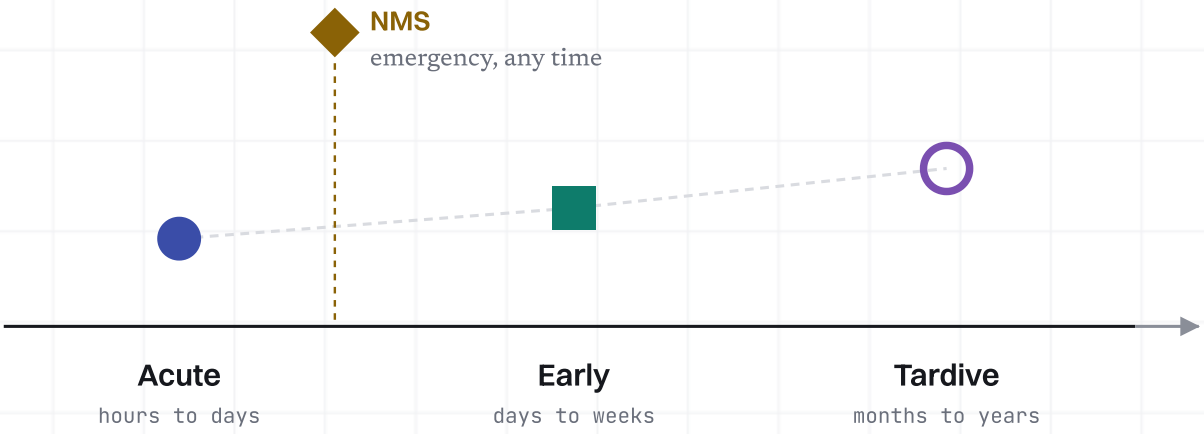


The Restless and the Rigid.

The drugs that quiet the mind can disturb the body, and they do it on a schedule. *Which movement disorder this is depends on what it looks like and when it started; what you do about it depends on getting one fork right.*

01 The two questions: what, and when

DEFINITIONAL

A patient on an antipsychotic is moving in a way they did not move before. The chart will call it extrapyramidal, a word that only means the motor trouble sits outside the pyramidal tract, in the basal ganglia, where blocking dopamine has consequences. The label settles nothing. Before reaching for an antidote, two questions decide almost everything: what does the movement look like, and when did it start. Get those two right and the disorder names itself; get the management fork that follows right, and you have done the harder half.

These movements are iatrogenic. They are the cost of dopamine blockade, and the clinician who prescribed the drug is the one placed to recognise and undo them. That is not a reproach; it is the reason vigilance is the whole skill. The same receptor blockade produces a family of disorders that differ mainly in their timing and their phenomenology, and the two axes below organise the rest of this issue.[1,54]

TWO AXES THAT SORT EVERY CASE

- **When: acute, early, or tardive.** Acute dystonia arrives within hours to days; akathisia and parkinsonism over days to weeks; the tardive syndromes only after months to years of exposure. The clock is the first discriminator, and it is why the same drug can cause a spasm in week one and a writhe in year three.
- **What: restless or rigid.** The hyperkinetic pole is restless, the dystonias, akathisia and dyskinesias that add movement. The hypokinetic pole is rigid, the parkinsonism and rabbit syndrome that take movement away. Most bedside confusion dissolves once the movement is placed on this axis.

THE CONCEPT CODES USED THROUGHOUT

BY ONSET ● Acute hours to days ■ Early days to weeks ○ Tardive months to years

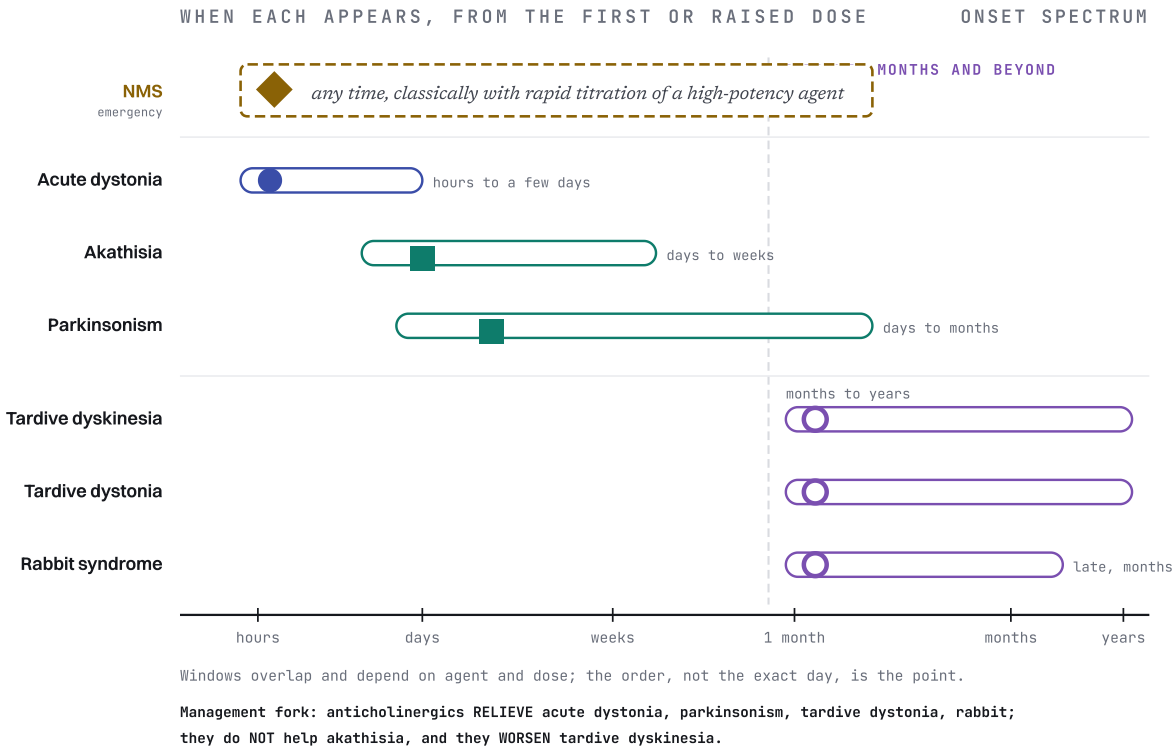
◆ Emergency NMS, any time

1 in 3 **The stakes of the acute reactions.** Up to a third of antipsychotic-naive, first-episode patients given haloperidol develop acute dystonia;[7] overall incidence with conventional neuroleptics is about 5%, much higher with high-potency agents and concentrated in young men.[6]

Each colour is also a shape, so the codes survive a greyscale photocopy. The timeline overleaf places every disorder on the onset axis at once; it is the map the rest of the issue fills in.

The single most useful thing to hold about extrapyramidal effects is that they appear on a schedule. The acute reactions cluster in the first days and weeks; the tardive ones only after prolonged exposure; and one entry on the map, neuroleptic malignant syndrome, is not on the spectrum at all but an emergency that can strike at any time, usually as the dose is pushed. Reading the figure left to right is reading the natural history of dopamine blockade.[1,54]

FIGURE 1 **When each appears, from the first or raised dose**



HOW TO READ THIS Scan left to right as elapsed time from the first or raised dose; each bar's colour and shape repeats the onset legend, and the order of the bars, not the exact day, is the teaching point.

