VESTIBULAR PHYSIOLOGY

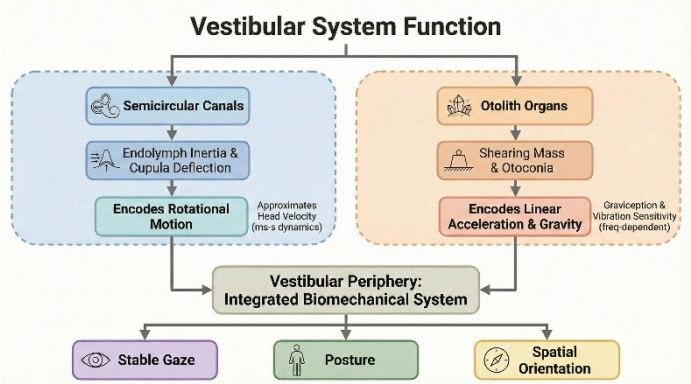
Clinical Quick-Reference · Based on ADC Comprehensive Clinician Review

Companion to the Vestibular Anatomy Cheat Sheet

The ADC Vestibular Anatomy Cheat Sheet mapped the ***structures*** of the vestibular labyrinth — the semicircular canals, otolith organs, membranous labyrinth, and central connections. This sheet explains ***how those structures work***. Together, they form a complete foundation for understanding vestibular function, clinical testing, and the physiological basis of dizziness.

This reference covers all 20 episodes of the ADC Clinician Audio Series: **Physiology of the Vestibular System**. It is organised across four pages: **(1) Peripheral Transduction** — hair cell mechanics, molecular channels, and otolith organs; **(2) Afferent Coding & Canal Mechanics** — semicircular canal biophysics, frequency tuning, and Ewald's Laws; **(3) Central Processing** — the VOR, cerebellum, and cortical vestibular pathways; **(4) Clinical Application** — test frequency spectrum, pharmacology, and vestibular compensation.

Clinical pearls (♥) *throughout highlight the direct clinical implications of each physiological concept — where the bench meets the bedside.*



HAIR CELL TRANSDUCTION

Stereocilia & Tip Links

- **Deflection toward kinocilium:** tip links stretch → MET channels open → K^+/Ca^{2+} influx → depolarisation (~1 ms)
- **Away from kinocilium:** channels close → hyperpolarisation; resting open probability ~10%
- **Adaptation:** Ca^{2+} enters → myosin motor resets tip-link length → sensitivity maintained across stimulus range
- K^+ recycling: endolymph (+80 mV endocochlear potential) provides driving force; K^+ exits via perilymph

TMC1/2 — The MET Channel

- **TMC1 and TMC2** (transmembrane channel-like proteins) form the tip-link–gated cation pore
- TMC2 predominates in neonates; TMC1 takes over at maturity; TMC2 compensates in TMC1 knockout
- **TMC1 loss-of-function** → DFNB7/11 hereditary deafness; vestibular function also impaired
- Non-selective cation channel: K^+ dominant influx; Ca^{2+} entry triggers fast adaptation
- **Gene therapy:** AAV-mediated TMC1 delivery restores MET function in deaf mouse models; human trials in progress

Adaptation Mechanisms

- **Fast adaptation (ms):** Ca^{2+} influx → calmodulin on myosin-1c → reduces tip-link tension → channel re-closes
- **Slow adaptation (10–100 ms):** myosin-1c motor slides along stereocilium actin core → resets operating point
- Both mechanisms maintain hair cell sensitivity across different static displacement levels

♥ *Aminoglycosides preferentially destroy irregular afferents (high-gain, wide-bandwidth) before regular afferents — explains high-frequency VOR failure before low-frequency caloric dysfunction in early ototoxicity.*

