Gaze Holding & Nystagmus Examination:

A Comprehensive Clinical Review

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Section 3A — Oculomotor Assessment | Vestibular Function Testing Series

How to Use This Review

This document is the companion clinical literature review to the gaze stability and nystagmus evaluation video series on the ADC education hub at www.australiandizzinessclinics.com. It is designed for vestibular physicians, audiologists, and neurologists building expertise in laboratory vestibular function testing.

The review follows clinical testing sequence: from theoretical foundations and neural substrates through methodology, normative values, interpretation frameworks, and clinical application. Callout boxes throughout identify clinically high-yield points and evidence-based pearls.

Callout box guide:

 Clinical Insight: *Clinically relevant observations derived directly from the basic science — the bridge between laboratory findings and patient management.*

 Clinical Pearl: *High-yield, memorable clinical points — the key facts that separate a competent clinician from an expert in vestibular function testing.*

 Key Point: *Foundational concepts and summary statements that anchor the clinical framework. Master these to interpret the full testing battery.*

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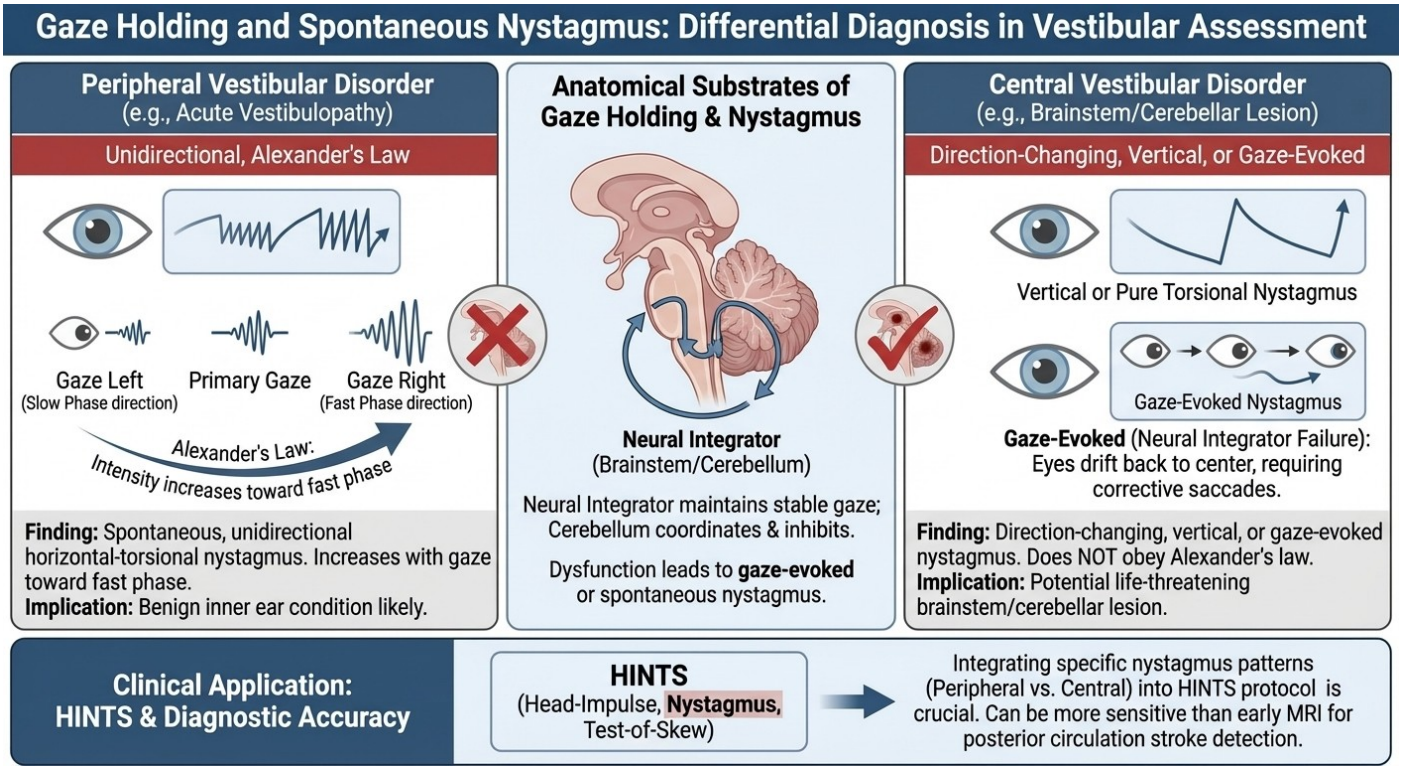
Introduction: Gaze Holding and Spontaneous Nystagmus in Vestibular Diagnosis

For the vestibular physician, assessment of gaze-holding function and spontaneous nystagmus provides a direct window into brainstem and cerebellar integrity. The ability to maintain the eyes steadily on a target (gaze-holding) and the presence of nystagmus at rest are “fingerprints” of specific neural circuit dysfunction [1]. Abnormalities in these domains often draw the line between peripheral and central vestibular disorders, guiding critical decisions such as the need for urgent neuroimaging. For example, a patient with acute vertigo and a unidirectional horizontal-torsional nystagmus that obeys Alexander’s law (increases when gazing toward the fast phase) is likely suffering a peripheral vestibulopathy, whereas direction-changing or vertical nystagmus strongly points to a central lesion [2]. Thus, careful examination of gaze stability and spontaneous

nystagmus is indispensable in differentiating benign inner ear conditions from life-threatening brainstem or cerebellar strokes.

Clinically, these oculomotor signs serve as high-yield clues. A stable gaze-holding system ensures that, after a rapid eye movement (saccade), the eyes remain fixed on target. Failure of this mechanism leads to gaze-evoked nystagmus – a telltale sign of neural integrator or cerebellar dysfunction. Likewise, spontaneous nystagmus (nystagmus present in primary gaze without any provocation) indicates an imbalance in vestibular tone or central vestibular pathways. In the emergency setting, integrating these findings into protocols like HINTS (Head-Impulse, Nystagmus, Test-of-Skew) dramatically improves diagnostic accuracy. Indeed, specific nystagmus patterns can be more sensitive than early MRI in detecting a posterior circulation stroke [2].



This comprehensive review, tailored for neuro-otologists, will delve into the neurophysiology of gaze holding, the mechanisms and types of nystagmus, and their clinical relevance – matching the depth and structured approach of prior reviews on saccades and optokinetic nystagmus. We will explore how the neural integrator and cerebellum maintain eccentric gaze, how to examine gaze-holding at the bedside, the spectrum of pathological nystagmus (from gaze-evoked to seesaw), and the nuances of interpretation in various clinical scenarios. Both basic neuroanatomy and clinical pearls will be emphasized, so that by the end, the reader can translate these oculomotor observations into precise localization and management decisions.

Neurophysiology and Anatomical Substrates

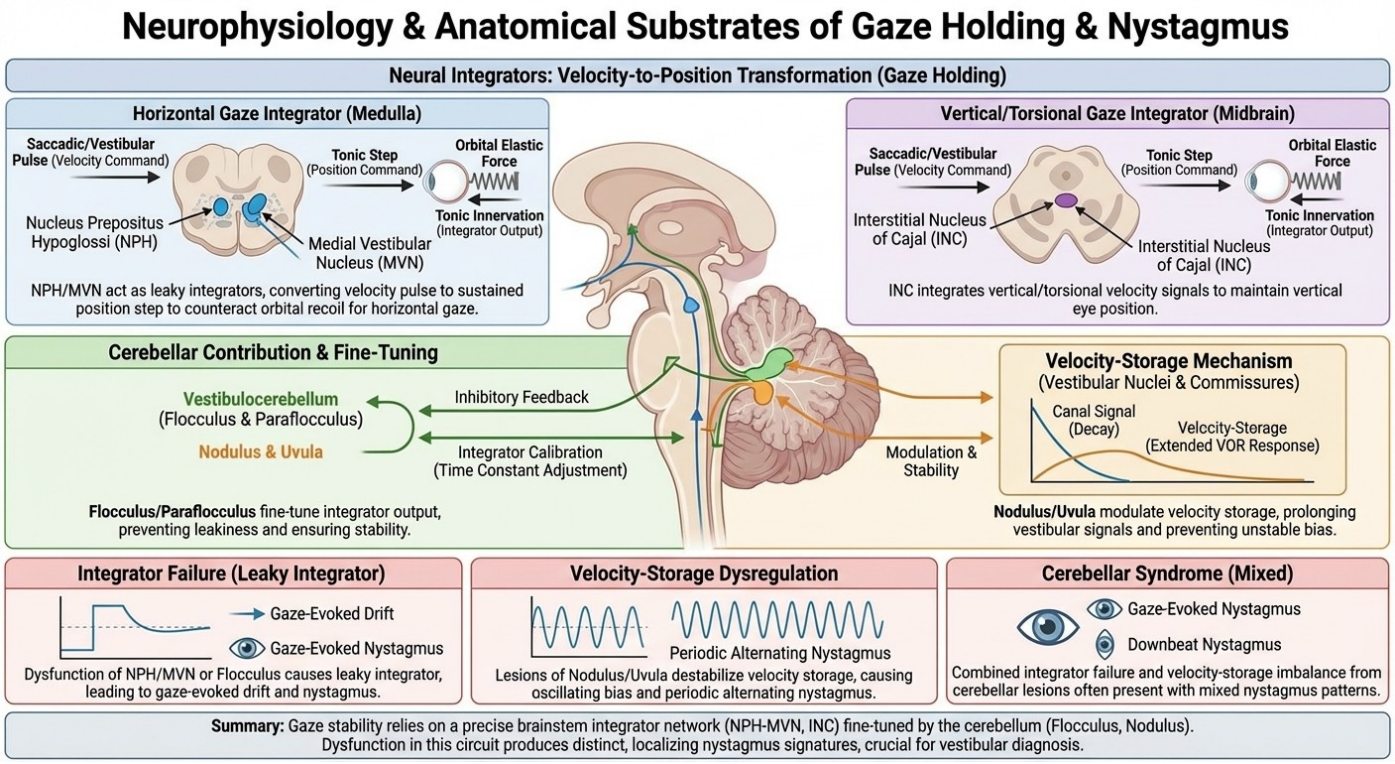
Neural Integrators – The Velocity-to-Position Transformers: When the eyes move to a new eccentric position, the orbit's elastic forces naturally pull them back toward centre. To hold gaze steady, the brain must continuously counteract this recoil by converting a transient velocity command into a sustained position command. This conversion is handled by the neural