WHAT THE SCHEDULE BUYS YOU

- **The clock narrows the differential before you touch the patient.** A spasm in the first week and a writhe in the third year are different problems on the same drug, and the onset alone rules half the list in or out.
- **The acute reactions are the reversible ones.** Dystonia, akathisia and parkinsonism settle when the drug is adjusted; the tardive syndromes are the ones that may not, which is why the right of the figure carries the weight and why prevention matters most there.
- **One entry ignores the schedule.** Neuroleptic malignant syndrome can arrive at any point on the line, so fever and rigidity are never filed under timing. They are filed under emergency, and they come off the antipsychotic at once.

A note on the word tardive: it means late, not permanent. But the tardive syndromes are the ones most likely to persist, which is why their place at the far right of this figure carries the most weight.

02 The whole differential, on one grid

THE MASTER TABLE

This is the table to remember. Each row is a disorder, coded by its onset class; the columns move from recognition to management in the order a clinician actually uses them. The bottom row is not an extrapyramidal effect at all but the emergency it is most often confused with, placed here because the first job at the bedside is to exclude it. The per-disorder sections that follow expand each row; the citations live there.

TABLE 1 **Extrapyramidal effects, side by side**

Disorder	ONSET	Key features	MECHANISM	RISK FACTORS	First management move
● **Acute dystonia** ACUTE	Hours to days	Sustained spasm: oculogyric crisis, torticollis, trismus, tongue. Laryngeal spasm is an airway emergency	Acute striatal D2 blockade; dopamine-acetylcholine imbalance	Young, male, high-potency FGA, naive, high dose	**Anticholinergic** IM (or promethazine); benzodiazepine
■ **Akathisia** EARLY	Days to weeks	Subjective inner restlessness with objective fidgeting; the anxiety and agitation mimic	Mesocortical dopamine plus noradrenergic; less D2-bound	High-potency, high dose; occurs with any agent	**Propranolol**; mirtazapine; reduce dose
■ **Parkinsonism** EARLY	Days to months	Bradykinesia, rigidity, often symmetric; postural tremor; masked face. The depression mimic	Striatal D2 occupancy above about 80%	Older, female, high potency and dose	**Reduce or switch**; anticholinergic or amantadine
○ **Tardive dyskinesia** TARDIVE	Months to years	Choreoathetoid orofacial, lingual and buccal movements; limbs and trunk	D2 receptor supersensitivity (leading hypothesis)	Older, FGA, longer or higher exposure, early EPS	**VMAT2 inhibitor**; withdraw anticholinergic; clozapine
○ **Tardive dystonia** TARDIVE	Months (prolonged)	Sustained twisting postures; axial, retrocollis, trunk. Persistent	Chronic D2 blockade; overlaps tardive dyskinesia	Younger, male, co-existing tardive dyskinesia	**Anticholinergic may help**; botulinum; clozapine
○ **Rabbit syndrome** TARDIVE	Months	Fine, rapid, rhythmic vertical perioral chewing at about 5 Hz; tongue spared	Drug-induced parkinsonism spectrum, not dyskinesia	Long-term typical antipsychotics	**Anticholinergic** (responds); reduce or switch
◆ **NMS** EMERGENCY	Any time	Fever, lead-pipe rigidity, altered consciousness, autonomic instability; raised CK	Acute massive central D2 blockade	Rapid or parenteral loading, high potency, dehydration, agitation	**Stop the drug**; supportive; dantrolene or bromocriptine

Read down the onset column and the figure on the previous page reappears; read across any row and you have the disorder. The single thread that ties the management column together is the anticholinergic decision, mapped in Figure 3.

QUICK CHECK

A young, antipsychotic-naive man develops a fixed upward deviation of the eyes 18 hours after his first haloperidol dose. Which row of the table, and what is the first move?

A Acute dystonia (onset hours to days; an oculogyric crisis): an intramuscular anticholinergic, fast, and protect the airway if the voice or breathing changes.[3,7]

03 Acute dystonia

HOURS TO DAYS

Acute dystonia is the earliest and most dramatic of the reactions: a sustained, involuntary muscle spasm that pulls the eyes, neck, jaw or tongue into a fixed abnormal posture. The classic forms are oculogyric crisis, torticollis or retrocollis, trismus and tongue protrusion, and at the extreme opisthotonus.[3] Onset is fast. The large majority occur within the first few days of starting or raising a high-potency agent, most within 48 to 72 hours.[1,2] The one presentation that must never be missed is laryngeal or pharyngeal dystonia, which can obstruct the airway, producing stridor and desaturation, and demands immediate reversal.[3,4]

Why it happens, and to whom. The mechanism is acute blockade of striatal D2 receptors, tipping the local balance toward a relative cholinergic excess; high-potency agents that bind D2 tightly carry the most risk, and the strong serotonergic blockade of the atypicals mitigates it.[5] The risk profile is one of the most stereotyped in psychiatry. Overall incidence with conventional neuroleptics is around 5%, much higher with butyrophenones than phenothiazines, and concentrated in young men.[6] In antipsychotic-naive, first-episode patients given haloperidol, up to a third develop dystonia.[7] Young age, male sex, high-potency first-generation agents, never having taken an antipsychotic, and a higher dose are the classic predictors.[8]

MANAGEMENT, IN ORDER

1. **Reverse it fast.** A parenteral anticholinergic relieves acute dystonia within minutes: in India, intramuscular promethazine is the common ward agent, with oral or parenteral trihexyphenidyl once the spasm is controlled; benztropine and biperiden are alternatives where stocked. A benzodiazepine is an effective second option.[1,3]

2. **Protect the airway first if the larynx is involved.** Stridor, dysphagia or voice change in a patient who has just started an antipsychotic is an emergency: secure the airway and give the anticholinergic at once.[3,4]

3. **Anticipate recurrence.** A single dose of antidote is shorter-acting than the antipsychotic, so continue oral anticholinergic cover for roughly 48 to 72 hours after the acute episode, or the spasm can return.[9]

4. **Prevent the next one.** In high-risk patients, young men started on high-potency agents, anticholinergic prophylaxis cuts incidence several-fold and is reasonable for about a week, after which it can usually be stopped; routine long-term prophylaxis is not recommended.[8,2]

A frightening reaction, but a reversible one. Telling the patient and family that explicitly is part of the treatment, because the fear of a recurrence is a common reason adherence collapses. The antidote here, the anticholinergic, is specific: it relieves dystonia and parkinsonism, but not akathisia, tardive dyskinesia or NMS.[10]

04 Akathisia

DAYS TO WEEKS

Akathisia is the most missed of the extrapyramidal effects, because its defining feature cannot be seen. It is a subjective inner restlessness, an unbearable urge to move, usually but not always accompanied by visible fidgeting, pacing and rocking; it is not diagnosed on observed movement alone. The Barnes Akathisia Rating Scale separates exactly these elements, the objective movements, the subjective awareness of restlessness, and the distress, and remains the standard instrument.[11] It is common: estimates run from about 14% to 35% of patients on antipsychotics, with one Barnes-scale cohort finding 19.5%, and the dose is an independent driver.[12,13]

The trap, and the harm. Because the core symptom is internal, akathisia is repeatedly misread as anxiety, agitation, or worsening psychosis. That error is not neutral: mistaking it for psychotic agitation prompts an increase in the antipsychotic, which worsens the akathisia, which looks like further agitation.[12] The condition also carries a real affective burden. It is associated with dysphoria, irritability and aggression, and with suicidal ideation.[12] The link to suicide should be held as an association of genuine concern rather than proven cause: the primary data are mixed, and at least one nested case-control study found no significant association with completed suicide.[14] The clinical instruction is the same either way, treat the akathisia, do not escalate the antipsychotic.

