

# Physiology of the Vestibular System

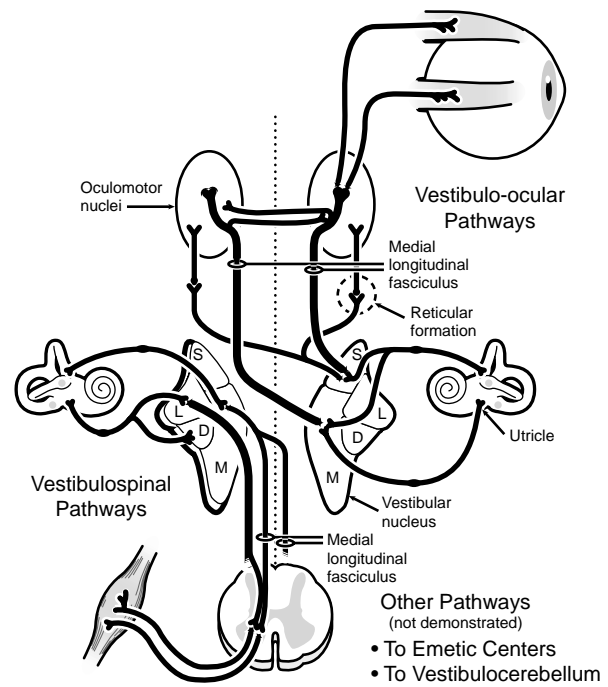
John A. Rutka, MD, FRCSC

Within the inner ear are specialized sensory receptors responsible for the perception of the forces associated with head movement and gravity. Control centers within the brainstem integrate this information along with other biologic signals derived from vision and proprioceptive sensors in the final determination of an individual's orientation in three-dimensional space.<sup>1</sup> Although anatomically developed and responsive at birth, the vestibular system matures along with other senses in the first 7 to 10 years of life.<sup>2</sup>

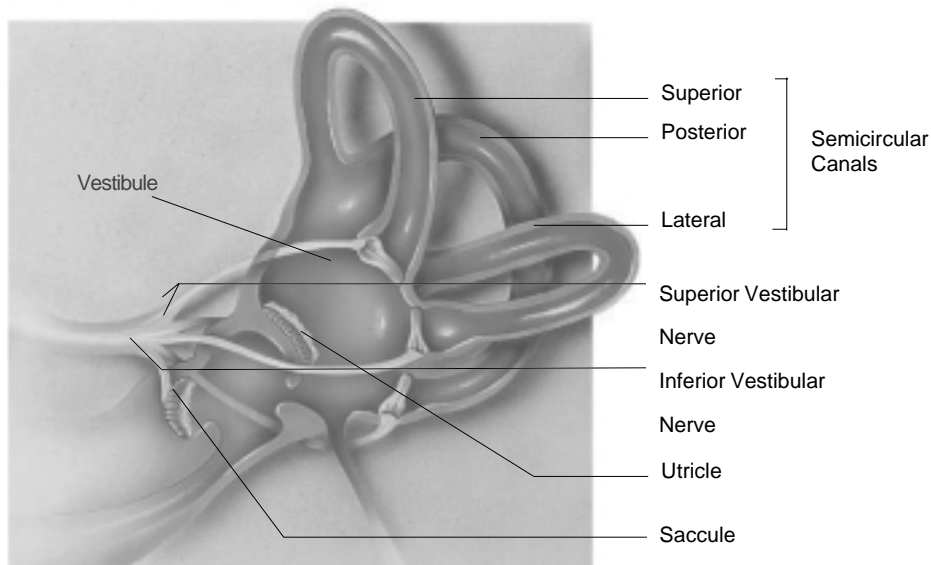
Recognition of the head's movement relative to the body is provided by the linear (otolithic macula) and angular (semicircular canals) acceleration receptors of the inner ear. Electrical activity generated within the inner ear travels along the vestibular nerve (primary afferent neuronal pathway) to the central vestibular nuclei of the brainstem, forming second-order neuronal pathways that become the vestibulo-ocular reflex (VOR), the vestibulospinal tracts, and the vestibulo-cerebellar tracts. Pathways derived from vestibular information also travel to the brainstem emetic centers, which serves to explain vegetative symptoms such as nausea, vomiting, and perspiration that a patient typically experiences following an acute unilateral vestibular loss (Figure 2-1).

