Tardive Dyskinesia

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Cause / differential	Clinical clues	Suggested investigations	Clinical pitfalls
Tardive dyskinesia from DRBAs — antipsychotics, metoclopramide and other dopamine-blocking antiemetics	Delayed onset after months–years of exposure; stereotyped **oro-bucco-lingual** movements, chewing, tongue protrusion, facial grimacing; limb/truncal choreiform or stereotypic movements	**Medication history is the key investigation**: current + previous antipsychotics/antiemetics, dose, duration, withdrawals. Document phenomenology with **AIMS** and ideally video	Missing remote exposure; assuming second-generation antipsychotics cannot cause TD; overlooking metoclopramide/prochlorperazine exposure. TD may first become obvious after dose reduction/withdrawal because DRBA treatment can suppress its appearance.
Tardive dystonia	Sustained twisting/posturing; retrocollis, axial extension, cranial dystonia; may coexist with classic TD	Examination defining dystonic vs choreiform phenomenology; medication history	Calling all tardive syndromes “TD.” This matters because treatment strategy and botulinum-toxin suitability differ
Tardive akathisia / stereotypy	Inner restlessness with repetitive pacing/rocking vs purposeless repetitive movements	Clinical observation; ask specifically about subjective restlessness	Akathisia may be mislabelled as agitation/anxiety or TD
Drug-induced parkinsonism (DIP)	Bradykinesia, rigidity, reduced arm swing, relatively rhythmic tremor; often temporally closer to DRBA initiation/dose escalation	Neurological exam; medication chronology. Dopaminergic imaging only if genuine diagnostic uncertainty with degenerative parkinsonism	**Treatments move in opposite directions:** anticholinergics may improve DIP but can worsen TD. TD and DIP can coexist
Idiopathic Parkinson disease / Lewy-body disease	Asymmetric bradykinesia/rigidity, rest tremor, non-motor prodrome; dyskinesias usually related to dopaminergic therapy	Movement-disorder exam; DAT imaging selectively if diagnosis remains unclear	Attributing parkinsonism to antipsychotic treatment without recognising unmasked neurodegeneration
Levodopa-induced dyskinesia	Established PD and temporal relationship to levodopa peaks/dose cycle	Medication–movement diary; observe ON/OFF relationship	Can look choreiform, but drug chronology is completely different
Huntington disease	Progressive generalized chorea, behavioural/cognitive change, family history; typically no necessary DRBA relationship	**HTT genetic testing** with appropriate counselling if phenotype suggests HD; neuroimaging supportive	Antipsychotic exposure is common in HD and can falsely anchor the clinician on TD
Other inherited choreas — Wilson disease, benign hereditary chorea/NKX2-1, neuroacanthocytosis, spinocerebellar disorders, etc.	Younger onset, family history, systemic or neurological features	Guided genetic/metabolic work-up	Broad genetic panels are low yield without phenotype-directed evaluation
Wilson disease	Younger patient; dystonia, tremor, dysarthria, psychiatric/hepatic features	Ceruloplasmin, serum/24-h urinary copper, slit-lamp examination ± genetics/hepatology evaluation	Must not miss in a younger patient with unexplained movement disorder; serum ceruloplasmin alone is not definitive

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Autoimmune / paraneoplastic chorea	Subacute onset; encephalopathy, psychiatric change, seizures, autonomic/systemic features	MRI brain, CSF, autoimmune/paraneoplastic testing guided by phenotype; malignancy search where appropriate	Extensive antibody panels in a chronic stable stereotypy have poor pre-test probability
Structural basal-ganglia lesion — stroke, tumour, demyelination, hypoxic injury	Acute/subacute onset, hemichorea, focal neurological findings	**MRI brain**	Routine imaging is usually unnecessary in archetypal TD, but unilateral or abrupt-onset movements should trigger imaging
Metabolic/endocrine chorea — hyperthyroidism, hyperglycaemia, electrolyte disturbance, hepatic/renal disease	Acute/subacute onset or systemic illness	Glucose/HbA1c, electrolytes/Ca/Mg, renal/liver function, **TSH** ± other tests according to context	Overlooking hyperglycaemic hemichorea or thyrotoxicosis in an apparently “psychiatric” presentation
Systemic autoimmune disease — SLE/APS	Chorea plus thrombotic, obstetric, rheumatological or multisystem history	ANA/ENA, complements, antiphospholipid antibodies if clinically indicated	Low-specificity serology should not be sent indiscriminately
Functional movement disorder	Inconsistency, distractibility, variability, incongruent phenomenology; positive functional signs	Diagnosis from positive clinical features; targeted testing only to exclude credible organic alternatives	Functional disorder and organic TD can coexist; avoid diagnosing purely because investigations are normal
Tics / Tourette syndrome	Premonitory urge, suppressibility, stereotyped motor/vocal tics; usually earlier onset	History and examination	Orofacial tics can closely resemble TD; ask specifically about urge and suppressibility
Edentulous / spontaneous orofacial dyskinesia	Older age, poor dentition/dentures, predominantly oral movements without DRBA exposure	Dental/oral examination; verify medication history	Spontaneous dyskinesias occur in older adults, so **movement phenomenology alone does not prove TD**
Seizure / epilepsia partialis continua	Paroxysmal, stereotyped, episodic movements ± altered awareness	EEG when clinically plausible	Routine EEG is not indicated for chronic classic dyskinesia