MANAGEMENT, IN ORDER

1. **Recognise it, by asking.** The highest-yield step is to ask directly about inner restlessness and use the Barnes scale, rather than waiting to see movement. Mechanistically akathisia is tied less to striatal D2 blockade than to mesocortical dopamine and a compensatory noradrenergic overactivity, which is why noradrenergic drugs work.[11,15]

2. **Beta-blockade first.** Low-dose propranolol, around 20 to 80 mg a day, significantly reduces akathisia within days in controlled trials; the effect is specific to beta-blockade.[16,17]

3. **Then mirtazapine, or a benzodiazepine.** Mirtazapine 15 mg a day is among the best-supported options, ranked highly in the 2024 network meta-analysis; benzodiazepines help where distress is prominent.[18,13]

4. **Reduce the dose or switch.** Dose is an independent driver, so lowering it or moving to a lower-liability agent treats the cause.[13]

The one move to avoid: reaching reflexively for an anticholinergic. Unlike in dystonia and parkinsonism, anticholinergics are not reliably effective for akathisia and add their own burden; reserve them for coexisting parkinsonism.[15] In Indian practice propranolol, clonazepam and mirtazapine are all cheap and available, so the evidence-based ladder is fully within reach.

05 Drug-induced parkinsonism

DAYS TO MONTHS

Drug-induced parkinsonism is the quiet one: bradykinesia, rigidity, a tremor and a masked face that develop over days to weeks, sometimes months, after starting or raising a dopamine-blocking drug.[19] It is the second commonest cause of parkinsonism in older people after Parkinson's disease itself, and in a thirty-year population study it accounted for about 12% of all incident parkinsonism, with a clear female predominance.[21,22] In an individual patient it can be clinically indistinguishable from idiopathic disease, but the differences are teachable: drug-induced parkinsonism is more often symmetric, its tremor is more often postural or action than a classic asymmetric rest tremor, and its tempo tracks the recent drug change. A normal dopamine-transporter scan, where available, settles it.[20]

The mechanism is a number. Parkinsonism is dose-dependent striatal D2 blockade made visible. Occupancy studies define a window: antipsychotic effect emerges around 65 to 70% striatal D2 occupancy, prolactin elevation higher, and extrapyramidal signs become significantly more likely once occupancy passes roughly 78 to 80%.[23,24] Clozapine, which sits low on that curve, carries the least risk. The practical message is that parkinsonism is often a sign the dose has climbed past the therapeutic window, not that another drug is needed.

THE MIMIC

When the side effect looks like the illness

The bradykinesia, masked facies and psychomotor slowing of drug-induced parkinsonism overlap closely with depression and with the negative symptoms of schizophrenia. Empirically, antipsychotic-induced akinesia accounts for much of the apparent link between extrapyramidal signs and low mood, so the motor side effect masquerades as affective flattening.[25] Reading these drug-induced negative symptoms as worsening primary illness invites the wrong move, escalating dopamine blockade rather than easing it. Before adding anything for apparent depression or negative symptoms in a patient on an antipsychotic, examine for rigidity and bradykinesia.

Management follows the mechanism: reduce the dose, or switch to a lower-potency or atypical agent, with anticholinergics or amantadine for symptomatic relief in persistent cases.[19,20] Most cases resolve once the drug is withdrawn, though full recovery can take months; in a minority, up to around 10%, the parkinsonism persists, and the drug is taken to have unmasked subclinical Parkinson's disease.[20]

06 Tardive dyskinesia

MONTHS TO YEARS

Tardive dyskinesia is the one that lasts. It is a persistent, potentially permanent disorder of insidious onset caused by chronic exposure to dopamine-blocking drugs, conventionally appearing after months to years.[26] The movements are rhythmic, repetitive, choreoathetoid, predominantly of the face, mouth and tongue, often spreading to the limbs and trunk; severity is rated with the Abnormal Involuntary Movement Scale (AIMS), which sums movements across seven body regions and is the standard endpoint in the pivotal trials.[30,31]

How common, and in whom. Annualised incidence is higher with first-generation antipsychotics than second: a meta-analysis of head-to-head trials found about 6.5% per year on first-generation arms against 2.6% on second-generation.[27] Pooled cross-sectional prevalence in antipsychotic-treated patients is around 25%, higher on current first-generation than second-generation treatment, and lower in Asian than Western cohorts, a point worth holding before quoting the global figure to an Indian audience.[28] The established risk factors are older age, longer and higher cumulative exposure, first-generation agents, early extrapyramidal effects, mood disorder, diabetes, and, importantly, anticholinergic co-treatment.[29]

Mechanism and prognosis. The leading hypothesis is post-synaptic D2 receptor supersensitivity from chronic blockade, though it is one of several incomplete explanations and the pathogenesis remains unsettled.[26] The prognosis is the reason tardive dyskinesia dominates the prevention conversation: it is often persistent, frequently does not remit even when the drug is stopped, and may transiently worsen on abrupt withdrawal.[26,29] Because it is so often irreversible, the governing principle is prevention, the lowest effective dose, a preference for lower-liability agents, and regular AIMS monitoring to catch it early.

The management of established tardive dyskinesia is its own page, because here the antidote logic of the acute reactions inverts: the anticholinergic that rescues a dystonia is a risk factor that worsens this one.

