider stigma

Mnemonic: **PSSC-P**, "Psychiatry Still Struggles Changing Perceptions"

Q15

What does ISMI measure, how many items does it have, and name its five subscales?

ISMI = Internalized Stigma of Mental Illness scale

Measures: Self-stigma

Items: 29

Subscales: Alienation, Stereotype Endorsement, Discrimination Experience, Social Withdrawal, Stigma Resistance

Mnemonic: "**All Students Deserve Social Recognition**" → A, S, D, S, R

Q16

Rank anti-stigma strategies by strength of evidence.

1. **Contact-based** (strongest, sustained attitude change; in-person > video > social media)
2. **Education** (moderate, short-term knowledge change)
3. **Protest** (weakest, suppresses expression but doesn't change underlying attitudes)

Mnemonic: **PEC** (weakest to strongest: Protest → Education → Contact)

Q17

Name the five domains of the WHO CBR Matrix.

1. Health
2. Education
3. Livelihood
4. Social
5. Empowerment

Mnemonic: **HELSE** (Norwegian/Danish for "health")

Q18

What is Individual Placement and Support (IPS)? Give two evidence-based facts.

IPS = evidence-based supported employment model for people with severe mental illness.

Key features: Zero exclusion, direct competitive employment (no lengthy pre-vocational training), job coach support in real workplace, integrated with clinical care.

Evidence:

1. IPS produces competitive employment rates **2–3 times higher** than traditional vocational rehabilitation
 2. Cochrane reviews confirm superiority over standard vocational services
-

Q19

What are the four components of decision-making capacity?

1. **Understand** the relevant information
2. **Appreciate** how it applies to their own situation
3. **Reason** through options and consequences
4. **Communicate** a decision

Mnemonic: **UARC**

MHCA 2017: capacity is **presumed** for all adults; must demonstrate specific incapacity for a specific decision at a specific time.

Q20

Distinguish supported decision-making from substituted decision-making.

	SUPPORTED	SUBSTITUTED
Who decides	The person (with support)	Guardian/proxy
Legal basis	UNCRPD Article 12	Traditional guardianship
Standard	Person's own will/preferences	"Best interests"
MHCA 2017	Advance directives + nominated representative	Emergency involuntary provisions

Supported = UNCRPD-aligned, preferred. Substituted = older model, being phased out globally.

Q21

Name three rights of persons with mental illness under MHCA 2017.

Any three from: Access to mental health care, Community living, Protection from cruel/inhuman treatment, Equality and non-discrimination, Confidentiality, Advance directives, Nominated representative, Free legal aid, Right to personal records, Right to make complaints.

Full mnemonic: **FACE-CLARN** or **MHCA gives you the right to FACE CLAN**

Q22

What are the WHO 8 steps of Psychological First Aid?

1. Contact and engagement
2. Safety and comfort
3. Stabilization
4. Information gathering
5. Practical assistance
6. Connection with social supports
7. Information on coping
8. Linkage to collaborative services

Mnemonic: **CESSI-CPL** / "Can Every Scared Soul In Crisis Please Live?"

Q23

Why is universal Critical Incident Stress Debriefing (CISD) not recommended?

Three reasons:

1. **No RCT evidence** that CISD prevents PTSD when applied universally
2. **Possible harm**, forcing premature structured disclosure of trauma in groups may interfere with natural recovery or increase PTSD risk in some individuals
3. **PFA is superior** as an immediate, flexible, non-intrusive alternative

The Cochrane review of psychological debriefing found it no better than no intervention and potentially harmful.

Q24

Name the two-tier structure of Tele-MANAS.

- **Tier 1:** Trained counselors (non-specialist), supportive counseling, psychoeducation, triage
- **Tier 2:** Clinical psychologists and psychiatrists, complex cases, clinical management

NUMBER: 14416	AVAILABLE: 24x7	LAUNCHED: OCTOBER 2022

Integration: Links to eSanjeevani and DMHP for referral and follow-up.

Q25

What is the CAM (Confusion Assessment Method)? State the diagnostic criteria.

CAM = Confusion Assessment Method for delirium diagnosis. Sensitivity ~94–100%, Specificity ~90–95%.