integrator network in the brainstem and cerebellum [3]. For **horizontal gaze, the primary integrator elements are the nucleus prepositus hypoglossi (NPH) and adjacent medial vestibular nucleus (MVN) in the medulla, whereas vertical (and torsional) gaze holding is governed by the interstitial nucleus of Cajal (INC) in the midbrain** [4]. These nuclei mathematically integrate the "pulse" of eye velocity (from a saccade or other movement) into a "step" of tonic innervation that holds the eye at its new position. In essence, the NPH/MVN and INC act as leaky batteries that charge up during an eye movement and then discharge at a steady rate to hold the eyes against orbital spring forces.

Cerebellar Contribution – Flocculus, Paraflocculus, and Nodulus: The cerebellum fine-tunes this gaze-holding integrator to ensure accuracy and stability. The flocculus and paraflocculus (vestibulocerebellum) provide critical inhibitory feedback to the vestibular nuclei and NPH, calibrating the neural integrator's time constant [5]. Floccular Purkinje cells fire in relation to eye velocity and adjust the integrator output; lesions of the flocculus make the neural integrator "leaky," resulting in gaze-holding failure and a combination of gaze-evoked drift plus downbeat nystagmus [6]. The nodulus and uvula (midline cerebellar structures) chiefly modulate the vestibular velocity-storage mechanism (which extends the duration of vestibular signals). Lesions in the nodulus can destabilize velocity storage, leading to periodic or direction-changing nystagmus (such as periodic alternating nystagmus) by allowing an unchecked oscillation of stored vestibular bias [7,8]. In summary, the brainstem integrator holds the eyes, but the cerebellum keeps that hold rock steady. Damage to any part of this network – the integrator nuclei or their cerebellar supervision – can impair the velocity-to-position transformation and cause the eyes to drift off target.

The Velocity-Storage Mechanism: While not a gaze-holding system per se, the velocity-storage network is an important vestibular substrate that interacts with gaze stability. Located in the vestibular nuclei and their commissural connections, it prolongs the vestibulo-ocular reflex (VOR) response to sustained rotation. Normally, a head rotation signal from the semicircular canals decays in a few seconds, but velocity-storage extends this to ~20 seconds, improving low-frequency VOR performance. When this network is dysregulated, it produces characteristic nystagmus patterns. A hyperactive velocity-storage (often from floccular dysfunction) biases upward drift and manifests clinically as downbeat nystagmus, whereas an unstable, oscillating velocity-storage bias produces the classic cycling of periodic alternating nystagmus [9]. Lesions of the nodulus/uvula or conditions like Wernicke encephalopathy are well-known causes of such velocity-storage disturbances [10]. Thus, neural integrator failure and velocity-storage imbalance often coexist in central vestibular disorders – explaining why cerebellar diseases frequently present with mixed gaze-evoked and positional nystagmus.

Summary of Key Structures: To hold gaze on target, the oculomotor system relies on a network that spans the medulla, pons, midbrain, and cerebellum. The NPH-MVN (horizontal integrator) and INC (vertical integrator) generate the persistent firing ("step") to counteract elastic drift [3,4]. The vestibulocerebellum (flocculus/paraflocculus) adjusts this firing to prevent under-holding (drift back to centre) or over-holding (oscillation), while the nodulus adjusts prolonged vestibular responses to prevent abnormal nystagmus biases [5]. This intricate circuit underscores why gaze-holding deficits are a sensitive indicator of central pathology: even a small lesion in this network can produce a signature nystagmus that betrays its location.



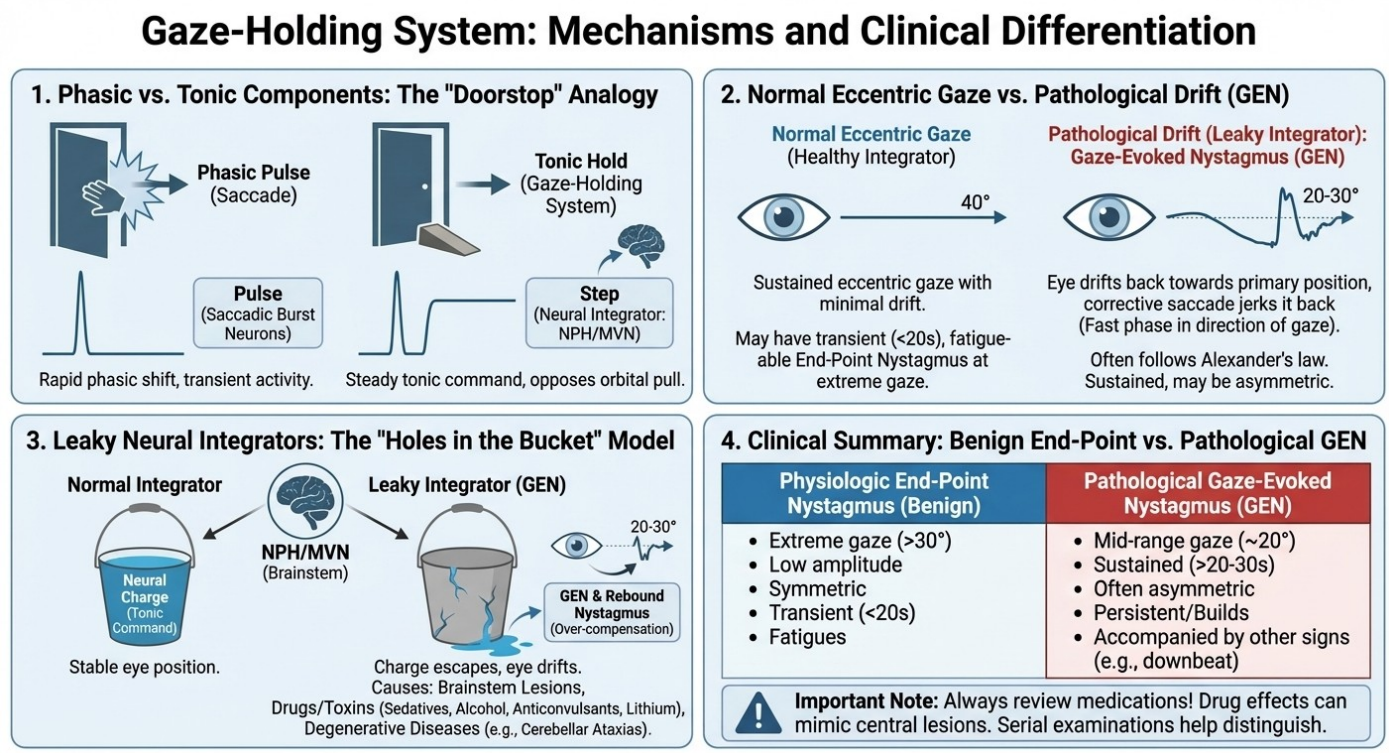
Gaze-Holding System and Mechanisms

Tonic vs. Phasic Eye Movements: Eye movements have phasic components (quick shifts) and tonic components (steady holding). Saccades, for instance, are rapid phasic shifts driven by a burst of neural activity (the “pulse”), but to maintain the new eye position, a tonic “step” of firing must follow. The gaze-holding system provides this tonic output. It works continuously in the background to oppose the orbital tissues’ pull that wants to return the eyes to primary position [11]. In a normal system, the phasic pulse (from saccadic premotor burst neurons) is perfectly integrated into a step by the neural integrator, and the eyes remain still once the target is acquired. Tonic gaze holding refers to this maintained contraction of extraocular muscles, whereas phasic movements (saccades, quick phases) are transient. A useful analogy is holding a door open: a phasic push opens the door, but a doorstop (tonic hold) is needed to keep it from swinging shut.