OTOLITH ORGANS

Saccule & Utricle

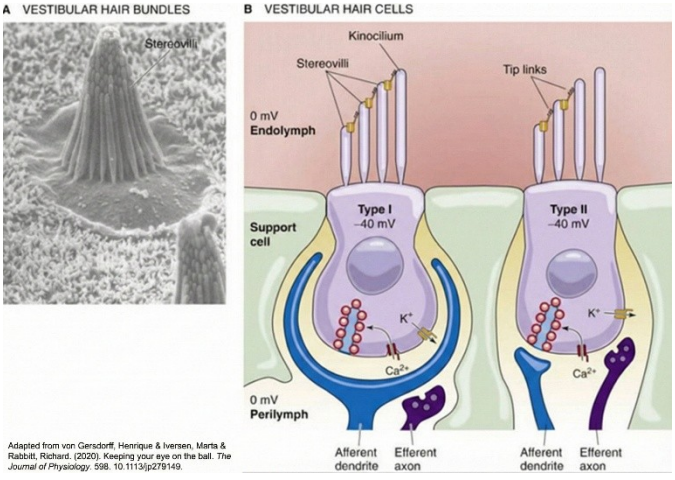
- **Utricle:** near-horizontal plane; ~35,000 hair cells; detects lateral + fore–aft linear acceleration + tilt
- . **Ephaptic dominance at high frequency:** provides 5–10 ms
- **Saccule:** vertical plane; ~40,000 hair cells; vertical linear acceleration + bone-conducted vibration
- Striola divides each macula → mirror-image polarity reversal; broader dynamic range across frequencies
- Otoconia: $CaCO_3$ crystals; density 2.71 g/cm³; inertial lag creates shear force on hair bundles
- **Utriculosaccular duct:** connects utricle and saccule → leads to endolymphatic sac
- **Ductus reuniens:** saccule ↔ scala media; slow endolymph pressure equalisation

Two Mechanical Modes

- **Accelerometer (low freq):** otoconia shift with head tilt/acceleration → SVV/SVH; gravity reference
- **Seismometer (high freq):** otoconia inertial; macula vibrates with bone-conducted sound → VEMP

♥ *VEMP circuit: cVEMP = saccule → inferior vestibular nerve → ipsilateral SCM (inhibitory). oVEMP = utricle → superior vestibular nerve → contralateral inferior oblique (excitatory). Nerve division localised without imaging.*

♥ *Tullio phenomenon: SSCD creates a third window → sound energy shunts into vestibular labyrinth → activates saccule + anterior canal. cVEMP threshold reduced (<80 dBnHL), oVEMP amplitude increased. Confirmed by sub-mm CT temporal bones*



TYPE I vs TYPE II HAIR CELLS

Type I — Flask-Shaped

- **Morphology:** flask-shaped; calyceal afferent synapse; surrounded by large cup-shaped calyx terminal
- **Afferent type:** irregular firing; high gain; striolar zone; fast VOR; primarily in central zone of macula / crista
- **Ephaptic coupling:** K^+ accumulates in narrow calyx cleft → depolarises post-synaptic membrane without vesicular release → ultra-fast, non-quantal transmission
- TC of velocity storage reduced by: nodulus lesion, alcohol, certain

latency required for VOR during head impulses (vHIT range)

Type II — Cylindrical
- **Morphology:** cylindrical; multiple small bouton afferent terminals; peripheral zone
- **Afferent type:** regular firing; lower gain; narrow bandwidth; tonic postural responses
- Irregular (Type I): high dynamic sensitivity, wide bandwidth → transient head movements
- Regular (Type II): lower gain, narrow bandwidth → sustained linear/gravitational signals

Coefficient of Variation (CV)
- CV = standard deviation of inter-spike interval / mean ISI
- Regular afferents: CV < 0.1; Irregular afferents: CV > 0.2
- **Clinical relevance:** caloric tests low-frequency regular fibres; vHIT tests high-frequency irregular fibres

♥ *Irregular afferents disproportionately lost in early aminoglycoside toxicity and superior vestibular neuritis — explains high-frequency VOR failure (abnormal vHIT) before low-frequency dysfunction (normal caloric) early in the disease course.*

POTASSIUM RECYCLING & ENDOLYMPH

K^+ Recycling Pathway
- K^+ influx through MET channel → exits basal face of hair cell into perilymph
- K^+ → supporting cells → fibrocytes → stria vascularis → re-secreted into endolymph
- **Stria vascularis:** highly vascularised; Na^+/K^+-ATPase + NKCC co-transporter maintain +80 mV endocochlear potential
- Endocochlear potential = driving force for K^+ influx through MET channels
- **Ductus reuniens and endolymphatic sac** regulate endolymph volume and pressure