AT THE BEDSIDE

A 62-year-old on long-term haloperidol shows choreoathetoid lip and tongue movements, scored across the seven AIMS regions. She is also on trihexyphenidyl for an old dystonia. This is tardive dyskinesia, and that anticholinergic is now a risk factor, not a treatment: the first move is to taper it, not to add to it.[29,30]

6.5 vs 2.6% **Annualised tardive-dyskinesia incidence, per year.** First-generation antipsychotics against second-generation in head-to-head trials: the single strongest reason to prefer a lower-liability agent and the lowest effective dose.[27]

06 / cont. Treating the tardive syndromes

WITHDRAW, DEPLETE, AND THE TWO EXCEPTIONS

Two things have changed the management of tardive dyskinesia: the recognition that anticholinergics belong nowhere near it, and the arrival of the VMAT2 inhibitors. The American Academy of Neurology now grades the VMAT2 inhibitors valbenazine and deutetrabenazine as established and effective at the highest evidence level for tardive dyskinesia.[33]

BY STRENGTH OF EVIDENCE

1. **VMAT2 inhibitors first.** In the KINECT-3 trial, valbenazine 80 mg a day reduced the AIMS dyskinesia score by a mean of 3.2 against 0.1 for placebo.[30] Deutetrabenazine, in the ARM-TD and AIM-TD trials, gave reductions of about 3.0 to 3.3 in the active arms against roughly 1.4 to 1.6 for placebo.[31,32] These are the only treatments at the top evidence tier.[33]

2. **Withdraw the anticholinergic.** Anticholinergics are a recognised risk factor that can worsen tardive dyskinesia, not a treatment; the Cochrane review found no supportive evidence and recommended that withdrawal itself be evaluated as a benefit.[37,38]

3. **Then clonazepam and ginkgo biloba.** Both are graded probably effective: clonazepam reduced dyskinesia by about a third in a controlled crossover, though tolerance develops, and Ginkgo biloba extract EGb-761 at 240 mg a day gave a 51% response against 5% on placebo in a 157-patient trial.[34,35]

4. **Amantadine, and switching to clozapine.** Amantadine is possibly effective; clozapine, with its very low tardive liability, is widely used in practice though the switch evidence is thin.[36,39]

INDIA

What the shelf actually holds

The Western algorithm names the VMAT2 inhibitors first, but valbenazine and deutetrabenazine are effectively unavailable and unaffordable in routine Indian practice, reachable only by named-patient import at a cost out of reach for almost all patients. That shifts the practical weight onto the older options: clonazepam and Ginkgo biloba, both cheap and available, and tetrabenazine, the one dopamine-depleter that is marketed and affordable in India, as the realistic VMAT2-class choice. The single most actionable Indian-practice point is the cheapest: trihexyphenidyl is very commonly co-prescribed here, and because it worsens tardive dyskinesia, tapering it is often the first and least costly intervention.[33,38] The Indian Psychiatric Society schizophrenia guidelines anchor antipsychotic selection and side-effect monitoring for local practice.[55]

THE TWO TARDIVE EXCEPTIONS, WHERE THE ANTICHOLINERGIC HELPS

Tardive dystonia (sustained axial twisting, about 3% on long-term treatment) can, unlike classic tardive dyskinesia, respond to anticholinergics, which diminished it in 46% of the classic series; botulinum helps focal forms and clozapine is the antipsychotic of choice when one must continue.[40,41,42] **Rabbit syndrome** (fine 5 Hz perioral chewing with the tongue spared, the discriminator from oral tardive dyskinesia) belongs to the parkinsonism spectrum, not the dyskinesias, and responds to anticholinergic drugs.[43,44,45] Both are late, and both are helped by the very drug that worsens classic tardive dyskinesia.

07 NMS: the emergency that is not EPS

DO NOT MISS

Neuroleptic malignant syndrome is on this map only because it must be excluded first. It is a rare, life-threatening reaction to dopamine blockade, defined by a tetrad of hyperthermia, generalised lead-pipe rigidity, altered mental status and autonomic instability, and it must be considered in any patient on an antipsychotic who develops fever with a change in conscious level.[46,47] The supportive laboratory findings are a markedly raised creatine kinase, from sustained muscle rigidity, and leukocytosis; the international Delphi consensus set the critical CK threshold at four times the upper limit of normal.[48] It is rare, with an incidence of roughly 0.02 to 0.2% of exposed patients and a mortality near 6% that has fallen with earlier recognition.[49] Rapid or parenteral loading, high-potency agents, dehydration, agitation and a prior episode are the risk factors.[47]

ACT NOW

Suspected NMS

01 **Stop the antipsychotic immediately.** Cessation of the offending dopamine antagonist is the single most important step.[47]

02 **Support aggressively.** Intravenous fluids to protect the kidneys from rhabdomyolysis, active cooling, and monitoring at an intensive level.[53]

03 **Add specific agents in severe cases.** Dantrolene for the rigidity and hyperthermia, bromocriptine or another dopamine agonist to counter the blockade, benzodiazepines for agitation.[49,50]

04 **Reserve ECT** for cases refractory to drugs, and rechallenge only after a washout, with a lower-potency agent, slowly.[49,53]

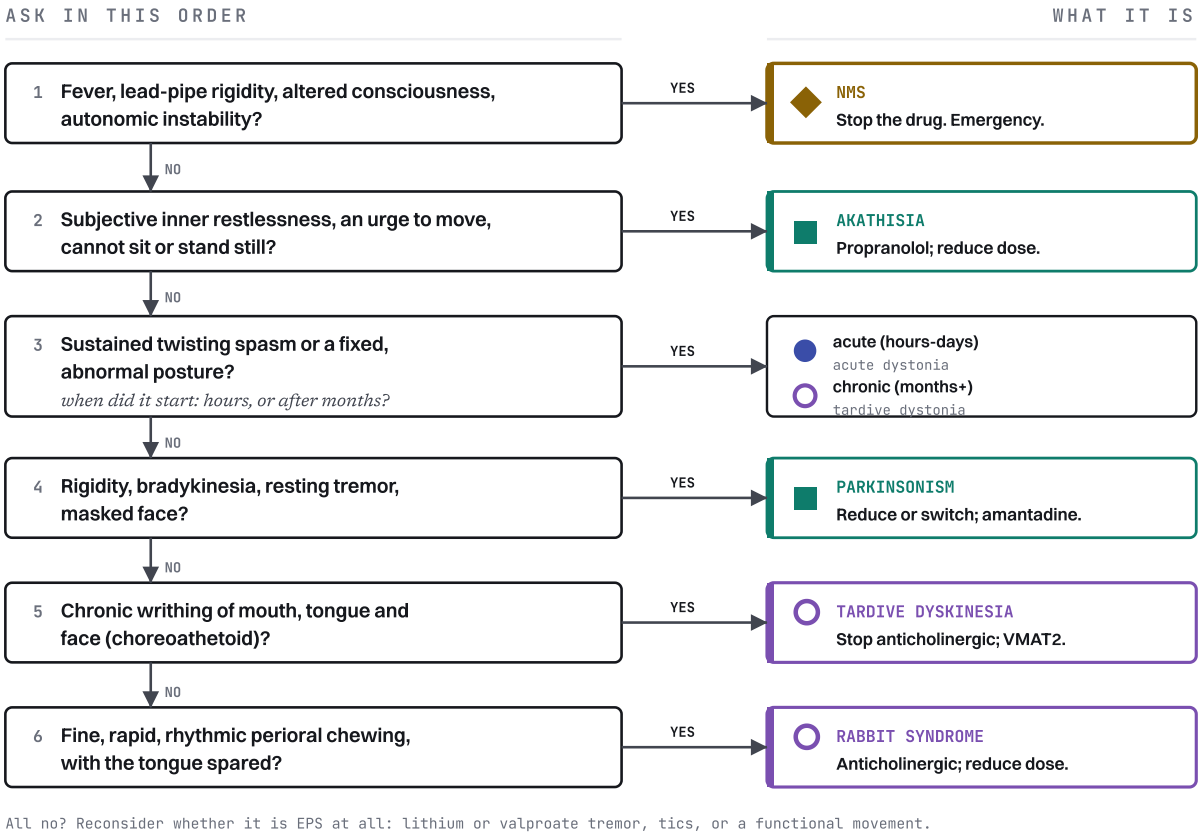
The other look-alike: serotonin syndrome. The syndrome most often confused with NMS is not an extrapyramidal effect either. Serotonin syndrome comes from excess serotonergic activity and produces neuromuscular hyperactivity, clonus and hyperreflexia, more pronounced in the legs, with autonomic instability and altered mental status; it is diagnosed by the Hunter criteria in a patient on a serotonergic drug.[51,52] The two discriminators are reflexes and time: NMS gives rigidity with hyporeflexia evolving over one to three days after a dopamine antagonist; serotonin syndrome gives clonus and hyperreflexia evolving over hours after a serotonergic agent.[50,51] The distinction is safety-critical because the antidotes are syndrome-specific, and giving a dopamine antagonist to a serotonin-syndrome patient makes things worse.[53]