Normal Eccentric Gaze vs. Pathological Drift: Healthy individuals can sustain eccentric gaze (30° or more from centre) with minimal drift due to a well-functioning neural integrator. At extreme gaze (especially beyond ~40°), a slight physiological end-point nystagmus may appear – a few beats of jerk nystagmus with small amplitude that fatigue within seconds. By contrast, gaze-evoked nystagmus (GEN) is an abnormal, sustained nystagmus that occurs when the patient tries to look eccentrically, due to a leaky integrator that cannot hold the eye steady [12]. In GEN, the eyes drift back toward primary position (because the neural integrator’s output decays), then a corrective saccade jerks them back to the intended eccentric gaze position – resulting in repetitive jerk nystagmus. The fast phase beats in the direction of gaze (e.g. right-beating nystagmus on right gaze, left-beating on left gaze). This pattern often follows Alexander’s law (nystagmus is stronger when looking toward the fast phase side) [13]. Crucially, pathologic GEN persists as long as the eccentric gaze is maintained (unlike the transient end-point nystagmus), may be asymmetric (present in one direction more than the other), and is frequently accompanied by other ocular motor signs like downbeat nystagmus in primary gaze [1,12].

Leaky Neural Integrators – "Holes" in the Gaze-Holding Bucket: A useful way to conceptualize gaze-holding deficits is to imagine the neural integrator as a bucket that holds neural charge; if it has a leak, the charge (tonic command) gradually escapes. The eye then slides back toward centre with an exponential trajectory. The rate of drift (slow-phase velocity) is proportional to how "leaky" the integrator is [11]. Once the drift error is large, a corrective saccade fires to pull the eye back to target – producing a jerk nystagmus. Common causes of a leaky integrator include structural lesions in the dorsomedial medulla (affecting NPH/MVN), drug intoxications, and degenerative disorders. For example, anticonvulsant toxicity, sedative use, alcohol intoxication, and lithium are classic reversible causes of gaze-evoked nystagmus, as they depress neural integrator function [14]. In degenerative cerebellar diseases (like spinocerebellar ataxias), loss of Purkinje cells removes the stabilizing influence on the integrator, leading to prominent gaze-evoked drift and often accompanying downbeat nystagmus [5,15]. Importantly, GEN indicates a central dysfunction – either brainstem or cerebellum, or the influence of a drug – in contrast to peripheral vestibular nystagmus which is typically present in primary gaze (spontaneous) and does not require eccentric gaze to appear. A related phenomenon is rebound nystagmus, which can be thought of as an integrator over-compensation: after holding an eccentric gaze for a long time, the integrator becomes biased; when the patient returns to primary gaze, the stored bias causes a transient nystagmus in the opposite direction (eyes drift toward the previous eccentric position then snap back) [16]. Rebound nystagmus usually lasts only a few seconds and is highly suggestive of cerebellar pathology (often accompanying gaze-evoked nystagmus in diseases like multiple sclerosis or cerebellar degeneration).

In summary, a robust gaze-holding system produces minimal nystagmus even at far gaze, whereas a deficient system yields characteristic drifts. Distinguishing physiologic end-point nystagmus from pathological gaze-evoked nystagmus is clinically important. Features favouring a physiologic (benign) end-point nystagmus include: only at extreme gaze (usually >30°), low amplitude, symmetric in both directions, and fatiguing within a few beats. In contrast, a nystagmus that is sustained >20–30 seconds, especially if asymmetric (present in one direction but not the other) or present even at mid-range eccentric gaze (20°), is pathological. Always consider medications and alcohol in the differential: a patient on high-dose anti-seizure medications or benzodiazepines may have mild gaze-evoked nystagmus from the drug effect rather than a structural lesion [14]. When in doubt, serial examinations (after holding gaze a few seconds) can help – physiologic nystagmus tends to diminish with repeated attempts or as the patient tires, whereas pathological GEN remains robust or may even build in intensity as the integrator saturates.

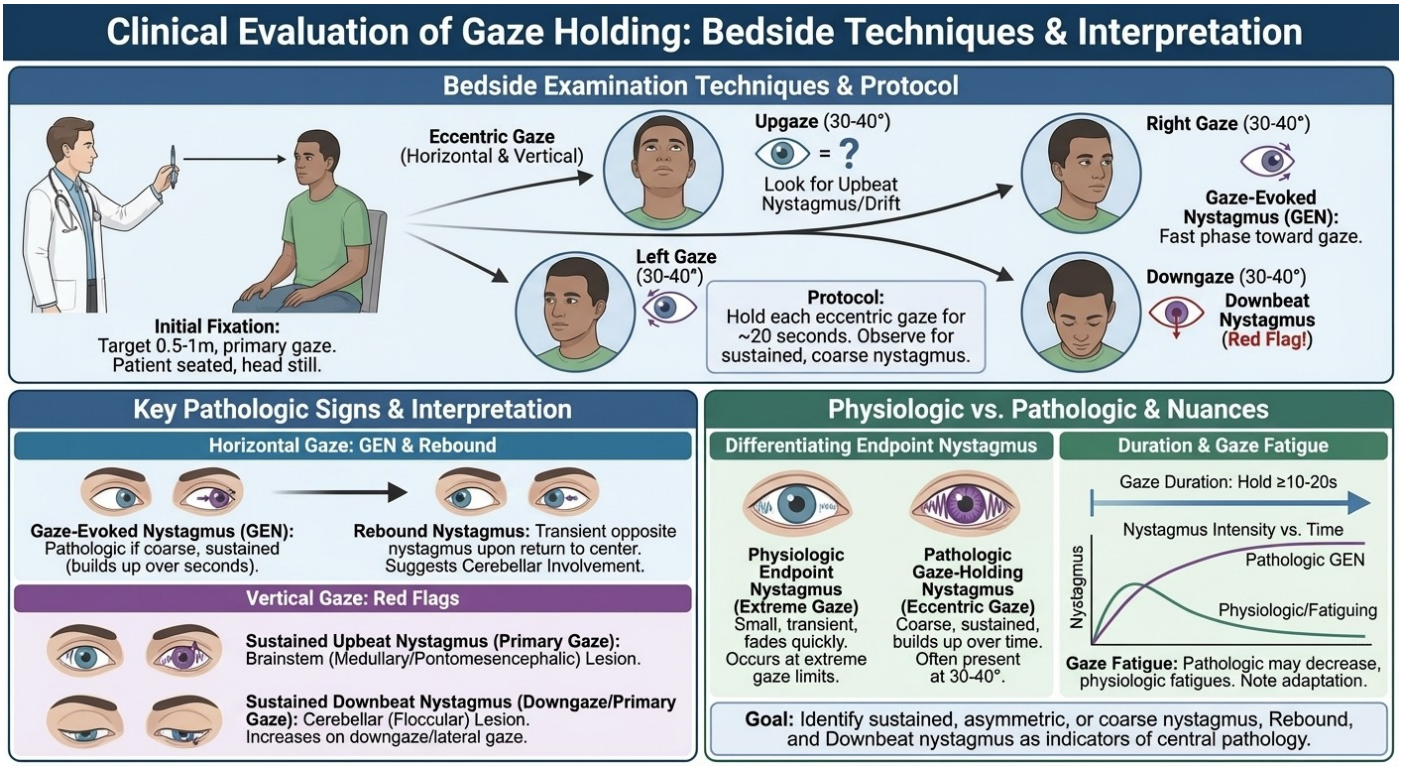


Clinical Evaluation of Gaze Holding

Bedside Examination Techniques: Evaluating gaze holding is straightforward but nuanced. The patient is asked to fixate on a target (such as the examiner's finger or a pen) at about 0.5 to 1 meter away and then to look eccentrically to the right, left, up, and down without turning the head. Typically, holding each eccentric gaze for about 20 seconds allows observation for nystagmus. It is important to test at least 30° to 40° off centre, as more subtle integrator leaks may not manifest at smaller gaze angles. During horizontal gaze holding, observe for any jerk nystagmus (fast phase toward the gaze direction indicates gaze-evoked nystagmus). In upward gaze, look for up-beating nystagmus or down-beating drift, and in downward gaze, note any downbeat nystagmus (a red flag for central pathology). Gaze-Evoked Nystagmus (GEN) is identified by a fast phase in the direction of eccentric gaze (e.g. right-beating on right gaze), whereas rebound nystagmus is checked by returning the eyes to centre after a prolonged eccentric gaze and watching for a few beats in the opposite direction [16]. The examiner should differentiate these from a small, endpoint physiologic nystagmus at extreme gaze. One approach is to bring the eyes just to the limit where any nystagmus starts; if the nystagmus is coarse, sustained, or the patient complains of inability to hold gaze, it likely indicates pathology.