Endolymphatic Hydrops
- Increased endolymph pressure → mechanical distortion of membranes → episodic hair cell dysfunction
- Low-frequency hearing loss + tinnitus + aural fullness + episodic vertigo = Ménière's syndrome
- **SLC26A4 (Pendrin) mutations:** impaired endolymph resorption → Pendred syndrome with vestibular hypofunction

♥ *Vestibular hydrops dissociation: abnormal low-frequency function (caloric) with preserved high-frequency vHIT is a biomarker of endolymphatic hydrops. Explains the paradox of normal vHIT in active Ménière's.*

SEMICIRCULAR CANAL MECHANICS

Steinhausen Torsion-Pendulum Model
- **Endolymph inertia** → cupular deflection proportional to angular velocity (integrates acceleration)
- **Mechanical TC ≈7 s:** governed by endolymph viscosity / cupula elasticity (TC = η/δ)
- Canal acts as angular velocity transducer across 0.1–10 Hz; below 0.1 Hz → progressive phase lead error
- **Velocity storage** (brainstem) extends TC to ~15 s → perceived rotation outlasts stimulus

Ewald's Laws
- **1st Law:** eye movement in the plane of the stimulated canal
- **2nd Law:** ampullofugal flow in lateral SCC excites; ampullofugal in vertical SCCs inhibits (reversed for vertical canals)
- **3rd Law:** excitatory response > inhibitory — basis of canal paresis asymmetry on caloric/vHIT
- **Coplanar pairs:** L Lat ↔ R Lat | R Ant ↔ L Post | L Ant ↔ R Post (three orthogonal planes)

♥ *Velocity storage: commissural vestibular nucleus connections prolong canal signal. Nodulus/uvula regulate duration — nodulus lesion → prolonged post-rotatory nystagmus and periodic alternating nystagmus (PAN).*

VESTIBULAR NUCLEI & SIGNAL INTEGRATION

Temporal Integration
- **Velocity storage mechanism:** VN nuclei prolong head velocity signal beyond mechanical TC (~7 s) to ~15 s
- Commissural inhibition between bilateral VN nuclei: lesion removes inhibition → spontaneous nystagmus toward intact side

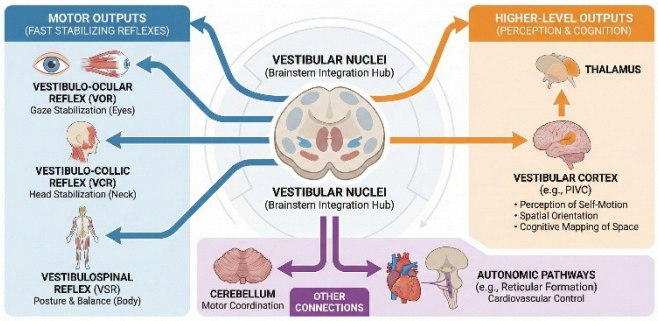
drugs; increased in dark

Spatial Integration
- VN nuclei receive inputs: semicircular canals, otoliths, visual cortex (optokinetic), cerebellum, spinal cord
- **Otolith-canal convergence:** VN neurons combine linear + angular motion signals → tilt-translation disambiguation
- **Graviceptive signalling:** VN neurons encode gravity reference for SVV/SVH; disrupted in lateral medullary infarct (Wallenberg)

Pharmacology at the Vestibular Nuclei
- AMPA receptors: fast temporal precision (sub-ms); dominate during VOR transmission
- NMDA receptors: modulate velocity storage TC; NMDA antagonists shorten post-rotational nystagmus
- **GABAergic inputs:** cerebellum (Purkinje) → VN inhibition; benzodiazepines potentiate → suppress spontaneous nystagmus
- H1/muscarinic receptors: antihistamines reduce VN excitability; effective anti-nausea/anti-vertigo effect

♥ *Canal paresis formula (Jongkees): CP = [(RW+RC)–(LW+LC)] / (RW+RC+LW+LC) × 100%; >25% = unilateral canal paresis. Caloric probes ~0.003 Hz; vHIT probes 1–6 Hz: caloric normal + vHIT abnormal = high-frequency selective lesion.*