Disruption of peripheral (inner ear and the vestibular nerve) or central vestibular pathways as a result of, for example, trauma, ototoxicity, or surgical deafferentation leads to the patient experiencing a distortion in orientation. The patient often uses the term "dizziness," which is an all-encompassing yet relatively nonspecific term that can include symptoms such as giddiness, lightheadedness, and floating sensation. Clinically, the term "vertigo" is best suited to describe a precise type of dizziness—a hallucination of movement involving oneself (subjective vertigo) or the surrounding environment (objective vertigo) that is apt to occur when there is an acute interruption of vestibular pathways.<sup>1</sup>

Of all the human vestibular pathways, the VOR remains the most important and most studied. At its simplest level the VOR is required to maintain a stable retinal image with active head movement. When an active head movement is not accompanied by an equal but opposite conjugate movement of the eyes, retinal slip occurs. When the VOR is affected bilaterally (as could occur from systemic aminoglycoside poisoning) patients characteristically complain of visual blurring with head movement, better known as oscillopsia, in addition to having significant complaints of imbalance and ataxia.<sup>3</sup> True vertigo is typically not a feature of a bilateral peripheral vestibular loss.



**Figure 2-1** Schematic representation of the vestibular system and its pathways.



**Figure 2-2** Anatomic organization of the peripheral vestibular system (vestibular end-organs and the vestibular nerve). Reproduced with permission from Solvay Pharma, Canada.

## ANATOMY OF THE VESTIBULAR SYSTEM

### Peripheral Vestibular System

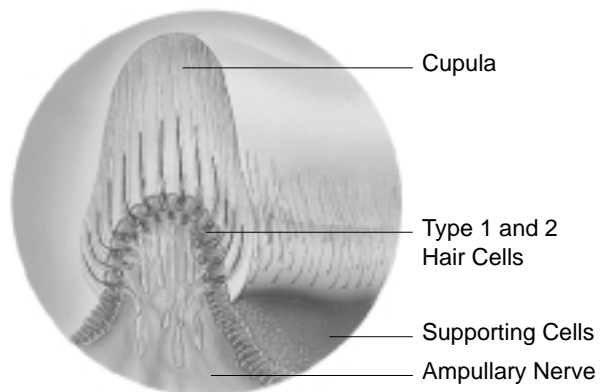
The peripheral vestibular system includes the paired vestibular sensory end-organs of the semicircular canals (SCCs) and the otolithic organs. These receptors are found within the fluid-filled bony channels of the otic capsule (the dense endochondral-derived bone that surrounds the labyrinth and cochlea) and are responsible for perception of both the sense of position and motion. The vestibular nerve (both superior and inferior divisions of the VIIIth nerve) is the afferent connection to the brainstem nuclei for the peripheral vestibular system (Figure 2-2).

Perception of angular accelerations is chiefly the responsibility of the three paired SCCs (superior, posterior, and lateral). Within the ampullated portion of the membranous labyrinth are the end-organs of the cristae, containing specialized hair cells that transduce mechanical shearing forces into neural impulses.

