PVM09CHEATSHEET

Ototoxicity and Drug-Induced Vestibular Dysfunction

Drug-Induced Balance and Hearing Disorders in Children

WHY THIS MATTERS

Ototoxic drugs cause permanent SNHL and vestibular damage in children. Vestibular damage is often subclinical but causes lifelong oscillopsia and imbalance. Aminoglycosides and platinum chemotherapy are the most important agents. Children have longer life expectancy with the deficit — early identification and rehabilitation are critical. The combination of furosemide + aminoglycoside is synergistically toxic and must never be co-prescribed.

HIGH-RISK OTOTOXIC DRUGS

Drug	Damage type	Key risk factor
Gentamicin / tobramycin	Vestibular > cochlear; bilateral BVH	Cumulative dose; renal impairment; MT-RNR1 m.1555A>G mutation
Amikacin	Cochlear > vestibular	Cumulative dose; prolonged course; renal impairment
Netilmicin	Cochlear + vestibular (less than gentamicin)	Safer than gentamicin; still requires monitoring
Cisplatin	High-frequency cochlear; delayed vestibular	Cumulative dose >400 mg/m²; combined cranial radiation
Carboplatin	Cochlear (children more sensitive than adults)	Age <5 years; combined with cisplatin
Furosemide (high IV dose)	Synergistic cochlear + vestibular with aminoglycosides	NEVER co-prescribe — absolute contraindication
Vancomycin (IV)	Cochlear + vestibular	Synergistic with aminoglycosides; renal impairment
Quinine (high dose)	Reversible cochlear predominant	High dose; rarely relevant in paediatric practice today

MITOCHONDRIAL AMINOGLYCOSIDE HYPERSENSITIVITY

Aspect	Detail
Gene variant	MT-RNR1 m.1555A>G (mitochondrial 12S rRNA)
Frequency	~1:500 European populations; higher in some East Asian populations
Effect	Single standard gentamicin dose causes profound irreversible bilateral SNHL
Test	Mitochondrial DNA blood test — rapidly available; simple blood sample
Rule	Test before first aminoglycoside dose if clinically feasible; mandatory in elective settings
Family history	Maternal-line post-aminoglycoside deafness = pathognomonic for MT-RNR1
Emergency use	If aminoglycoside required urgently and test unavailable: document risk-benefit; consent family

VESTIBULAR TOXICITY — CLINICAL FEATURES

Feature	Detail
Oscillopsia	Bouncing/blurred vision with head movement — pathognomonic of bilateral VOR loss
Gait	Wide-based; unsteady in dark; Romberg positive
Dynamic visual acuity	≥3 line logMAR drop with 2 Hz head oscillation — objective oscillopsia measure
vHIT finding	Bilateral absent or severely reduced VOR gain (<0.6); covert + overt saccades
Timing	Vestibular damage occurs during treatment; may progress after stopping
Reversibility	No pharmacological reversal — vestibular hair cell loss is permanent; VRT is the only treatment

MONITORING PROTOCOL — OTOTOXICITY SURVEILLANCE

Phase	Test	Timing	Action if abnormal
Before treatment	PTA + DPOAE baseline; MT-RNR1 if feasible	Before first dose	Document; counsel family; review antibiotic choice
During aminoglycoside (>7 days)	DPOAE or high-frequency hearing screen	Every 3–5 days	Any shift → urgent audiology; review drug necessity
During cisplatin	High-frequency PTA or DPOAE 4–8 kHz	Before each cycle	SIOP grade ≥2B → halt or substitute if oncologically safe
3 months post-treatment	Full PTA + word discrimination + vHIT	After course completion	SNHL or BVH → hearing aids + VRT referral
Annual (confirmed SNHL)	PTA + vestibular screen	Yearly for 5 years	Late cisplatin deterioration is well-documented
School entry	PTA	Prior to school entry	Catch late presenters from neonatal aminoglycoside exposure

CISPLATIN OTOTOXICITY — SIOP GRADING

SIOP Grade	Threshold change	Action
Grade 1	4 kHz bilateral ≥20 dB; no speech impact	Monitor; continue treatment; counsel family
Grade 2A	4 kHz + 3 kHz bilateral ≥20 dB	Audiologist review; consider dose modification
Grade 2B	Shift at 2 kHz; speech frequency impact	Oncology team — cisplatin substitution if oncologically safe
Grade 3	Shift at ≤1 kHz; profound speech impact	Hearing aids immediately; CI assessment; educational support
Grade 4	Profound loss; CI required	CI evaluation urgently; educational planning; sign language if appropriate

VRT FOR BILATERAL VESTIBULAR HYPOFUNCTION

- Gaze stabilisation exercises (VOR x1 and x2) are the mainstay — head movement while fixating targets; build speed progressively.
- Balance retraining on foam, tandem stance, single-leg, and in low-light conditions trains substitution strategies.
- Dynamic visual acuity improvement is the key treatment goal — not normalisation of VOR gain.
- Refer to vestibular physiotherapist with experience in bilateral BVH — standard "vestibular exercises" are insufficient.
- School physical education adaptations: avoid unlit areas, open swimming alone, activities requiring accurate head orientation in dark.

OUTCOME AND LONG-TERM MONITORING

Aspect	Detail
Audiological improvement	Partial hearing recovery possible if ototoxicity identified early and drug stopped promptly
Vestibular improvement	VOR gain may slowly increase post-aminoglycoside if damage partial; bilateral profound loss is permanent
VRT outcomes in BVH	Dynamic visual acuity improves significantly with VRT; functional compensation without VOR gain normalisation is achievable
Quality of life	Oscillopsia and gait impairment markedly improved with structured VRT; independent ambulation maintained in most
Late cisplatin deterioration	SNHL may worsen months–years after completion of cisplatin; annual audiology surveillance mandatory for 5 years post-treatment
School impact	Hearing aids, FM systems, preferential seating; vestibular physiotherapy for balance; avoid dark environments for BVH

WHEN TO REFER

- **► All NICU gentamicin graduates — audiology follow-up at 3 months corrected age as minimum standard**
- **► Bilateral vestibular hypofunction on vHIT post-aminoglycoside — vestibular physician + physiotherapist urgently**
- **► Progressive hearing loss during cisplatin — oncology + ENT; SIOP grading guides management**
- **► Maternal-line aminoglycoside deafness — MT-RNR1 test BEFORE any dose; single doses are dangerous in carriers**
- **► Confirmed oscillopsia + bilateral VOR loss — vestibular physician; structured BVH rehabilitation programme**

♦ Aminoglycoside vestibular toxicity is a silent epidemic in NICU survivors. An estimated 1 in 20 NICU graduates has significant bilateral VOR hypofunction from gentamicin — but most are never tested. These children present as "clumsy" with school and sport difficulties attributed to developmental delay. A bedside head impulse test takes 30 seconds. Refer for formal vHIT if abnormal — this is a completely underdiagnosed, potentially preventable cause of lifelong disability.

♦ Furosemide + aminoglycoside synergy is the most dangerous ototoxic combination in clinical practice. Furosemide disrupts the blood-labyrinth barrier and dramatically increases aminoglycoside entry into the cochlea and labyrinth. This combination should never be co-prescribed. If there is genuinely no alternative, the shortest possible aminoglycoside course with audiological monitoring from day one is mandatory — and the risk-benefit discussion must be documented.