Features:

- Feature 1: Acute onset + fluctuating course (**required**)
- Feature 2: Inattention (**required**)
- Feature 3: Disorganized thinking
- Feature 4: Altered level of consciousness

Diagnosis of delirium: Feature 1 + Feature 2 + (Feature 3 **OR** Feature 4)

Q26

What is the Werther effect and the Papageno effect in suicide prevention?

Werther effect: Media-driven suicide contagion, prominent, detailed, romanticized media coverage of a suicide increases copycat suicides in vulnerable individuals (named after

Goethe's novel whose publication was associated with copycat suicides).

Papageno effect: Protective effect of media stories showing people who overcame suicidal crisis, reduces suicide risk in readers / viewers. Named after the character in Mozart's Magic Flute who was talked out of suicide.

Clinical application: Media guidelines for suicide reporting aim to harness Papageno and suppress Werther.

Q27

Name five evidence-based means restriction interventions for suicide prevention.

1. **Coal gas detoxification** (UK 1960s), ~30% reduction in suicide rate
2. **Paracetamol pack-size restriction** (UK), significant reduction in paracetamol-related deaths
3. **Bridge barriers** (San Francisco Golden Gate, UK railway), prevention with minimal method substitution
4. **Pesticide restriction** (Sri Lanka, Bangladesh, India, Paraquat, endosulfan), major rural suicide reduction
5. **Firearm legislation** (Australia), reduced firearm suicide and mass shootings

Mnemonic: **COBRA**

Q28

State the stepped care principle and name the five steps for depression.

Principle: Match treatment intensity to severity. Start with least intensive effective intervention. Step up if no response in 6–8 weeks. Step down when stable.

Five steps:

1. Recognition + watchful waiting
2. Low-intensity CBT / guided self-help
3. High-intensity CBT / IPT / antidepressants
4. Multidisciplinary + crisis assessment
5. Inpatient / ECT consideration

Mnemonic: **RWSHC**

Q29

Name three gatekeeper training programmes with their duration.

PROGRAMME · DURATION

QPR (Question, Persuade, Refer) 1–2 hours

safeTALK 3–4 hours

ASIST (Applied Suicide Intervention Skills Training) 2 days

Mental Health First Aid 8 hours (1 day)

QPR steps: Q = Question (ask directly), P = Persuade (listen, offer support), R = Refer (connect to professional help).

Q30

Summarise the four principles of medical ethics and their main tension point in psychiatry.

PRINCIPLE · CORE MEANING

Autonomy Respect patient's right to make informed decisions

Beneficence Act in patient's best interest

Non-maleficence Avoid harm

Justice Fair resource distribution; equal treatment

Main tension in psychiatry: Autonomy vs Beneficence, involuntary treatment may be in the patient's best interest (beneficence) but overrides their right to refuse (autonomy).

MHCA 2017 attempts to resolve this by requiring both imminent danger AND incapacity before involuntary treatment, and mandating MHRB review.

Second tension: Justice, mental illness affects 10.6% of India's population but receives <1% of the health budget. This is a structural justice failure.

RAPID RECALL STRIP: Cut-and-keep facts

ITEM · ANSWER

NMHP launched 1982

DMHP piloted 1996, 27 districts

India psychiatrist density 0.3/100,000

WHO recommended 3/100,000

NMHS prevalence 10.6%

NMHS treatment gap 83.45%

Median DUP India ~5 years

mhGAP launched 2008

RPwD Act categories 21

Benchmark disability $\geq 40\%$

MHCA 2017 in force May 2018

ISMI items/subscales 29 items / 5 subscales

CBR domains 5 (HELSE)

IPS vs traditional employment 2–3× higher

Capacity components 4 (UARC)

PFA steps 8 (CESSI-CPL)

Tele-MANAS number 14416

Tele-MANAS launched October 2022

NSPS launched 2022

India suicide rate ~12–12.4 / 100,000

India suicides/year ~170,000–180,000

Strongest anti-stigma Contact-based

Strongest suicide prevention Means restriction

All names and case references fictitious. Quick review is a recall tool, verify clinical decisions against primary guidelines.

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