Practical investigation set

Stage	What I would do
1. Establish phenomenology	Observe at rest and with activation/distraction; assess face, tongue, jaw, trunk and limbs; distinguish chorea, stereotypy, dystonia, akathisia, tremor and myoclonus
2. Reconstruct drug exposure	Pharmacy/GP/psychiatric records where necessary: antipsychotics, **metoclopramide**, prochlorperazine and other DRBAs; include drugs stopped months or years earlier
3. Quantify	Baseline **AIMS** and longitudinal reassessment; video can be invaluable for progression and treatment response.
4. Minimal laboratory screen if atypical	FBC, electrolytes/Ca/Mg, renal/liver function, glucose/HbA1c, TSH; further tests phenotype-driven
5. MRI brain	Acute/subacute onset, unilateral/markedly asymmetric syndrome, focal neurology, rapid progression or absent convincing DRBA exposure
6. Specialist testing	Wilson work-up in appropriate age/phenotype; HTT testing for suspected Huntington disease; CSF/autoimmune/genetic investigations only when supported by history/examination

High-yield clinical pitfalls

- **The medication chronology is often more diagnostic than any investigation.** A convincing history of DRBA exposure plus compatible delayed-onset movements is central to diagnosis.
- **Do not equate every movement occurring during antipsychotic therapy with TD.** DIP, akathisia, acute dystonia and underlying neurological disease are common alternatives.
- **Do not exclude TD because the offending drug has been discontinued.** Symptoms may persist and can become more apparent following dose reduction or withdrawal.
- **Anticholinergics are a particular trap:** useful for some parkinsonian/dystonic adverse effects but can exacerbate classical TD.
- **DRBA escalation can temporarily mask TD**, creating the false impression that increasing the antipsychotic has “treated” it.
- **AIMS is a severity/monitoring instrument, not a stand-alone diagnostic test.** The diagnosis still depends on history, examination and exclusion of plausible mimics.
- Red flags against straightforward TD include **rapid progression, altered cognition, seizures, focal/asymmetric findings, marked weakness/sensory signs, systemic illness, or no credible DRBA exposure**.

The most useful bedside distinction is often **TD versus drug-induced parkinsonism**: TD tends toward irregular choreiform/stereotypic oro-lingual and limb movements, whereas DIP is dominated by bradykinesia/rigidity ± rhythmic tremor; critically, both can occur simultaneously.

Well-established dopamine receptor–blocking agents (DRBAs).

Chronic DRBA exposure is the classic pharmacological association with tardive syndromes.