08 How to act at the bedside

DIFFERENTIATE, THEN TREAT

With the disorders in hand, the bedside task is a short sequence: exclude the emergency, then sort the movement by what it is and when it began, then treat. The flow below runs the questions in the order that is safest, the emergency first, then the most-missed, then the rest. A single yes names the disorder and points to the first move.

FIGURE 2 **The bedside differentiation flow**



HOW TO READ THIS Ask the six questions top to bottom in this safety order, the emergency first and the most-missed second; the first YES names the disorder and its first move, and the colours and shapes repeat the onset legend.

QUICK CHECK

A patient on an antipsychotic has fever, lead-pipe rigidity and altered consciousness. Where does the flow send you, and what is the first move?

A Question one: this is NMS, not an extrapyramidal effect. Stop the antipsychotic at once and support; it is an emergency, not a movement to manage on the ward.[47]

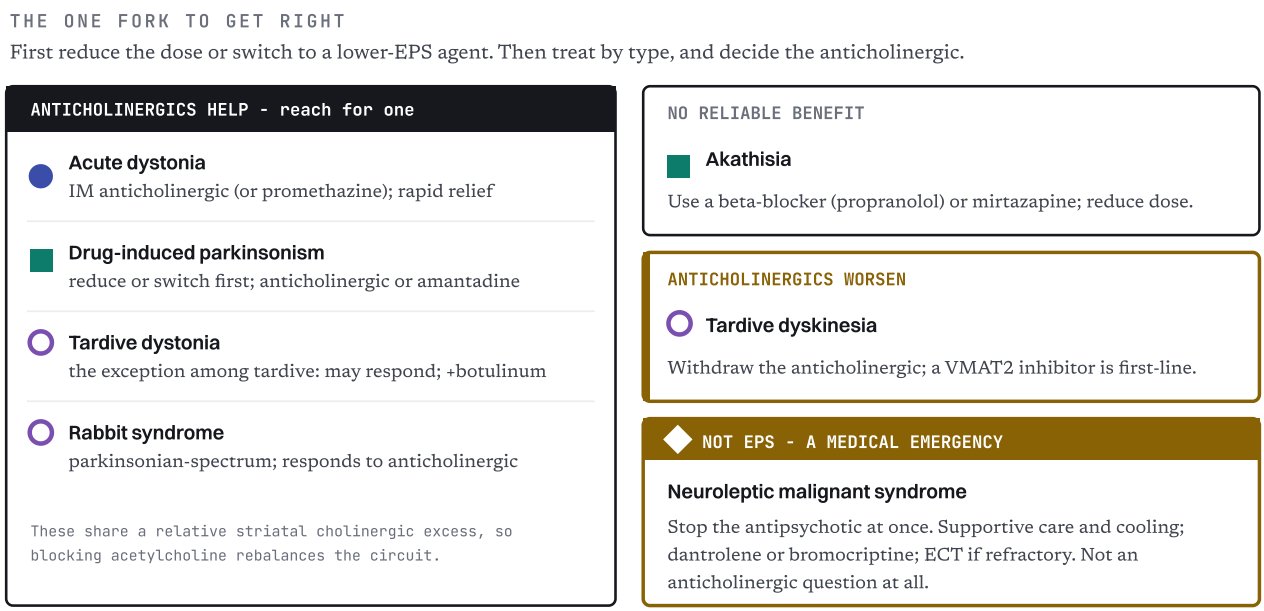
AT THE BEDSIDE

A man three weeks into risperidone paces the waiting room and says he cannot sit still; he has no fever and no posturing. Run the flow: question one, no; question two, yes. This is akathisia, the most-missed, and it wants propranolol and a lower dose, not the higher one that the restlessness invites.[12,16]

The fork, and the drugs

Once the disorder is named, management has a common opening, reduce the dose or switch to a lower-EPS agent, and then one decision that organises the rest: whether to give an anticholinergic, withhold it, or actively take it away. That fork is the correctness anchor of the whole topic, and the map below sorts every disorder by it.[1,10]

FIGURE 3 **The anticholinergic fork**



HOW TO READ THIS Three columns are the whole topic. Anticholinergics HELP on the left (the cholinergic-excess disorders), give no reliable benefit top-right (akathisia), or WORSEN lower-right (tardive dyskinesia); NMS sits apart, not an anticholinergic question at all.

TABLE 2 **The drugs, and when to reach for them**

Agent	Treats	Typical dose	Caution
Anticholinergic (trihexyphenidyl, promethazine)	Acute dystonia, parkinsonism, tardive dystonia, rabbit syndrome	THP 2 to 6 mg/day; promethazine 25 to 50 mg IM acutely	Worsens tardive dyskinesia; anticholinergic load in the elderly
Propranolol	Akathisia (first-line)	20 to 80 mg/day	Bradycardia, asthma, hypotension
Mirtazapine	Akathisia	15 mg/day	Sedation; well tolerated
Benzodiazepine (clonazepam)	Akathisia; tardive dyskinesia (probably effective)	0.5 to 2 mg/day	Tolerance, sedation, dependence
Amantadine	Parkinsonism; tardive dyskinesia (possibly)	100 to 300 mg/day	Renal dosing; insomnia
VMAT2 inhibitor (valbenazine, deutetrabenazine)	Tardive dyskinesia (highest evidence)	Valbenazine 40 to 80 mg/day	Largely unavailable and unaffordable in India
Tetrabenazine	Tardive dyskinesia and dystonia (depleter)	Titrated to effect	Available in India; depression, sedation
Dantrolene, bromocriptine	NMS (severe)	Per emergency protocol	Inpatient or intensive setting

08 / cont. What to examine, and with what

ASSESSMENT

Each disorder has an examination and, for several, a validated scale. The instruments matter for two reasons: they force the right examination, and they make change measurable across visits, which is how prevention turns into early detection. The one to use routinely is the AIMS, because tardive dyskinesia is the disorder where catching it early changes the outcome most.