OUTPUTS OF THE VESTIBULAR NUCLEI: MOTOR & HIGHER-LEVEL FUNCTIONS



AFFERENT CODING & FREQUENCY TUNING

Regular vs Irregular Afferents
- **Regular afferents:** low CV; tonic regular discharge; lower gain; narrow bandwidth; encode steady-state position and slow movements
- **Irregular afferents:** high CV; variable ISI; high dynamic sensitivity; wide bandwidth; encode transient, high-frequency head movements
- **Zone distribution:** irregular fibres concentrated in striola/central crista; regular in peripheral zones
- **Clinical relevance:** vHIT primarily tests irregular (high-frequency) fibres; caloric tests low-frequency regular fibres

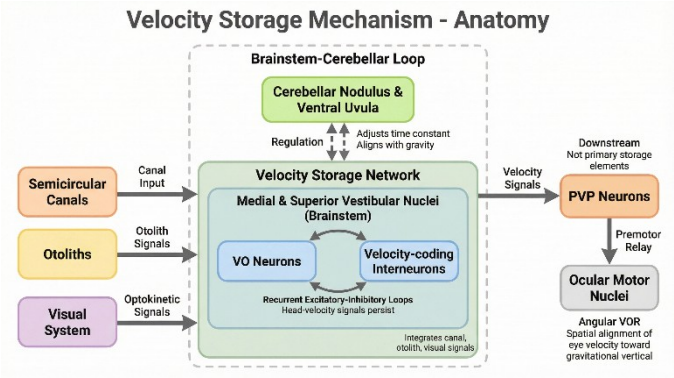
The Vestibular System as a Frequency Filter
- **Caloric:** ~0.003–0.01 Hz — very low frequency; lateral SCC only; sensitive, slow, labile
- **Rotational chair:** 0.01–2 Hz — full frequency range; VOR gain/phase/asymmetry; gold standard for BVH
- **vHIT:** 1–6 Hz — high frequency; all 6 SCCs tested individually; detects acute/severe hypofunction; insensitive to partial lesions
- **cVEMP:** 500 Hz air-conducted tone burst → saccule → inferior vestibular nerve → SCM; threshold <100 dBnHL; n23 inhibitory
- **oVEMP:** 500 Hz bone-conducted vibration → utricle → superior vestibular nerve → contralateral IO; n10 excitatory peak

♥ *Frequency dissociation: SVN = absent oVEMP + intact cVEMP. Inferior neuritis = absent cVEMP + intact oVEMP. Allows precise localisation without MRI. Caloric normal + vHIT abnormal in early Ménière's (low-freq loss only).*

CENTRAL PATHWAYS OVERVIEW

Three Primary Vestibular Reflexes
- **VOR:** labyrinth → VN → MLF → oculomotor nuclei → extraocular muscles; gain ~1.0; latency 5–10 ms
- **VSR:** VN → lateral/medial vestibulospinal tracts → limb extensors/neck; stabilises posture against gravitational load
- **VCR:** VN → spinal accessory nucleus → SCM; stabilises head position during body movement
- **Lateral VST (Deiters' nucleus):** facilitates ipsilateral extensor tone; inhibits ipsilateral flexors

Medial Vestibulospinal Tract (MVST)



Velocity Storage & Nystagmus

- Spontaneous nystagmus from unilateral VH: fast phase away from lesion (Alexander's Law: increases with gaze toward fast phase)
- Direction-changing positional nystagmus (DCPN) with non-fatiguing features: central pathology until proven otherwise
- **Post-rotational nystagmus:** outlasts stimulus because velocity storage extends VN signal beyond SCC mechanical TC

Otolith-Ocular Reflexes

- Skew deviation: utricular asymmetry → ipsilesional hypotropia; marker of otolith or brainstem/cerebellar lesion
- **Ocular counter-rolling:** utricle senses tilt → compensatory eye rotation in opposite direction (limited, ~10°)
- HINTS exam: Head Impulse + Nystagmus direction + Test of Skew — differentiates acute vestibular neuritis from stroke with >96% sensitivity for stroke

♥ *Alexander's Law: spontaneous nystagmus intensity increases with gaze toward fast phase. Reflects adaptive gaze-holding mechanism modulated by flocculus; present in peripheral, absent/direction-changing in central lesions.*

VESTIBULO-OCULAR REFLEX (VOR)