Vertical and Eccentric Gaze: Vertical gaze-holding is tested by having the patient look as far up and down as possible. A few beats of endpoint upbeating nystagmus in upgaze can occur normally, especially in older patients, but sustained vertical nystagmus (upbeat or downbeat in primary or slight vertical gaze) is always abnormal. Downbeat nystagmus that increases on downgaze or lateral gaze strongly suggests a cerebellar (floccular) lesion [6]. Upbeat nystagmus present on straight-ahead gaze, conversely, is often due to a brainstem lesion (such as in the medullary or pontomesencephalic region) [17]. Testing downgaze (asking the patient to look down 20–30°) can bring out subtle downbeat nystagmus that might not be obvious in primary gaze. Eccentric Gaze Duration: It's useful to sustain the gaze for at least 10–20 seconds if safe for the patient (some may develop eye strain). Pathologic gaze-evoked nystagmus often builds

up a few seconds after eccentric gaze is maintained, whereas a transient end-point nystagmus usually fades quickly.



Identifying Rebound and Other Nuances: To elicit rebound nystagmus, have the patient look far right for ~20 seconds, then quickly return to centre. Observe for any transient left-beating nystagmus immediately upon return to primary gaze; then do the same after a far-left gaze (checking for right-beating on return). Rebound nystagmus is a subtle sign – it usually lasts only 5–10 seconds and the patient may not be aware of it. Its presence, even if slight, is highly suggestive of cerebellar involvement [16]. Another phenomenon to check is "gaze fatigue" – sometimes with prolonged eccentric gaze, a pathologic nystagmus may actually decrease as the neural integrator exhausts, or a physiologic nystagmus may fatigue. Noting whether nystagmus intensity adapts or remains steady can be informative.

Interpreting Findings in Context: The vestibular physician must interpret gaze-holding findings in light of the patient's overall condition. **Age:** Elderly patients often have mildly impaired gaze holding due to age-related neural integrator degeneration – a mild, symmetric gaze-evoked nystagmus at the extremes of gaze can be a normal aging variant. This "senescent nystagmus" should be low amplitude and not accompanied by other neurologic signs. **Medications:** Many drugs can cause nystagmus or make existing nystagmus more pronounced. Barbiturates, benzodiazepines, anti-epileptics (phenytoin, carbamazepine), lithium, and even high doses of anti-depressants or antihistamines can produce gaze-evoked nystagmus as a side effect [14,18]. Always review the medication list before attributing GEN to a structural lesion. If a patient on such medications shows gaze nystagmus, consider re-examining after holding medications if possible. **Fatigue and alertness:** A drowsy or fatigued patient may have difficulty sustaining eccentric gaze, and nystagmus may appear simply because the eyes are drifting due to inattention. Ensure the patient is optimally alert during the exam; brief rest and refocus can help if the exam is prolonged. Ultimately, pathological gaze-holding deficits should correlate with other signs – for example, presence of limb ataxia or dysarthria would reinforce a central lesion if GEN

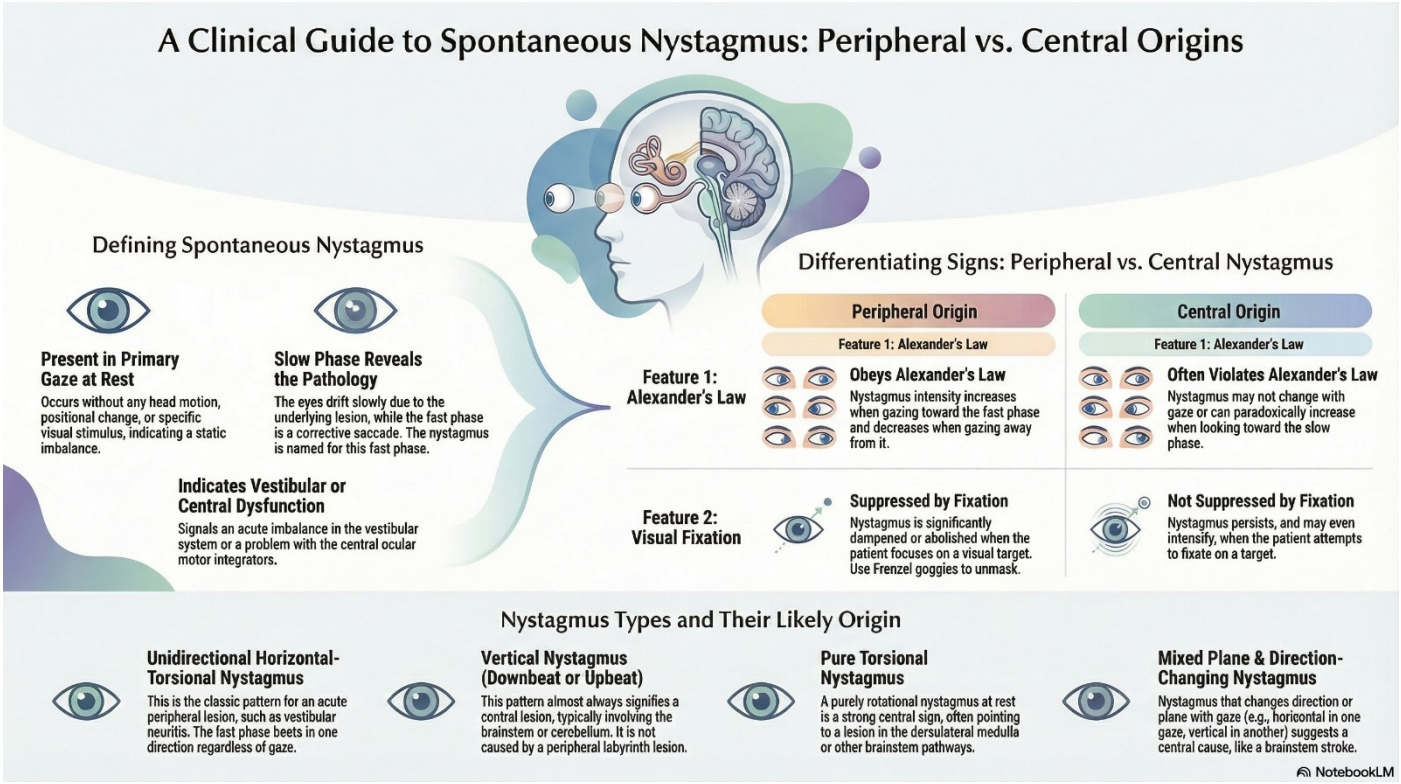
is observed. In contrast, an isolated mild gaze nystagmus in an older patient on sedatives, with an otherwise normal exam, might be observed over time rather than prompting an immediate MRI.

Spontaneous Nystagmus: Characteristics and Types

Definition and Fast/Slow Phases: Spontaneous nystagmus refers to nystagmus that is present in primary gaze (eyes looking straight ahead) without any deliberate provocation (no head motion, no positional change, no visual stimulus). It typically indicates an acute vestibular imbalance or central integrator dysfunction. Nystagmus consists of a slow drifting phase and a fast corrective phase; by convention it is named after the fast phase direction [1]. For example, if the eyes drift slowly to the left and then jerk back to the right, it is a right-beating nystagmus. The fast phase is a corrective saccade, while the slow phase reflects the pathological drift of the eyes away from the target. This slow phase is usually the hallmark of the underlying pathology (e.g., vestibular lesions cause slow phases toward the lesioned side). Clinically, jerk nystagmus is characterized by these distinct slow and fast components, whereas pendular nystagmus has oscillations without a clear fast phase (more often seen in congenital or certain central disorders).

Alexander's Law: Peripheral vestibular nystagmus usually follows Alexander's law, which states that the intensity of nystagmus increases when gazing in the direction of the fast phase and decreases when gazing in the opposite direction [13]. In practical terms, a patient with a right-beating spontaneous nystagmus will have the fastest slow-phase velocity and largest amplitudes when they look to the right (fast-phase direction), smaller nystagmus when looking straight ahead, and the nystagmus may almost vanish when they look to the left (away from the fast phase). This occurs because looking toward the fast phase effectively adds a gaze-holding load in the same direction as the drift, enhancing the imbalance, whereas looking away subtracts from it. Alexander's law is a useful clinical tool: if a spontaneous nystagmus is observed, checking gaze to either side will often reveal this pattern, supporting a peripheral vestibular cause [13,19]. (Central nystagmus, by contrast, often does not obey Alexander's law or may even paradoxically increase when looking in the direction of the slow phase, as can happen with some forms of upbeat nystagmus due to INC lesions [20].)