TABLE 3 **Assessment by disorder**

Disorder	Instrument	What to examine
Acute dystonia	Bedside	Sustained spasm of eyes, neck, jaw, tongue; ask onset (hours to days) and the drug change; check the airway if the voice or breathing is affected
Akathisia	Barnes Akathisia Rating Scale	Ask about subjective inner restlessness first, the diagnostic core; rate objective movement and distress separately; do not rely on observed movement alone
Parkinsonism	Simpson-Angus Scale	Rigidity, bradykinesia and tremor; note symmetry and postural versus rest tremor; distinguish from depression and negative symptoms; a dopamine-transporter scan if it persists
Tardive dyskinesia	AIMS (items 1 to 7)	Orofacial, lingual, limb and trunk movements with activation manoeuvres; rate at baseline and periodically; the standard trial endpoint
Tardive dystonia	Burke-Fahn-Marsden scale	Sustained twisting postures, axial and retrocollis; note chronicity and prolonged exposure
Rabbit syndrome	Bedside	Fine, rapid, rhythmic vertical perioral movements at about 5 Hz, with the tongue spared, the discriminator from oral tardive dyskinesia
NMS	Vitals plus labs	Temperature, blood pressure, heart rate, conscious level; creatine kinase (four times the upper limit or more) and leukocytosis; apply the consensus criteria

QUICK CHECK

Which single scale should be used routinely, and why this one over the others?

A The AIMS, items 1 to 7. Tardive dyskinesia is the disorder where catching it early changes the outcome most, so serial AIMS is what turns prevention into early detection.[30]

HOLD THIS

The fork is the lesson

Almost everything in this issue reduces to one decision made well. Anticholinergics relieve acute dystonia and drug-induced parkinsonism, and they help the two odd tardive syndromes, tardive dystonia and rabbit syndrome. They do not reliably help akathisia, which wants a beta-blocker. And they worsen tardive dyskinesia, where they should be withdrawn, not added. Get the disorder right by what it looks like and when it began, then get the fork right, and the management follows.

09 Three ways to get it wrong

PITFALLS

Treating the wrong restlessness. The commonest and most damaging error is to read akathisia as agitation or psychotic relapse and respond by raising the antipsychotic. The dose increase deepens the akathisia, which looks like further agitation, and a loop is built that can end in real harm. The fix is a question, not a drug: ask the patient whether the restlessness is inside them. Inner restlessness on a recently started or raised antipsychotic is akathisia until proven otherwise, and it wants a beta-blocker and a lower dose, not a higher one.[12,15]

Giving the anticholinergic reflexively. The anticholinergic that rescues an acute dystonia is the wrong instinct for two of the disorders it is most often reached for. In akathisia it does not reliably work; in tardive dyskinesia it is a recognised risk factor that worsens the movements and should be tapered, not added.[15,38] The reflex matters most in India, where trihexyphenidyl is so routinely co-prescribed that quietly worsening tardive dyskinesia is a real and avoidable harm. Before continuing an anticholinergic, ask which disorder it is actually for.

Mistaking the side effect for the illness. Drug-induced parkinsonism wears the face of depression and of negative symptoms, the slowing, the flat affect, the reduced movement.[25] Reading it as worsening illness invites the wrong move, more dopamine blockade, when the cause is too much already. And the gravest version of this error is missing NMS: rigidity with fever and a rising creatine kinase in a patient on an antipsychotic is not an extrapyramidal effect to be managed on the ward but an emergency to be stopped and supported at once.[47,48]

~25% **Pooled prevalence of tardive dyskinesia** in antipsychotic-treated patients.[28] Anticholinergic co-treatment is a recognised aggravator, so the reflexive trihexyphenidyl that is so routine in India is a real and avoidable harm.[38]

THE THREAD

All three share one root

Each pitfall is the same mistake in a different costume: acting on what the movement resembles instead of what it is. Akathisia resembles agitation, parkinsonism resembles depression, and an undertreated dystonia resembles a difficult patient. Naming the disorder by its phenomenology and its timing, before reaching for a drug, is what prevents all three.

10 Before you treat

Extrapyramidal effects are iatrogenic, which is the good news: the clinician who can recognise them is the one who can undo them. Almost all of the skill is two judgements made in order, what the movement is, and what the anticholinergic should do about it.

WHAT THIS ISSUE COMES DOWN TO

1. **Read the movement and the clock.** What it looks like, restless or rigid, and when it started, acute, early or tardive, names almost every case. The onset spectrum is the spine: dystonia in hours, akathisia and parkinsonism in days to weeks, the tardive syndromes only after months.
2. **Exclude the emergency first.** Fever, lead-pipe rigidity, altered consciousness and a raised creatine kinase are NMS, not EPS. Stop the drug and support; the antidote logic of the others does not apply.
3. **Get the anticholinergic fork right.** It relieves acute dystonia and parkinsonism and helps tardive dystonia and rabbit syndrome; it does not reliably help akathisia, which wants propranolol; and it worsens tardive dyskinesia, where it should be withdrawn.
4. **Prevent what you cannot reverse.** Tardive dyskinesia is the one that lasts, so the lowest effective dose, lower-liability agents, and routine AIMS monitoring matter more than any treatment. Where the VMAT2 inhibitors are out of reach, withdrawing the anticholinergic and using clonazepam, ginkgo or tetrabenazine is the realistic path.

REMEMBER

ANTICHOLINERGIC · HELPS, NO, WORSENS

It HELPS where a cholinergic excess drives the movement (acute dystonia, parkinsonism, tardive dystonia, rabbit syndrome); gives NO reliable help in akathisia (reach for a beta-blocker); and WORSENS tardive dyskinesia (withdraw it). One fork, and the whole issue turns on it.

BEDSIDE CHECK

A patient on an antipsychotic is moving abnormally

01 Fever, rigidity, altered consciousness, autonomic instability? Treat as NMS: stop the drug and support, do not give an anticholinergic.

02 Is the restlessness subjective, an inner urge to move? That is akathisia: propranolol and a lower dose, not a higher one, and not an anticholinergic.

03 When did it start, hours or months? Hours to days favours acute dystonia; months to years favours a tardive syndrome.

04 Is the movement a twisting posture, a parkinsonian slowing, or a choreoathetoid writhe? Each points to a different disorder, and a different first move.

05 If I am about to give an anticholinergic, which disorder is it for? It helps dystonia and parkinsonism, but worsens tardive dyskinesia.