3-Neuron Arc

- **1st neuron:** vestibular nerve → vestibulocochlear nerve (CN VIII) → vestibular nuclei
- **2nd neuron:** VN → medial longitudinal fasciculus (MLF) → oculomotor, trochlear, abducens nuclei
- **3rd neuron:** oculomotor nuclei → extraocular muscles
- **Latency:** 5–10 ms — fastest motor reflex in the body; demands direct oligosynaptic pathway
- **Normal gain:** ~1.0 (eye velocity = head velocity); reduced in unilateral/bilateral hypofunction

VOR Gain Control

- **VOR cancellation:** flocculus/paraflocculus suppress VOR during smooth pursuit + gaze fixation on moving target
- **Gain adaptation:** flocculus detects retinal slip → modifies parallel fibre → Purkinje cell → VN synapse
- VOR gain: increase (magnifying lens) or decrease (minifying lens) via opposing LTP/LTD at PF-PC synapse
- **vHIT:** tests high-frequency VOR (1–6 Hz); covert saccades indicate compensatory brainstem rerouting

Alexander's Law & Clinical Correlates

- Nystagmus intensity ↑ on gaze toward fast phase — floccular gaze-holding modulation
- **Fixation suppression failure:** unable to suppress nystagmus with fixation — central sign (cerebellar/brainstem)
- **Bruns nystagmus:** large-amplitude slow-phase nystagmus ipsilesional + high-frequency nystagmus contralesional = CPA mass

♥ *vHIT covert saccades: when VOR gain is reduced, the brain generates a corrective saccade during the head impulse. Covert are harder to detect clinically; vHIT reveals them. Overt saccades occur after the impulse.*

VESTIBULO-SPINAL & COLIC REFLEXES

Lateral Vestibulospinal Tract (LVST)

- MVN → ipsilateral limb extensors; stabilises posture against gravitational load; activated by otolith signals
- **Head direction cells (entorhinal/subiculum):** encode allocentric
- MVN → bilateral cervical muscles; head–neck stabilisation during angular motion
- **Cervico-ocular reflex (COR):** neck proprioception → small supplementary eye movement; impaired in cervicogenic dizziness

VEMP Circuitry

- **cVEMP:** saccule → inferior vestibular nerve → inferior VN → descending MLF → ipsilateral SCM inhibition; threshold <100 dBnHL; amplitude 50–150 µV
- **oVEMP:** utricle → superior vestibular nerve → superior VN → MLF → contralateral IO (CN III); n10 amplitude; measured below eye

♥ *oVEMP n10 amplitude asymmetry >35% and cVEMP threshold asymmetry >10 dBnHL are significant. Both together map the full otolith-nerve axis — essential for pre-surgical planning in SSCD and Ménière's.*

CEREBELLUM AS PREDICTIVE ENGINE

Flocculus — VOR Adaptation & Cancellation

- **Flocculus (FL):** receives mossy fibres from VN and pontine nuclei; receives climbing fibres from inferior olive (IO) encoding retinal slip
- Purkinje cells in FL → VN inhibition; modify VOR gain based on visual feedback
- **LTD at PF-PC synapse:** simultaneous CF + PF activation → long-term depression of PF-PC synapse → reduces PC firing → disinhibits VN → increases gain
- **VOR cancellation:** FL suppresses VOR during voluntary gaze on moving target (smooth pursuit)

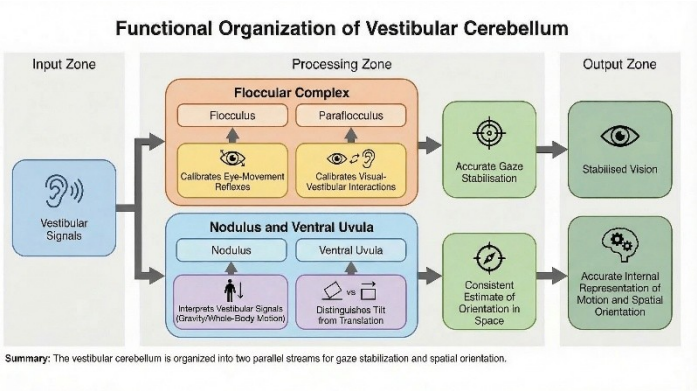
Nodulus/Uvula — Velocity Storage Control