Fixation Suppression: One of the most distinguishing features of peripheral vs. central spontaneous nystagmus is the effect of visual fixation. In peripheral vestibular nystagmus, the nystagmus is significantly damped by visual fixation – if the patient fixes their gaze on a target (like the examiner's face or a distant letter), the cortical and cerebellar mechanisms (especially the flocculus) act to suppress vestibular nystagmus [5,21]. This is why we often use Frenzel goggles or remove fixation (darkness) to unmask a peripheral nystagmus during exam. A patient with acute vestibular neuritis may have minimal nystagmus when staring at an acuity chart (eyes open, fixating), but pronounced nystagmus when vision is removed (eyes closed or Frenzel lenses). In central nystagmus, by contrast, fixation typically does not suppress the nystagmus well [2,21]. A downbeat nystagmus from a brainstem lesion, for instance, will be readily visible even as the patient tries to fixate, and might even intensify with visual effort. This difference arises because peripheral nystagmus is driven by the vestibular nuclei, which are subject to cerebellar suppression via the vestibulo-cerebellum during fixation [5]. Central nystagmus originates within the brain's ocular motor network itself, often downstream of where fixation suppression can be effective.



Types of Spontaneous Nystagmus: Spontaneous nystagmus can manifest in various planes:

- **Unidirectional Horizontal-Torsional:** The classic acute peripheral vestibular nystagmus (e.g., in vestibular neuritis) is largely horizontal with a slight torsional component (the top poles of the eyes often beat toward the healthy ear) [19,21]. It is unidirectional – meaning the fast phase beats the same direction regardless of gaze (albeit with Alexander's law intensity changes).
- **Vertical Nystagmus:** This includes downbeat nystagmus (fast phase down, slow drift up) and upbeat nystagmus (fast phase up, drift down). Vertical nystagmus almost always signifies a central lesion [15,17]. Downbeat nystagmus is often evident in primary gaze and increases on looking down or lateral-down; upbeat is usually primary gaze or upgaze, sometimes increasing on upward gaze. These are never caused by a simple peripheral labyrinth lesion. Instead, they indicate brainstem or cerebellar pathology (discussed further below).
- **Pure Torsional Nystagmus:** A purely rotational (clockwise or counter-clockwise) nystagmus in primary gaze is also a central sign, usually implicating a lesion in the brainstem (such as the **dorsolateral medulla)** affecting specific vestibular pathways. Peripheral torsional nystagmus is typically seen in positional manoeuvres (like the torsional-upbeating nystagmus of posterior canal BPPV during Dix-Hallpike) but not as a sustained spontaneous nystagmus at rest. If torsional nystagmus is present spontaneously, one must think of central causes (or possibly an uncommon unilateral lesion affecting the anterior and posterior canals simultaneously, but this is rare).
- **Mixed Plane Nystagmus:** Many spontaneous nystagmus do not confine to a single pure plane. A brainstem stroke, for example, might cause a mixed horizontal-torsional nystagmus that changes with gaze direction (appearing more vertical-torsional in one gaze direction). Seesaw nystagmus, a rare form, has a torsional and vertical pendular oscillation (one eye rises and intorts while the other falls and extorts, then alternates) –

this too can appear as a mixed form of spontaneous nystagmus in certain parasellar or midbrain conditions (discussed later).

Oscillopsia and Symptoms: Patients with spontaneous nystagmus often experience oscillopsia – the illusion that the world is moving or bouncing – especially if the nystagmus is acquired and of high frequency. Interestingly, patients with longstanding infantile nystagmus may not have oscillopsia at all, as the brain adapts to ignore the oscillation [22]. In acute spontaneous nystagmus (like vestibular neuritis), oscillopsia is usually severe at onset (everything appears to "slip" with head or eye movement), and then gradually lessens over days as central compensation kicks in. Always ask patients about their perception of movement: this can help differentiate nystagmus from other eye movements (e.g., voluntary nystagmoid oscillations or minor intrusions usually don't cause oscillopsia).

Central vs. Peripheral Nystagmus Patterns

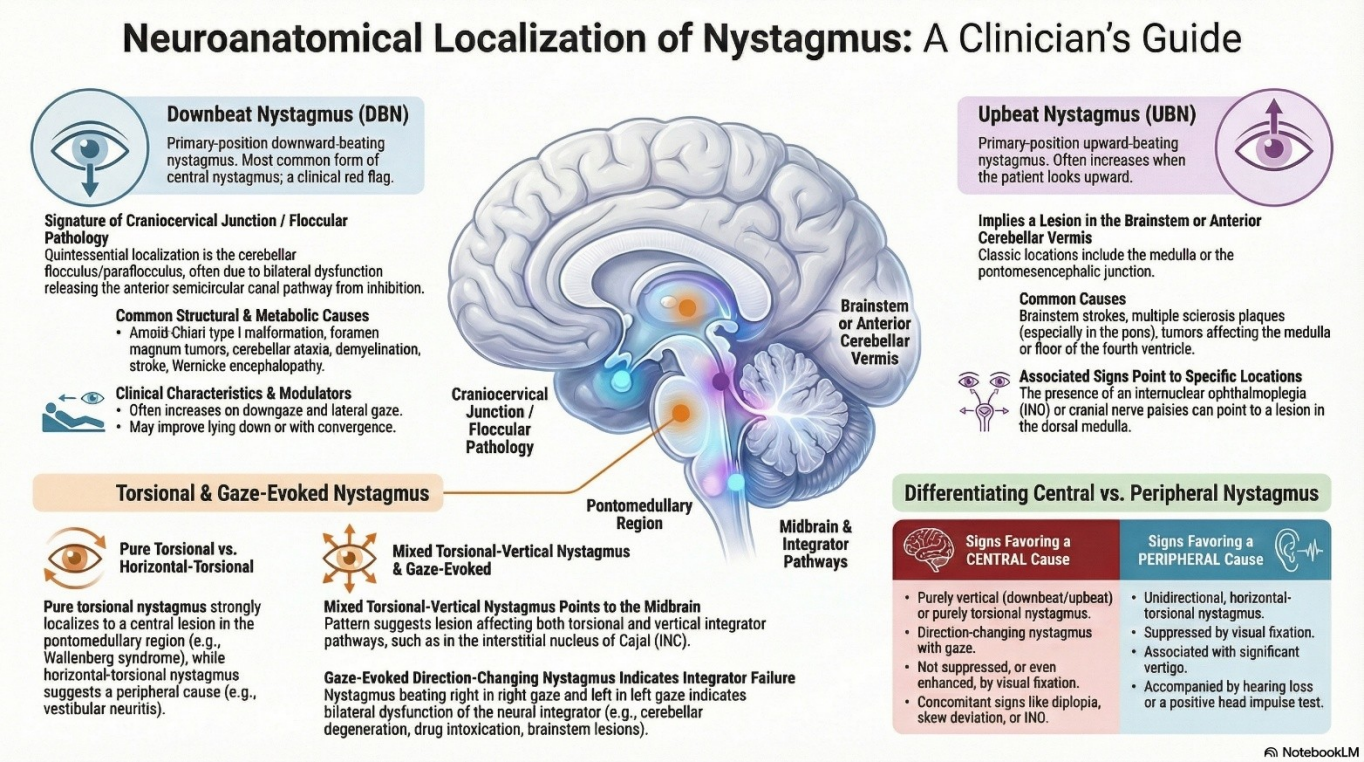
A major role of assessing gaze holding and spontaneous nystagmus is determining whether a vestibular disorder is peripheral (inner ear or VIII nerve) or central (brainstem/cerebellum). The table below summarizes key distinguishing features:

Feature	Peripheral Vestibular Nystagmus	Central Vestibular Nystagmus
Direction of Nystagmus	Unidirectional (fast phase usually away from lesion). Often mixed horizontal-torsional [19].	May be direction-changing with gaze (e.g. right-beat in right gaze, left-beat in left gaze) [12]. Can be pure vertical or pure torsional [17,21].
Alexander's Law	Follows Alexander's law (nystagmus intensifies when looking toward fast phase, diminishes looking away) [13].	Often does not follow Alexander's law; nystagmus may even invert or behave paradoxically with eccentric gaze [20].
Effect of Fixation	Strong fixation suppression [21]. Enhanced by removing fixation (e.g., Frenzel goggles).	Little or no fixation suppression [2,21]. May only be slightly more apparent in darkness.
Associated Vertigo	Typically, severe vertigo, nausea, vomiting at onset (patient truly feels spinning) [19,21].	Vertigo often less intense or absent; patient may report more dizziness or disequilibrium than true spinning [2,21].
Auditory Symptoms	Possible – e.g., tinnitus or hearing loss if labyrinth or nerve involvement (e.g. labyrinthitis, Ménière's).	Typically, none. If hearing loss is present, consider a labyrinthine stroke (AICA).
Gaze Dependency	Nystagmus direction is fixed (e.g. always right-beating), though intensity changes with gaze (Alexander's law).	Nystagmus often changes direction with gaze or position: e.g., purely horizontal in one gaze, beating opposite in another (gaze-evoked).
Other Ocular Motor Signs	None typical, aside from vestibular ocular reflex (VOR) deficits (e.g., positive head impulse test).	Often accompanies other abnormalities: gaze-evoked nystagmus, impaired smooth pursuit or saccadic dysmetria, skew deviation, etc. [2].
Positional Testing	Positional manoeuvres (e.g., Dix-Hallpike) may provoke nystagmus with	Positional nystagmus (if present) often has no latency and no fatigue with repetition [24].

	latency and fatigability [23].	