R References

ALL PUBMED-VERIFIED

1 Holloman LC, Marder SR. Management of acute extrapyramidal effects induced by antipsychotic drugs. Am J Health Syst Pharm. 1997. PMID 9359953

2 Boyer WF, Bakalar NH, Lake CR. Anticholinergic prophylaxis of acute haloperidol-induced acute dystonic reactions. J Clin Psychopharmacol. 1987. PMID 3597801

3 Christodoulou C, Kalaitzi C. Antipsychotic drug-induced acute laryngeal dystonia: two case reports and a mini review. J Psychopharmacol. 2005. PMID 15888517

4 Yaginuma K, et al. Haloperidol-induced dystonia due to sedation for upper gastrointestinal endoscopy: a pediatric case report. Case Rep Emerg Med. 2019. PMID 31032123

5 Pierre JM. Extrapyramidal symptoms with atypical antipsychotics: incidence, prevention and management. Drug Saf. 2005. PMID 15733025

6 Spina E, et al. Prevalence of acute dystonic reactions associated with neuroleptic treatment with and without anticholinergic prophylaxis. Int Clin Psychopharmacol. 1993. PMID 8097213

7 Aguilar EJ, et al. Predictors of acute dystonia in first-episode psychotic patients. Am J Psychiatry. 1994. PMID 7977894

8 Arana GW, et al. Efficacy of anticholinergic prophylaxis for neuroleptic-induced acute dystonia. Am J Psychiatry. 1988. PMID 2899403

9 Corre KA, Niemann JT, Bessen HA. Extended therapy for acute dystonic reactions. Ann Emerg Med. 1984. PMID 6696308

10 Vanegas-Arroyave N, et al. An evidence-based update on anticholinergic use for drug-induced movement disorders. CNS Drugs. 2024. PMID 38502289

11 Barnes TR. A rating scale for drug-induced akathisia. Br J Psychiatry. 1989. PMID 2574607

12 Jouini L, et al. Akathisia: prevalence and associated clinical features in patients with chronic psychosis. Clin Neuropharmacol. 2022. PMID 35696611

13 Gerolymos C, et al. Drug efficacy in the treatment of antipsychotic-induced akathisia: a systematic review and network meta-analysis. JAMA Netw Open. 2024. PMID 38451521

14 Reutfors J, et al. Antipsychotic drug use and risk of suicide: a nested case-control study. Hum Psychopharmacol. 2016. PMID 27108775

15 Musco S, McAllister V, Caudle I. Dopamine-receptor blocking agent effects: managing antipsychotic-induced akathisia. Ther Adv Psychopharmacol. 2020. PMID 32922732

16 Adler LA, Peselow E, Rosenthal M, Angrist B. A controlled comparison of the effects of propranolol, benztropine, and placebo on akathisia. Psychopharmacol Bull. 1993. PMID 8290678

17 Dumon JP, et al. Randomized, double-blind, crossover, placebo-controlled comparison of propranolol and betaxolol in the treatment of neuroleptic-induced akathisia. Am J Psychiatry. 1992. PMID 1349458

18 Poyurovsky M, et al. Low-dose mirtazapine: a new option in the treatment of antipsychotic-induced akathisia. J Clin Psychopharmacol. 2003. PMID 12826992

19 Conn H, Jankovic J. Drug-induced parkinsonism. Expert Opin Drug Saf. 2024. PMID 39419777

20 Lopez-Sendon JL, Mena MA, de Yebenes JG. Drug-induced parkinsonism. Drugs Aging. 2012. PMID 22250585

21 Thanvi B, Treadwell S. Drug induced parkinsonism: a common cause of parkinsonism in older people. Postgrad Med J. 2009. PMID 19528308

22 Savica R, et al. Incidence and time trends of drug-induced parkinsonism: a 30-year population-based study. Mov Disord. 2017. PMID 27779780

23 Kapur S, Zipursky R, Jones C, Remington G, Houle S. Relationship between dopamine D2 occupancy, clinical response, and side effects: a double-blind PET study of first-episode schizophrenia. Am J Psychiatry. 2000. PMID 10739409

24 Farde L, et al. Positron emission tomographic analysis of central D1 and D2 dopamine receptor occupancy in patients treated with classical neuroleptics and clozapine. Arch Gen Psychiatry. 1992. PMID 1352677

25 Muller MJ, Kienzle B, Dahmen N. Depression, emotional blunting, and akinesia in schizophrenia: overlap and differentiation. Eur J Health Econ. 2002. PMID 15609162

26 Frei K. Tardive dyskinesia: who gets it and why. Parkinsonism Relat Disord. 2018. PMID 30522959

27 Carbon M, et al. Tardive dyskinesia risk with first- and second-generation antipsychotics in comparative randomized controlled trials: a meta-analysis. World Psychiatry. 2018. PMID 30192088

28 Carbon M, et al. Tardive dyskinesia prevalence in the period of second-generation antipsychotic use: a meta-analysis. J Clin Psychiatry. 2017. PMID 28146614

29 Solmi M, et al. Clinical risk factors for the development of tardive dyskinesia: a systematic review and meta-analysis. J Neurol Sci. 2018. PMID 29439776

30 Hauser RA, et al. KINECT 3: a phase 3 randomized, double-blind, placebo-controlled trial of valbenazine for tardive dyskinesia. Am J Psychiatry. 2017. PMID 28320223

31 Fernandez HH, et al. Randomized controlled trial of deutetrabenazine for tardive dyskinesia: the ARM-TD study. Neurology. 2017. PMID 28446646

32 Anderson KE, et al. Deutetrabenazine for treatment of involuntary movements in patients with tardive dyskinesia (AIM-TD): a double-blind, randomised, placebo-controlled trial. Lancet Psychiatry. 2017. PMID 28668671

33 Bhidayasiri R, Jitkritsadakul O, Friedman JH, Fahn S. Updating the recommendations for treatment of tardive syndromes: a systematic review of new evidence and practical treatment algorithm. J Neurol Sci. 2018. PMID 29454493

34 Thaker GK, et al. Clonazepam treatment of tardive dyskinesia: a practical GABAmimetic strategy. Am J Psychiatry. 1990. PMID 1969244

35 Zhang WF, et al. Extract of Ginkgo biloba treatment for tardive dyskinesia in schizophrenia: a randomized, double-blind, placebo-controlled trial. J Clin Psychiatry. 2010. PMID 20868638

36 Pappa S, et al. Effects of amantadine on tardive dyskinesia: a randomized, double-blind, placebo-controlled study. Clin Neuropharmacol. 2010. PMID 21121175

37 Bergman H, Soares-Weiser K. Anticholinergic medication for antipsychotic-induced tardive dyskinesia. Cochrane Database Syst Rev. 2018. PMID 29341071

38 Desmarais JE, et al. Anticholinergics in the era of atypical antipsychotics: short-term or long-term harm? Ther Adv Psychopharmacol. 2014. PMID 25489477

39 Takeuchi H, Mori Y, Tsutsumi Y. Pathophysiology, prognosis and treatment of tardive dyskinesia. Ther Adv Psychopharmacol. 2022. PMID 36312846

40 van Harten PN, Kahn RS. Tardive dystonia. Schizophr Bull. 1999. PMID 10667744

41 Kang UJ, Burke RE, Fahn S. Natural history and treatment of tardive dystonia. Mov Disord. 1986. PMID 2904118

42 Ricciardi L, et al. Treatment recommendations for tardive dyskinesia. Can J Psychiatry. 2019. PMID 30791698

43 Schwartz M, Hocherman S. Antipsychotic-induced rabbit syndrome: epidemiology, management and pathophysiology. CNS Drugs. 2004. PMID 15015902