- Nodulus/uvula Purkinje cells → inhibit velocity storage neurons in VN
- Nodulus lesion → prolonged post-rotatory nystagmus, PAN, gravity-dependent direction changes
- **Otolith-canal conflict resolution:** nodulus integrates otolith signals to suppress canal-driven nystagmus at end of rotation

Cerebellar Vestibular Syndromes

- Downbeat nystagmus: flocculus/parafloccular lesion; upgaze pathway preserved; 4-aminopyridine may help
- Upbeat nystagmus: anterior vermis or pontine tegmentum lesion
- Direction-changing gaze-evoked nystagmus: cerebellar gaze-holding failure

♥ *Cerebellar stroke mimicking acute vestibular neuritis: HINTS distinguishes — normal vHIT + direction-changing nystagmus + skew deviation = central; abnormal vHIT + unidirectional nystagmus + no skew = peripheral. HINTS superior to CT for acute posterior fossa stroke.*



VESTIBULAR CORTEX & SPATIAL PERCEPTION

Thalamo-cortical Pathway

- **Thalamo-cortical path:** VN → VPLo/VL thalamus → PIVC (parieto-insular vestibular cortex) → area 2v; multisensory convergence
- **PIVC:** primary cortical area for vestibular processing; subjective visual vertical, tilt perception
- **Area 2v:** secondary somatosensory/vestibular area; body tilt representation
- **MST (medial superior temporal):** visual-vestibular integration for optic flow and heading direction

Spatial Perception & Disorientation

- **SVV (subjective visual vertical):** measure of graviceptive processing; tilted ipsilesionally in acute UVH

head direction; vestibular input essential for updating
- **Grid cells, place cells:** hippocampal spatial navigation; disrupted by vestibular deafferentation
- Cognitive effects of bilateral VH: spatial memory impairment, hippocampal atrophy over years

Visual-Vestibular Mismatch — VID & PPPD
- **VID (visual-induced dizziness):** excessive visual weighting over vestibular; triggered by optic flow, patterns, crowds
- **PPPD:** cortical hypervigilance to vestibular/spatial signals; perpetuates dizziness after structural recovery; CNS fails to update internal model
- Cortical reweighting failure: PIVC + area 2v over-activated by visual stimuli → persistent spatial disorientation

♥ *Why Your Brain Miscalculates Gravity (Ep 17): PIVC lesion from stroke → contralesional SVV tilt → apparent body tilt sensation. Partial recovery via cortical reweighting over weeks. Persistent SVV tilt >2° at 3 months indicates incomplete compensation.*

VESTIBULAR TEST FREQUENCY SPECTRUM

Full Test Battery Overview – Biological bandpass filter: different structures, afferent types, frequency windows — no single test sufficient – Caloric: ~0.003–0.01 Hz; lateral SCC only; chronic stable hypofunction; labile, position-sensitive – Rotational chair: 0.01–2.0 Hz; all SCCs; VOR gain/phase/asymmetry; gold standard for BVH – vHIT: 1–6 Hz; all 6 SCCs individually; acute/severe hypofunction; covert/overt saccades – cVEMP: 500 Hz air-conducted → saccule → inferior nerve → ipsilateral SCM; threshold + asymmetry – oVEMP: 500 Hz BC → utricle → superior nerve → contralateral inferior oblique; n10 amplitude

Frequency Dissociation — Clinical Interpretation – Normal caloric + abnormal vHIT: high-frequency selective lesion — incomplete neuritis, early Ménière's – Abnormal caloric + normal vHIT: low-frequency selective; favour pharmacological/reversible cause – Absent cVEMP + present oVEMP: inferior nerve division; Absent oVEMP + present cVEMP: SVN pattern – All abnormal: panvestibular dysfunction — gentamicin, autoimmune, bilateral Ménière's

♥ Frequency dissociation = cornerstone of syndromic vestibular diagnosis. Battery must be interpreted together — caloric and vHIT can disagree, both can be right.

