DRUG

Drug-Induced Vestibular Toxicity & Ataxia — Cheat Sheet for Vestibular Physicians

Take a drug history in every unexplained imbalance, and test the vestibular system — not just hearing — in everyone on aminoglycosides or cisplatin.

► Why drug-induced toxicity matters

A common, under-recognised and largely PREVENTABLE cause of progressive imbalance. Two targets: peripheral vestibulotoxicity (aminoglycosides, cisplatin, loop diuretics) and central drug-induced ataxia (antiepileptics, lithium, metronidazole, cytarabine, alcohol). Highest-risk groups: ICU aminoglycosides, platinum oncology, long-term phenytoin. The temporal link to the drug IS the diagnosis — and it is the thing most often missed.

Indications — when this work-up applies

- New bilateral imbalance, oscillopsia, or gait ataxia after exposure to an ototoxic or cerebellotoxic drug.
- Unexplained unsteadiness in ICU survivors, cystic fibrosis, platinum oncology, or long-term antiepileptic therapy.
- Delayed walking or wide-based gait in a child after aminoglycoside or cisplatin exposure.
- Distinguish from stroke, MS, paraneoplastic disease, B12/E deficiency, and idiopathic bilateral vestibulopathy.

Mechanism — how drugs injure balance

Mechanism	Process	Clinical relevance
Aminoglycoside hair-cell death	MET-channel entry, iron–ROS, apoptosis	Permanent bilateral vestibular loss; audiogram may be normal
Platinum oxidative injury	ROS + Pt–DNA adducts in OHC and stria	High-frequency SNHL; vestibular loss in 30–40%
Loop-diuretic strial effect	Na–K–2Cl inhibition; falls endocochlear potential	Reversible alone; synergistic with aminoglycosides
AED cerebellar toxicity	Na-channel block; chronic Purkinje-cell loss	Gaze-evoked nystagmus; chronic atrophy (phenytoin)
Other central toxins	Lithium, metronidazole, cytarabine, alcohol	Cerebellar ataxia; metronidazole reversible

Pearl — Aminoglycosides are vestibulotoxic at cochlea-sparing doses: profound bilateral vestibular loss can coexist with a NORMAL audiogram. Sensitivity hierarchy: utricle > saccule > crista > cochlear outer hair cells. Gentamicin and streptomycin are the worst offenders.

Causality — establishing the drug link

Domain	Requirement
Exposure	Documented ototoxic / cerebellotoxic drug preceding onset
Syndrome	Peripheral (bilateral vestibular hypofunction) or cerebellar pattern on exam
Tempo	Subacute over days–weeks (AED, lithium) or delayed weeks (gentamicin)
Dechallenge	Improvement or stabilisation on stopping / substituting the drug
Exclusion	Stroke, MS, paraneoplastic, B12/E, structural causes excluded
Support (not required)	Toxic drug level; dentate-nucleus or atrophy MRI; Naranjo score

Pearl — No formal criteria; diagnosis is clinical — drug exposure + compatible syndrome + exclusion of mimics + improvement on dechallenge (use the Naranjo scale). A normal MRI does not exclude reversible cerebellotoxicity, and a single drug level is supportive, not decisive.

Investigations — vestibular + audiological

Test	Purpose	When to order
Video head-impulse test (vHIT)	Bilateral canal VOR gain + corrective saccades	All suspected vestibulotoxicity
Caloric / rotatory chair	Quantify and confirm symmetric bilateral loss	Confirmatory; low-frequency canal function
cVEMP / oVEMP	Otolith function; often falls first	Baseline and after each aminoglycoside course
High-frequency audiogram + DPOAE	Earliest outer-hair-cell injury	Baseline, during, and post (ototoxic drugs)
MRI brain + drug level /	Exclude structural and metabolic mimics	Central (ataxic)

ammonia / B12		presentations
MT-RNR1 m.1555A>G	Aminoglycoside susceptibility	Before planned non-emergency aminoglycosides

Pearl — Audiometry alone is inadequate ototoxicity surveillance. Pair high-frequency audiometry + DPOAE with cVEMP + vHIT — the cVEMP often falls first in aminoglycoside vestibulotoxicity. A threshold shift over 15 dB should trigger action.

Differential diagnosis — high-yield mimics

Mimic	Key distinguishing features
Cerebellar stroke	Hyperacute onset; focal signs; vascular risk — MRI-DWI
Paraneoplastic / autoimmune cerebellitis	Subacute; no drug link; onconeural / GAD antibodies
Idiopathic bilateral vestibulopathy / CANVA	No ototoxic exposure; sensory neuropathy (RFC1) in CANVA
Wernicke's encephalopathy	Ataxia + ophthalmoplegia + confusion; at-risk host; give thiamine
Vitamin B12 / E deficiency	Sensory ataxia; positive Romberg in the light
Vestibular migraine / Ménière's	Episodic spinning vertigo — not the silent BVH pattern

► Red flags — refer / act urgently

The loop-diuretic + aminoglycoside combination is synergistically ototoxic — avoid it. New bilateral oscillopsia after gentamicin is vestibulotoxicity until proven otherwise. Offer MT-RNR1 (m.1555A>G) testing before planned non-emergency aminoglycosides — a single dose can cause permanent deafness in carriers. Severe lithium toxicity may need dialysis.

Management — prevention first, then rehabilitation

Tier	Intervention	Practice principles
Stop / substitute	Carboplatin for cisplatin; levetiracetam for phenytoin	Curative for reversible toxins where the indication allows
Aminoglycoside stewardship	Once-daily dosing; AUC-based TDM; shortest course	Lower sustained inner-ear concentrations
Avoid combinations	No loop diuretic + aminoglycoside together	Synergistic ototoxicity — separate or substitute
Otoprotection	Sodium thiosulfate for eligible cisplatin	RCT evidence (SIOPEL 6; ACCL0431)
Genetic prevention	MT-RNR1 testing pre-aminoglycoside; counsel family	Maternally inherited; avoid agent if positive
Rehabilitation	Vestibular rehab — gaze stabilisation, balance, optic flow	Start early; drives functional compensation

Pearl — Prevention beats rehabilitation. Stop or substitute where safe (carboplatin for cisplatin; levetiracetam for phenytoin); use once-daily aminoglycoside dosing + TDM + shortest course; give sodium thiosulfate otoprotection for eligible cisplatin protocols.

Counselling and follow-up

- Outlook depends on mechanism — reversible toxins (metronidazole, sedatives, loop diuretics) recover; cell-killing agents (aminoglycoside, cisplatin) and chronic phenytoin leave permanent deficits.
- Start vestibular rehabilitation early — the plasticity window is widest early and narrows with age. Recovery is functional, not anatomical.
- Document the adverse drug reaction; counsel the patient and, for MT-RNR1 carriers, the whole maternal family to prevent re-exposure.
- Relapse is essentially a function of avoidable re-exposure; a patient who reacted to a given agent should avoid it for life.

Key refs — Forge & Schacht 2000 · Huth 2011 · Brock SIOP Boston 2012 · Brock STS NEJM 2018 · van Gaalen 2014 · Strupp Bárány 2017 · Hall/Herdman VRT CPG 2022