44 Rissardo JP, et al. A systematic review of antipsychotic-induced rabbit syndrome. Medicina (Kaunas). 2024. PMID 39202628

45 Yassa R, Lal S. Prevalence of the rabbit syndrome. Am J Psychiatry. 1986. PMID 2870650

46 Berman BD. Neuroleptic malignant syndrome: a review for neurohospitalists. Neurohospitalist. 2011. PMID 23983836

47 Caroff SN, Mann SC. Neuroleptic malignant syndrome. Med Clin North Am. 1993. PMID 8093494

48 Gurrera RJ, et al. An international consensus study of neuroleptic malignant syndrome diagnostic criteria using the Delphi method. J Clin Psychiatry. 2011. PMID 21733489

49 Pileggi DJ, Cook AM. Neuroleptic malignant syndrome. Ann Pharmacother. 2016. PMID 27423483

50 Perry PJ, Wilborn CA. Serotonin syndrome vs neuroleptic malignant syndrome: a contrast of causes, diagnoses, and management. Ann Clin Psychiatry. 2012. PMID 22563571

51 Boyer EW, Shannon M. The serotonin syndrome. N Engl J Med. 2005. PMID 15784664

52 Isbister GK, Buckley NA, Whyte IM. Serotonin toxicity: a practical approach to diagnosis and treatment. Med J Aust. 2007. PMID 17874986

53 Katus LE, Frucht SJ. Management of serotonin syndrome and neuroleptic malignant syndrome. Curr Treat Options Neurol. 2016. PMID 27469512

54 Bhidayasiri R, et al. Evidence-based guideline: treatment of tardive syndromes: report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. 2013. PMID 23897874

55 Grover S, Chakrabarti S, Kulhara P, Avasthi A. Clinical practice guidelines for the management of schizophrenia. Indian J Psychiatry. 2017. PMID 28216783

India availability and pricing details (trihexyphenidyl and propranolol ubiquity; the practical unavailability and unaffordability of valbenazine and deutetrabenazine; tetrabenazine availability) are drawn from current Indian pharmacy market listings, not from PubMed, and are stated as market fact rather than cited evidence. Antipsychotic formulations are covered in Aporia 07; treatment resistance, including clozapine, in Aporia 08.

Educational note. This clinical-reasoning essay is for clinicians and students. It is educational, not treatment advice for any individual. Care decisions belong with the treating clinician. At Weave, care is led by Dr. Niharika Reddy, Consultant Psychiatrist.

CRISIS SUPPORT

Tele-MANAS 14416, 1800-891-4416 (24x7, Government of India)

Emergency 112

iCall 9152987821 (Mon-Sat, 10am-8pm; hours may vary)

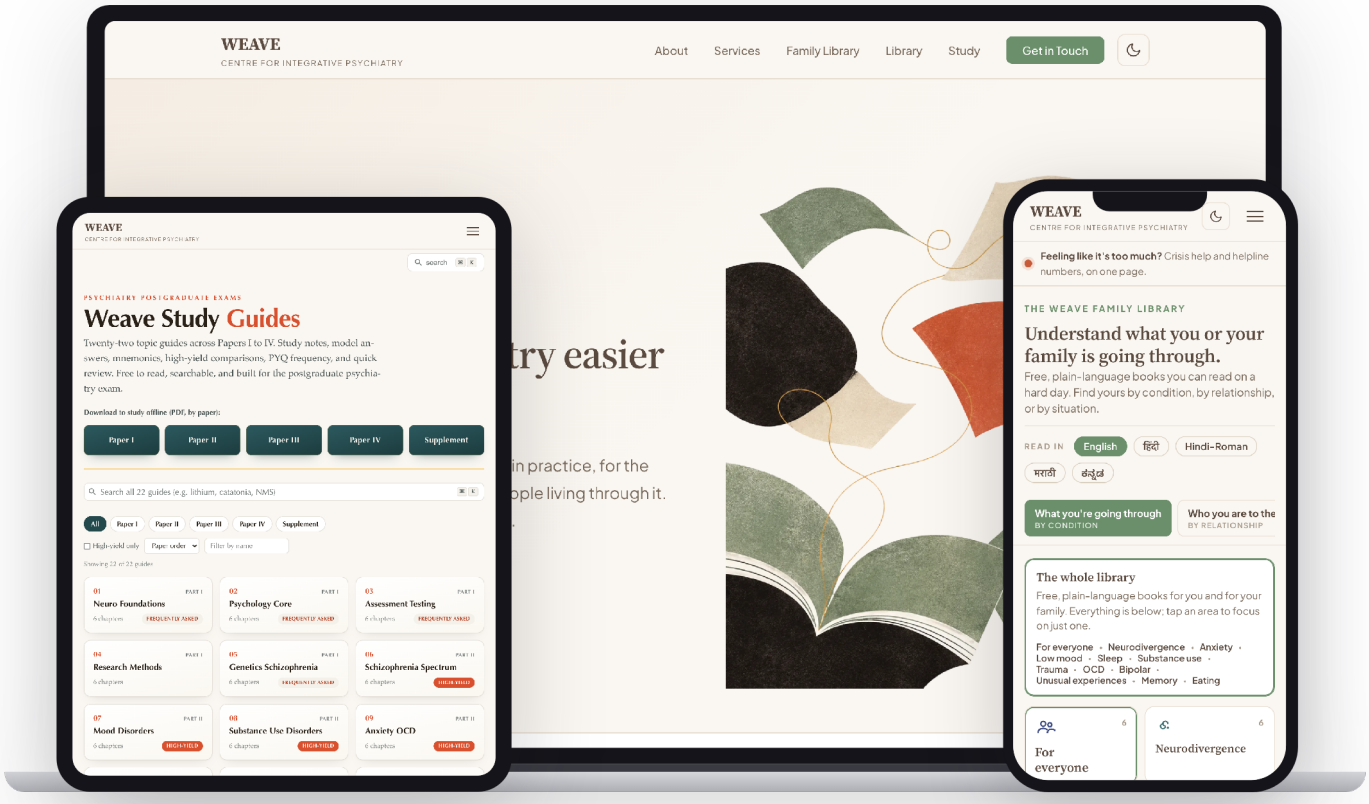
Vandrevala Foundation 1860-2662-345 (24x7)

AASRA 9820466726 (24x7)

CROSS-PROMOTION

More from Weave

Four free destinations for clinicians, students and families. Scan any code to open.



/library

Clinical field guides and references, most free to read and download.

/study

Postgraduate exam study guides across Papers I to IV.

/family

Plain-language books in English, Hindi, Hinglish, Marathi, Kannada.

/revision

A Paper a Day: the whole written exam in one free book.

weave.clinic · /library · /study · /family · /revision · study group · @doc.wilfred.md · @doc.niharika.md

WEAVE

CENTRE FOR INTEGRATIVE PSYCHIATRY

weave.clinic

wilfred@weave.clinic · niharika@weave.clinic

@doc.wilfred.md · @doc.niharika.md

Dr. Wilfred D'souza · Dr. Niharika Reddy