Drug / class	Typical use	DRBA relevance	TD / tardive-syndrome relevance	Clinical pearl
Haloperidol	Antipsychotic	Potent **D2 antagonist**	**Very well established**	High-potency first-generation antipsychotic; classic drug to identify in TD history. EMA documentation specifically recognizes tardive dyskinesia among extrapyramidal risks.
Fluphenazine	Antipsychotic	Potent D2 antagonist	**Very well established**	Depot formulations mean exposure can be prolonged and may be forgotten
Trifluoperazine	Antipsychotic	Potent D2 antagonist	**Very well established**	Ask about historical treatment for psychosis/agitation
Pimozide	Antipsychotic / tic disorders	Potent D2 antagonist	**Well established**	Older use in tic disorders can be an overlooked exposure
Chlorpromazine	Antipsychotic/antiemetic	D2 antagonist	**Very well established**	Lower-potency FGA does **not** mean negligible TD risk
Thioridazine	Historical antipsychotic	D2 antagonist	**Very well established**	Now uncommon, but relevant in older patients with remote exposure
Perphenazine	Antipsychotic	D2 antagonist	**Well established**	Also historically used in combination preparations
Flupentixol	Antipsychotic	D2 antagonist	**Well established**	Depot exposure important, especially in long psychiatric histories
Zuclopenthixol	Antipsychotic	D2 antagonist	**Well established**	Consider both oral and depot formulations
Sulpiride	Antipsychotic	Selective D2/D3 antagonist	**Well established**	Can also have been prescribed for non-psychotic indications in some jurisdictions
Amisulpride	Antipsychotic	D2/D3 antagonist	**Well established**	Often perceived as “atypical,” but remains a DRBA
Risperidone	Second-generation antipsychotic	Strong D2 antagonism	**Well established**	Among SGAs, clinically important EPS/TD exposure; do not dismiss because it is “atypical”
Paliperidone	Second-generation antipsychotic	D2 antagonist	**Well established**	Active metabolite of risperidone; include oral and depot formulations
Olanzapine	Second-generation antipsychotic	D2 + broader receptor antagonism	**Established**	Lower average TD risk than older FGAs, but certainly capable of causing TD
Quetiapine	Second-generation antipsychotic	Relatively weaker/transient D2 occupancy	**Established, lower relative propensity**	A previous switch *to* quetiapine does not negate earlier DRBA exposure
Clozapine	Second-generation antipsychotic	Relatively weak D2 blockade; broader pharmacology	**Low TD propensity but still a DRBA-spectrum antipsychotic**	Often used when TD coexists with psychosis; existing dyskinesia may reflect **prior** antipsychotics rather than clozapine itself

Drug / class	Typical use	DRBA relevance	TD / tardive-syndrome relevance	Clinical pearl
Aripiprazole	Third-generation antipsychotic	**D2 partial agonist**, rather than pure antagonist	**Can be associated with tardive syndromes**	Pharmacologically different from classical DRBAs; avoid assuming partial agonism eliminates TD risk
Brexpiprazole	Antipsychotic	D2 partial agonist	Tardive syndrome possible	Same conceptual caveat as aripiprazole
Cariprazine	Antipsychotic	D3>D2 partial agonist	Tardive syndrome possible	Not a classical antagonist, but clinically belongs in antipsychotic exposure history
Metoclopramide	Antiemetic/prokinetic	**Central D2 antagonist**	**Very well established**	The major **non-psychiatric DRBA to actively search for**. FDA labeling specifically warns that it can cause TD and describes it as a D2 antagonist.
Prochlorperazine	Antiemetic / phenothiazine	D2 antagonist	**Well established**	Frequently overlooked because patient remembers it only as an “anti-nausea tablet”
Promethazine	Antihistamine/antiemetic	Some dopamine antagonism in addition to H1 effects	Less prominent than metoclopramide/prochlorperazine	Do not give it the same evidential weighting as a potent DRBA
Droperidol	Antiemetic / perioperative	Potent D2 antagonist	**Established DRBA**	Usually episodic exposure; prolonged/repeated exposure is more relevant than a single perioperative dose
Domperidone	Antiemetic/prokinetic	**Peripheral D2 antagonist** with limited CNS penetration	Much weaker association with TD	It is pharmacologically a D2 antagonist, but limited blood–brain barrier penetration makes it quite different from metoclopramide for tardive risk. EMA describes domperidone as a D2 antagonist.

Priority	Ask specifically about
Highest-yield psychiatric exposures	**Haloperidol, chlorpromazine, fluphenazine, trifluoperazine, risperidone/paliperidone, olanzapine, amisulpride/sulpiride, depot antipsychotics**
Highest-yield non-psychiatric exposure	**Metoclopramide**
Often forgotten antiemetic exposure	**Prochlorperazine**, droperidol
Important historical exposure	Any antipsychotic taken **years previously**, including depot preparations
Don’t falsely exclude	SGAs and D2 partial agonists—TD risk is generally lower than with potent FGAs but **not zero**