VESTIBULAR PHARMACOLOGY

Drug Classes & Mechanisms – H1-antihistamines & phenothiazines: H1/muscarinic/D2 blockade → reduce VN excitability; antiemetic; impair compensation if used >72 h – Benzodiazepines: GABA-A potentiation → fastest vertigo relief; highest compensation impairment risk – Betahistine: H3 antagonist → maintenance for Ménière's only; not an acute suppressant

Suppression vs Compensation Trade-off – Suppressants mask VN asymmetry — the exact signal the cerebellum needs to drive compensation – Acute phase (<72 h): short-course suppressants acceptable; beyond 72 h taper and mobilise

♥ *The cerebellum cannot correct what it cannot detect. Taper suppressants beyond 72 h and mobilise — chronic use is a treatable cause of persistent dizziness.*

VESTIBULAR ADAPTATION & COMPENSATION

Compensation Timeline After UVH
- **Acute phase (0–72 h):** spontaneous nystagmus (fast phase away from lesion), severe oscillopsia, nausea, profound postural instability; driven by resting-rate asymmetry between bilateral VN
- **Static compensation (1–6 wk):** VN nuclei rebalance — contralateral VN downregulates to match reduced ipsilesional input; spontaneous nystagmus resolves at rest
- **Dynamic compensation (wks–months):** VOR gain recalibrated via flocculus/nodulus; requires active head movement with retinal slip; residual oscillopsia on fast movements reduces

Mechanisms of VOR Adaptation
- **Flocculus:** IO climbing fibre retinal-slip error signal → LTD at PF-PC synapse → modifies VN gain
- **Covert saccades:** compensatory saccades during head impulse indicate incomplete VOR adaptation; not a sign of failure — sign of ongoing adaptation
- VOR gain adaptation: increase or decrease via separate LTD/LTP mechanisms at floccular PF-PC synapse

Sensory Substitution Mechanisms
- Cervical proprioception partially substitutes during slow movements; cervico-ocular reflex (COR) contributes
- Visual flow (optokinetic system) suppresses dizziness at low velocities; fails in dark and at high head-movement speeds
- Somatosensory inputs increasingly weighted after BVH — good static balance on firm/well-lit surface, failure on foam or in dark

Predicting Compensation Outcomes
- **Poor prognostic factors:** bilateral VH, cerebellar disease, peripheral neuropathy, high anxiety, poor corrected visual acuity, older age, chronic suppressants
- **PPPD:** CNS fails to update internal model despite structural recovery; cortical hypervigilance perpetuates dizziness; SSRIs + CBT + VR therapy
- **Incomplete compensators (~30% UVH at 1 yr):** covert saccades persist on vHIT; benefit most from targeted vestibular rehabilitation exercises targeting canal-specific gain deficits

Why Early Mobilisation Works
- Active head movement → retinal slip → error signal → VOR recalibration (VOR adaptation requires the error)
- Bed rest removes the error signal. Suppressants mask the remaining asymmetry. Both delay adaptation.
- **Cawthorne-Cooksey / Herdman's VR protocol:** graded head movement exercises; visual stabilisation tasks; balance training

♥ *Early active mobilisation + targeted vestibular rehabilitation after UVH reduces time to compensation by 30–50%. Bed rest with suppressants is the worst management combination. Mobilise from day 2 after vertigo onset once safety confirmed.*

♥ *PPPD pathophysiology: after the acute insult resolves, the cortex maintains a heightened alert state monitoring spatial signals. This hypervigilance perpetuates dizziness even without active vestibular asymmetry. Treatment targets the cortical hypervigilance, not the inner ear*

Putting It Together — From Molecule to Clinic

Vestibular physiology begins at the hair cell — a single deflection of a stereocilium, a tip link stretched, a K^+ channel opened. That molecular event propagates through afferent fibres, vestibular nuclei, cerebellum, and cortex to produce the most fundamental of human experiences: the sense of where we are in space. When any step in this cascade fails, the result is dizziness.

The four key clinical principles that follow from this physiology: **(1)** No single test covers the full frequency range — always interpret the battery together. **(2)** Frequency dissociation is your most powerful localising tool. **(3)** Vestibular suppressants used beyond 72 hours actively impair the compensation the brain needs to perform. **(4)** Early active mobilisation is the most evidence-based intervention after acute vestibular loss.

For the complete 20-episode audio series, GP education resources, patient information leaflets, and the full vestibular condition library, visit **www.AustralianDizzinessClinics.com**. For the structural companion to this sheet, refer to the ***ADC Vestibular Anatomy Cheat Sheet***.