Localizing Clues – "Where is the Lesion?" Certain nystagmus patterns are virtually pathognomonic for specific neuroanatomic lesions:

- **Downbeat Nystagmus (DBN):** A primary-position downward-beating nystagmus is the signature of a **craniocervical junction or floccular pathology.** It is the most common form of central nystagmus [15]. DBN often increases on downgaze and on lateral gaze (downward drift with corrective downbeat saccade) [6,15]. Patients may report vertical oscillopsia (the world bouncing up and down). The quintessential localization for persistent downbeat nystagmus is the cerebellar flocculus/paraflocculus – bilateral floccular dysfunction (as in Arnold–Chiari type I malformation or degenerative cerebellar ataxias) **releases the anterior semicircular canal pathway from inhibition**, causing a tonic bias for upward drift corrected by downward quick phases [1,5]. Structural lesions at the cervico-medullary junction (foramen magnum area) such as Chiari I or a foramen magnum meningioma can cause DBN by compressing the floccular outflow or associated pathways. Other causes include demyelination, stroke, or nutritional deficiencies (e.g. Wernicke encephalopathy) affecting the medulla or vestibulocerebellum [10]. Clinically, DBN is a red flag; even if MRI is initially normal, an occult structural cause or a subtle metabolic cause should be sought. Some patients with downbeat nystagmus find it improves on lying down or with convergence **(a clue it's DBN, as convergence often dampens it).**
- **Upbeat Nystagmus (UBN):** An upward-beating nystagmus usually implies a lesion in the brainstem (medulla or pontomesencephalic junction) or sometimes the anterior cerebellar vermis [17]. UBN often increases on looking upward (sometimes called a primary position upbeat) [20]. Classic causes are brainstem strokes (e.g., in the medulla), multiple sclerosis plaques in the medial longitudinal fasciculus region of the pons, or tumours affecting the medulla or fourth ventricle floor. Unlike DBN, which is often persistent, UBN can be more transient and may even resolve spontaneously as the acute phase of a lesion passes [17]. If UBN is present acutely, one must search for other signs like an INO (internuclear ophthalmoplegia) or cranial nerve palsies that might point to an area like the dorsal medulla (e.g., a medullary infarct affecting perihypoglossal nuclei can cause UBN in the acute stage). Notably, UBN that increases on downward gaze or converts to DBN on upgaze has been associated with lesions of the INC in the midbrain (reflecting an unstable vertical integrator) [4].



- **Torsional Nystagmus:** Pure torsional nystagmus (with no or minimal horizontal/vertical component) strongly localizes to a lesion in the **pontomedullary region**, often affecting the vestibular nuclei or their interconnections [21]. For example, a **lateral medullary (Wallenberg) syndrome** can have a prominent torsional nystagmus (typically with a slight upbeat or downbeat bias) along with an ocular tilt reaction. The torsional fast phase is usually directed toward the side of the lesion if a vestibular nucleus is involved. In contrast, a torsional nystagmus with a vertical component (sometimes called mixed torsional-vertical) can indicate a midbrain lesion, such as in the interstitial nucleus of Cajal or rostral midbrain, where the torsional and vertical integrator pathways are both affected [4]. Peripheral vestibular lesions (like acute unilateral labyrinthectomy) often produce a torsional component to the nystagmus, but it's always coupled with horizontal movement (horizontal-torsional). Thus, isolated torsion implies a central cause, whereas torsion + horizontal suggests a peripheral axis (semicircular canal excitation).
- **"Cross-Coupled" or Gaze-Direction Changes:** A purely horizontal nystagmus in primary gaze that becomes direction-changing with gaze (right-beats in right gaze, left-beats in left gaze) is central – typically indicating **bilateral integrator dysfunction (often due to diffuse cerebellar or drug effect) or a paramedian brainstem lesion** [12,18]. A gaze-evoked nystagmus that changes direction (right-beating on right gaze, left-beating on left gaze) by definition means the integrator cannot hold in either direction – common in cerebellar degenerations, drug intoxications, or lesions affecting the NPH-MVN bilaterally [5,15]. If such a patient also has **a primary position nystagmus (like a slight resting nystagmus), consider a combined peripheral + central issue (e.g., Wernicke's disease can cause both a vestibular imbalance and a gaze-holding failure)** [10].

In practice, distinguishing central vs. peripheral nystagmus is the first priority when confronting a patient with spontaneous nystagmus. The presence of any of the following strongly favours a central cause: purely vertical or torsional nystagmus [15,17], direction-changing nystagmus with

gaze [12], nystagmus not suppressed (or even enhanced) by fixation [2,21], concomitant diplopia or skew deviation (suggesting a brainstem lesion), or other ocular motor signs like INO or gaze palsy. Conversely, a unidirectional horizontal-torsional nystagmus with significant vertigo, especially if there's also hearing loss or a positive head impulse test, is almost always peripheral (acute vestibular neuritis or labyrinthine issue). These guidelines, combined with the HINTS examination, approach 100% sensitivity for stroke in acute vestibular syndrome when applied properly [2,75].

Types of Pathological Nystagmus

Beyond the broad central vs. peripheral distinction, nystagmus is further classified into specific named syndromes or types based on when and how it appears. Each has diagnostic significance:

7.1 Gaze-Evoked Nystagmus (GEN)

Definition: Gaze-evoked nystagmus is a jerk nystagmus that is absent in primary gaze but appears when the eyes are held eccentrically. The fast phase beats in the direction of gaze (e.g. right-beating in right gaze) [12]. It arises from a failure of the neural integrator to maintain the eccentric eye position, leading to a centripetal drift and corrective saccades.

Clinical Features: GEN is typically horizontal (sometimes with a slight torsional component) on lateral gaze and can be vertical on upgaze. It is sustained as long as the gaze is maintained (unlike the transient physiologic end-point nystagmus). Often, if the integrator lesion is asymmetric, GEN may be present in one direction more than the other (or even only in one direction). In many cases of cerebellar disease, horizontal GEN is accompanied by a downbeat nystagmus in upgaze or primary gaze [6,15].

Aetiologies: Anything that impairs the gaze-holding network can cause GEN. Common causes include drug intoxications (anticonvulsants like phenytoin, barbiturates, benzodiazepines, alcohol) [14], which acutely reduce the integrator efficacy; cerebellar degenerations (especially those affecting the flocculus, as in spinocerebellar ataxias) which make the integrator leaky [15]; demyelination (e.g., MS plaques in the brainstem or cerebellum); stroke or ischemia in the medulla or pons affecting the NPH/MVN; Arnold–Chiari malformation (downward tonsillar pressure on medulla/cerebellum); and intracranial tumours (particularly those in the posterior fossa compressing the brainstem or fourth ventricle). Even advanced age is a mild cause – many elderly have a low-amplitude GEN due to age-related neural integrator decay.

7.2 Rebound Nystagmus

Definition: Rebound nystagmus is a transient jerk nystagmus that appears upon return to primary gaze after sustained eccentric gaze. If a patient holds an eccentric gaze for ~20 seconds and then centres their eyes, the eyes will drift back toward the previous eccentric direction and then jerk to centre, for a brief period [16]. Essentially, the integrator was "wound up" or biased in one direction and needs a few seconds to recalibrate once gaze returns to neutral.

Significance: Rebound nystagmus is almost always a sign of cerebellar dysfunction, especially of the vestibulocerebellum. It often accompanies gaze-evoked nystagmus in conditions like cerebellar degenerative diseases, MS, or after cerebellar infarctions [5,16]. In a classic cerebellar ataxia patient, you might see gaze-evoked nystagmus when they look left or right, and when

they look back to centre, a few beats of rebound nystagmus opposite to the previous gaze. The patient may not notice these beats, but they are a valuable clinical clue.

7.3 Bruns' Nystagmus

Definition: Bruns' nystagmus is a combination of two coexisting nystagmus patterns classically seen in large cerebellopontine angle (CPA) tumours (like vestibular schwannomas > 2–3 cm). It has two components: when the patient gazes toward the lesion side, they exhibit a slow, large-amplitude nystagmus (drift toward the lesion with a coarse corrective saccade), and when gazing toward the healthy side, they exhibit a faster, fine, small-amplitude nystagmus (resembling a gaze-paretic type) [1,25]. In plain language, looking toward the tumour yields a slow but big nystagmus, looking away yields a fast but small nystagmus. Both are present simultaneously depending on gaze.

Mechanism: The classic explanation is that the tumour causes two problems:

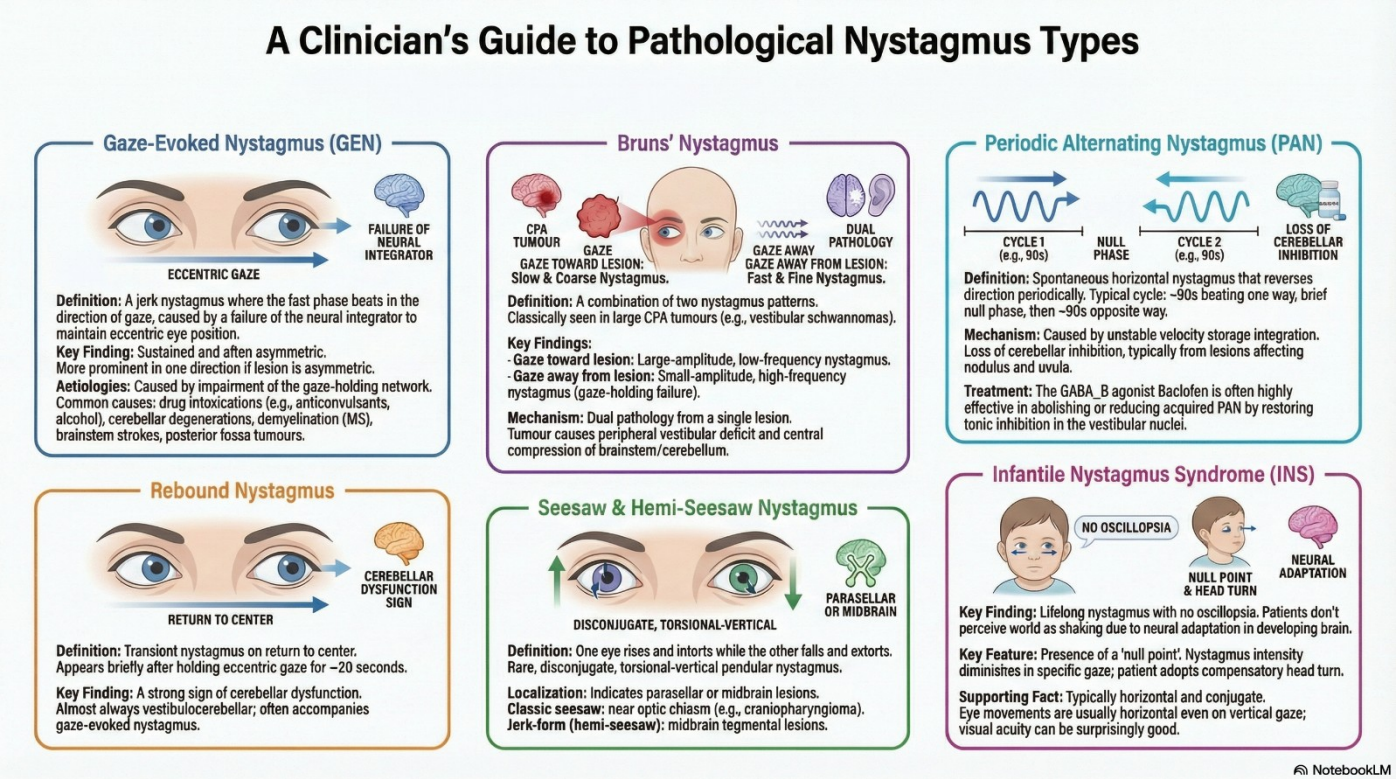
1. Vestibular nerve/inner ear deficit (peripheral) – this causes a vestibular nystagmus that beats away from the lesion side [19]. This nystagmus is typically low frequency but high amplitude when looking toward the lesion (since gaze toward lesion side requires slow phase toward healthy side, adding to the vestibular drift).
2. Brainstem or floccular compression (central) – the tumour compresses the cerebellar flocculus or brainstem gaze holding pathways, causing an ipsilateral gaze-holding failure [5,25]. This yields a gaze-evoked nystagmus when looking away from the lesion (e.g., looking left with a right CPA tumour) characterized by fast, small amplitude nystagmus (since the eye can't hold eccentric gaze to that side).

The net result is the Bruns combination. For example, a large right CPA meningioma: gaze right (toward tumour) → coarse right-beating nystagmus (vestibular component), gaze left → fine left-beating nystagmus (gaze-evoked component).

7.4 Seesaw and Hemi-Seesaw Nystagmus

Definition: Seesaw nystagmus is a rare pendular nystagmus in which one eye rises and intorts while the other eye falls and extorts, then they reverse – analogous to two kids on a seesaw [26]. In a full cycle, the eyes swap roles (the one that was up/intorting goes down/extorting and vice versa). If the movements have a jerk component (fast phase in one direction), it's termed hemi-seesaw nystagmus (one phase of the cycle is faster). Both are usually disconjugate and torsional-vertical in nature.

Localization: Seesaw nystagmus typically indicates a lesion in the parasellar region affecting the optic pathway and diencephalon, or sometimes a midbrain lesion interrupting interocular connections [26]. Classically, a large parasellar tumour such as a craniopharyngioma or pituitary adenoma compressing the chiasm and hypothalamus can produce seesaw nystagmus. Hemi-seesaw nystagmus (jerk form) has been associated with midbrain tegmental lesions (such as haemorrhages) and occasionally medullary lesions.



7.5 Periodic Alternating Nystagmus (PAN)

Definition: Periodic alternating nystagmus is a spontaneous horizontal nystagmus that periodically reverses direction every ~2 to 4 minutes [7,9]. A classic PAN cycle: about 90 seconds of right-beating nystagmus, a brief transition phase (maybe a few seconds of no nystagmus or small beats), then ~90 seconds of left-beating nystagmus, then repeat. The cycle length can vary. It is by definition conjugate horizontal nystagmus, oscillating in direction over time.

Mechanism and Localization: PAN is caused by an unstable velocity storage integrator in the vestibular system, often due to loss of **cerebellar inhibition from the nodulus and uvula** [7]. Think of it as the vestibular system's bias oscillating around zero – it points one way for a while, overshoots, points the opposite, and so on. Lesions or dysfunction of the nodulus are the most commonly implicated, as the nodulus normally dampens and resets the velocity storage mechanism.

Treatment: Baclofen, a GABA_B agonist, is famously effective in many cases of acquired PAN, often abolishing the nystagmus or greatly reducing it [8]. Baclofen presumably restores the tonic inhibition in the vestibular nuclei, rebalancing velocity storage. The standard dose is low (10–20 mg TID) and nystagmus may improve within days.

7.6 Congenital Nystagmus and Fixation Instability

Not all nystagmus indicates a new disease – some appear early in life due to congenital disorders of ocular motor control. **Infantile nystagmus syndrome (INS),** also simply called congenital motor nystagmus, is the most common form of congenital nystagmus. It usually manifests in the first few months of life as a **bilateral, conjugate horizontal oscillation** [22,27].

- It is typically **horizontal** (even on upgaze or downgaze, the movement remains horizontal).
- The nystagmus intensity often diminishes at a particular gaze position, known as the **null point** [27]. The child will adopt a head turn to bring their eyes to this null point, thereby improving their vision.
- **No oscillopsia:** Despite sometimes large amplitude eye movements, patients with lifelong nystagmus usually do not perceive the world as moving [22]. The brain adapts to the nystagmus during development by downweighting the errant visual feedback. Studies have shown reduced activity in motion-processing visual cortex (MT/V5) in these patients, explaining why they do not experience the "shaking" vision that an adult with new-onset nystagmus would.
- **Vision can be surprisingly good:** Visual acuity in INS can be near-normal in many patients (20/40 or better), because they develop strategies like foveation periods – brief moments in the nystagmus cycle where the eye velocity is near zero and the image is on the fovea [22].

Clinical Approach to Congenital Nystagmus: characterization of the nystagmus waveform and null point is essential. Surgical approaches (e.g., Kestenbaum-Anderson procedure) can be done to move the eyes' null position to primary gaze by rotating the muscles [27]. Pharmacologically, agents like memantine or gabapentin can modestly improve some cases of congenital nystagmus.

Nystagmus in Specific Clinical Scenarios

Having covered the mechanisms and types of nystagmus, we can apply these principles to real-world clinical scenarios:

8.1 Acute Vestibular Syndrome (AVS): This scenario demands rapid differentiation between vestibular neuritis (peripheral) and brainstem/cerebellar stroke (central). Nystagmus is a linchpin of this differentiation. In a classic vestibular neuritis, one finds a unidirectional, horizontal-torsional spontaneous nystagmus, usually beating away from the affected ear. This nystagmus will follow Alexander's law and will be readily suppressed by fixation – which is why such patients' nystagmus is much more pronounced when you remove fixation with Frenzel goggles [13,19]. The head impulse test (HIT) will be abnormal toward the lesion. In contrast, a central AVS (e.g., lateral medullary stroke or cerebellar infarction) often shows nystagmus that is atypical: it may be direction-changing gaze-evoked nystagmus, or a pure downbeat or upbeat nystagmus. Visual fixation does not eliminate the nystagmus [2]. These differences form the core of the HINTS exam: Head-Impulse, Nystagmus, Test-of-Skew. A HINTS "central" pattern has been shown to be more sensitive than early MRI for stroke [2,28].

8.2 Posterior Fossa Stroke: Different stroke locations produce characteristic nystagmus:

- **Lateral Medullary (Wallenberg) Syndrome:** A **torsional nystagmus** with the top of the eyes toward the lesion (**ipsiversive torsion**) is common, sometimes with a horizontal component that beats contralaterally. A subtle but specific sign in Wallenberg is **ocular tilt reaction** [21].
- **PICA Cerebellar Infarction:** This often causes **downbeat nystagmus and gaze-evoked nystagmus**, since the flocculus is highly sensitive to ischemia (PICA supplies it) [6,15].

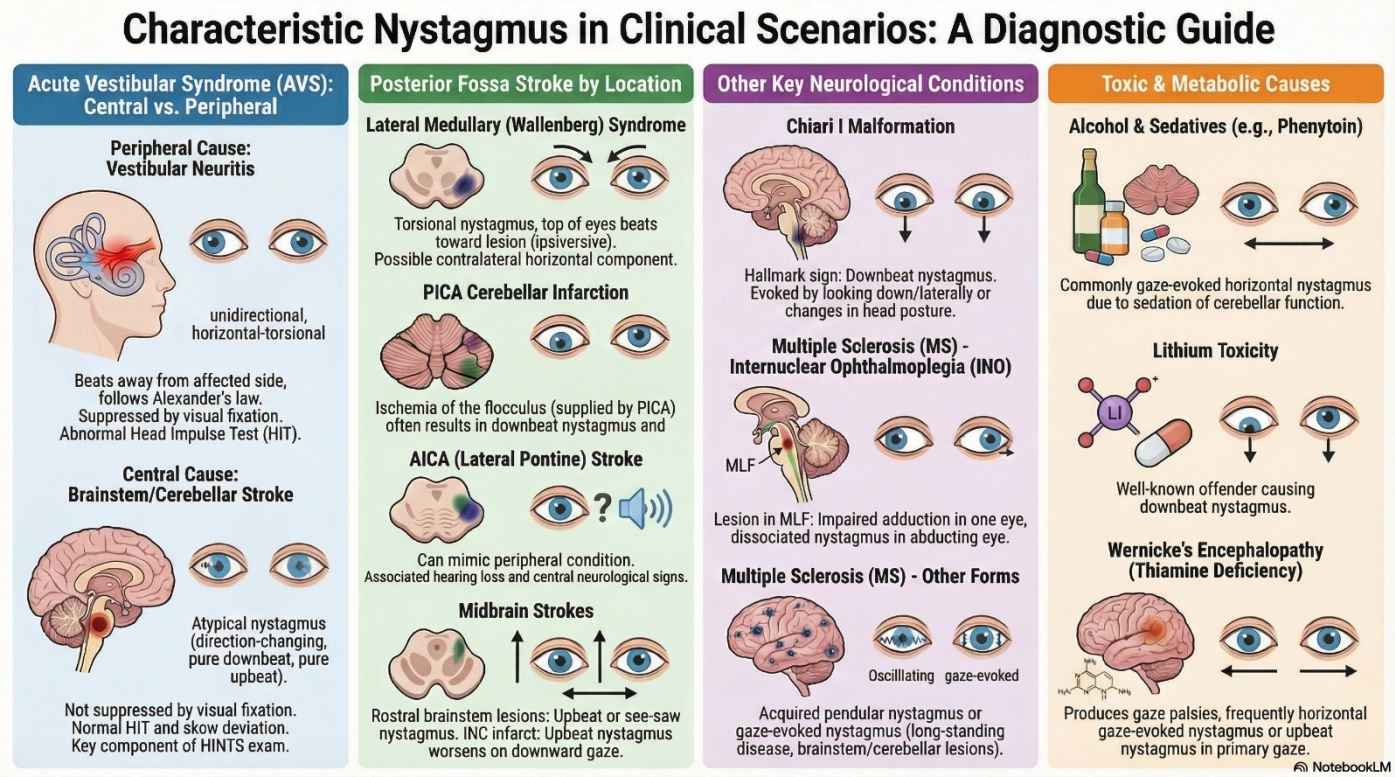
- **AICA (Lateral Pontine) Stroke:** can affect both the lateral pons and the inner ear. This can mimic a peripheral vestibular loss but often presents with hearing loss and other central signs [21].
- **Midbrain Strokes:** Infarcts in the rostral brainstem can cause **upbeat nystagmus or see-saw nystagmus.** For example, a paramedian midbrain infarct involving the INC can produce an UBN that increases when looking down [4,17].

In any suspected stroke with nystagmus, urgent neuroimaging and neurological consultation are warranted. In the first 1–2 days, small brainstem strokes can be MRI-negative (false negatives on DWI) [28,29].

8.3 Chiari I Malformation: The hallmark ocular motor sign is **downbeat nystagmus,** usually evoked in particular positions – especially on looking down and laterally or on changes in head posture [15].

8.4 Multiple Sclerosis: MS can cause a wide variety of nystagmus. Two classic ones are:

- **Internuclear Ophthalmoplegia (INO):** A lesion in the MLF causes impaired adduction of one eye and dissociated nystagmus of the abducting eye [1].
- **Pendular or Gaze-Evoked Nystagmus:** MS lesions in the brainstem or cerebellum can cause acquired pendular nystagmus, particularly in patients with long-standing disease.



8.5 Drug-Induced and Metabolic Nystagmus:

- **Alcohol:** notorious for causing gaze-evoked nystagmus due to sedation of cerebellar function [14].

- **Sedatives and Anticonvulsants:** Phenytoin toxicity is classic for causing nystagmus – usually gaze-evoked horizontal nystagmus [14,18]. Lithium is another common offender, known to cause a downbeat nystagmus [15].
- **Wernicke's Encephalopathy (Thiamine deficiency):** often associated with alcoholism; produces gaze palsies and frequently a horizontal gaze-evoked nystagmus or an upbeat nystagmus in primary gaze [10].

Laboratory and Video-Oculography Evaluation

Modern vestibular laboratories employ video-oculography (VOG) to quantify gaze-holding and nystagmus abnormalities. While the bedside exam is qualitative, VOG provides objective measurements such as slow-phase velocity (SPV) [30].

VOG objectively determines nystagmus direction and can identify subtle mixed nystagmus. For instance, it can quantify a small torsional component by tracking the torsional movement of the iris. It can also pinpoint a null point in congenital nystagmus. Lab recordings are particularly helpful to catch rebound nystagmus. In patients with suspected downbeat nystagmus, quantifying how much it increases on lateral gaze or with head position can also be done by recording in those positions. For example, a true BPPV nystagmus will show a crescendo-decrescendo waveform with a limited duration (<30s) on the trace and will fatigue with repetition [23].

Advanced Clinical Insights and Applications

Nystagmus Fatigue and Adaptation: In peripheral vestibular disorders, spontaneous nystagmus fatigues and central adaptation kicks in. Conversely, central nystagmus often does not "fatigue" in the same way – a downbeat nystagmus due to a structural lesion will persist until the lesion is treated [1,15]. A special case of fatigue is in BPPV positional nystagmus, where repeating the Dix-Hallpike leads to a smaller response [23].

HINTS Exam and Oculomotor Integration: The "N" (nystagmus) component is not just noting nystagmus presence but analysing its pattern [2]. Combining this with the head impulse and skew results increases confidence. Integration of all three signs plus considering gaze-holding function offers the best sensitivity. The advanced vestibular clinician also knows when HINTS might be misleading – for example, in a bilateral vestibular loss [28,29].

Integration with Other Ocular Motor Tests: A systematic ocular motor exam can localize lesions more precisely than any single test. For instance, if a patient has gaze-evoked nystagmus and hypermetric saccades and impaired smooth pursuit, the constellation strongly indicates a cerebellar lesion [1,5].

Therapeutic Monitoring and Prognosis: Nystagmus can be a biomarker for disease status. In degenerative cerebellar ataxias, tracking the progression of gaze-evoked nystagmus or downbeat amplitude can be a way to quantify disease worsening or therapeutic response (e.g., using 4-aminopyridine) [6].

In conclusion, gaze-holding function and spontaneous nystagmus are far more than physical exam curiosities – they are central to the art and science of neuro-otology. Mastery of their neurophysiological basis empowers the clinician to localize lesions with precision, distinguish peripheral from central causes of dizziness at the bedside, and provide timely, potentially vision

or life-saving, interventions. The vestibular physician who “listens” to the eyes can often discern the story of a patient’s disorder without a single invasive test.

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Accuracy and Currency

While every effort has been made to ensure the accuracy and completeness of the content, vestibular medicine is a rapidly evolving field. Clinicians are encouraged to verify specific protocols, normative values, and therapeutic recommendations against current published guidelines and primary literature.

References and Attribution

All referenced works are cited in good faith for educational purposes. Where specific normative data or clinical criteria are cited, the original sources should be consulted for full methodological detail and applicability to individual patient populations.

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Version 3.0 — April 2026 | Full ADC standard rebuild with front matter, table of contents, callout boxes, and image-preserving reformatting.

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