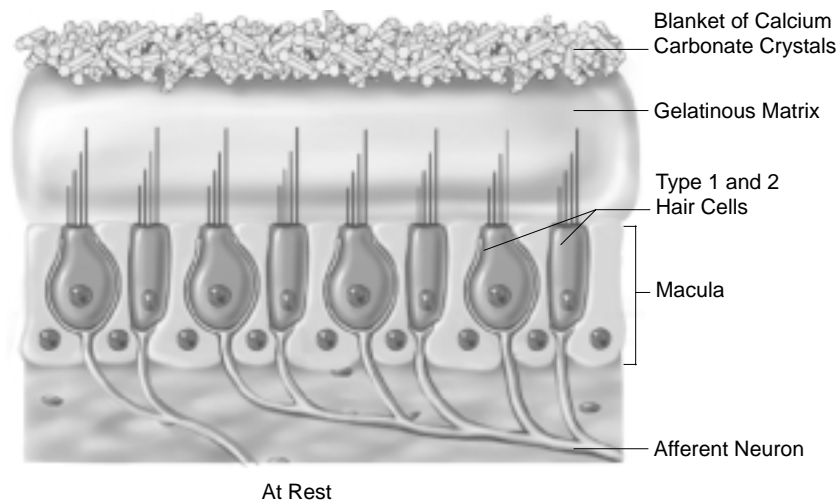
Histologically the hair cells of the ampulla are located on its surface. Their cilia extend into a gelatinous matrix better known as the cupula, which acts like a hinged gate between the vestibule and the canal itself (Figure 2-3).

The otolithic organs of the utricle and the saccule are found within the vestibule. Chiefly responsible for the perception of linear accelerations (eg, gravity, deceleration in a car), their end-organs consist of a flattened, hair cell-rich macular area whose cilia project into a similar gelatinous matrix. The matrix, however, differs from the matrix associated with the SCCs in its support of a blanket of calcium carbonate crystals better known as otoliths, which have a mean thickness of approximately 50  $\mu\text{m}$  (Figure 2-4).<sup>4</sup>

Information from the vestibular end-organs is transmitted along the superior (which receives information from the superior, horizontal SCCs and utricle) and inferior (which receives information from the posterior SCC and saccule) divisions of the vestibular nerve. Although its role is primarily afferent in the transmission of electrical activity to the central vestibular nuclei of the brainstem, an efferent system does exist that probably serves to modify end-organ activity.<sup>5</sup> Each vestibular nerve consists of approximately 25,000 bipolar neurons whose cell bodies are located in a structure known as Scarpa's ganglion, which is typically found within the internal auditory canal (IAC).<sup>6</sup> Type I neurons of the vestibular nerve derive information from corresponding type 1 hair cells, whereas type II neurons derive information from corresponding type 2 hair cells at its simplest.



**Figure 2-3** Stylized representation of the crista: angular acceleration receptor. Reproduced with permission from Solvay Pharma, Canada.



**Figure 2-4** Stylized representation of macular end-organ: linear acceleration receptor. Reproduced with permission from Solvay Pharma, Canada.

### Central Vestibular System

Primary vestibular afferents enter the brainstem dividing into ascending and descending branches. Within the brainstem there appears to exist a nuclear region with four distinct anatomic types of second-order neurons that have been traditionally considered to constitute the vestibular nuclei. It appears, however, that not all these neurons receive input from the peripheral vestibular system.<sup>4,7</sup> The main nuclei are generally recognized as the superior (Bechterew's nucleus), lateral (Deiters' nucleus), medial (Schwalbe's nucleus), and descending (spinal vestibular nucleus).

Functionally, in primate models, the superior vestibular nucleus appears to be a major relay station for conjugate ocular reflexes mediated by the SCCs. The lateral vestibular nucleus appears to be important for control of ipsilateral vestibulospinal (the so-called "righting") reflexes. The medial vestibular nucleus, because of its other connections with the medial longitudinal fasciculus, appears to be responsible for coordinating eye, head, and neck movements. The descending vestibular nucleus appears to have an integrative function with respect to signals from both vestibular nuclei, the cerebellum, and an amorphous area in the reticular formation postulated to be a region of neural integration. Commonly referred to as the "neural integrator" among neurophysiologists, it is responsible for the ultimate velocity and position command for the final common pathway for conjugate versional eye movements and position.<sup>8</sup>

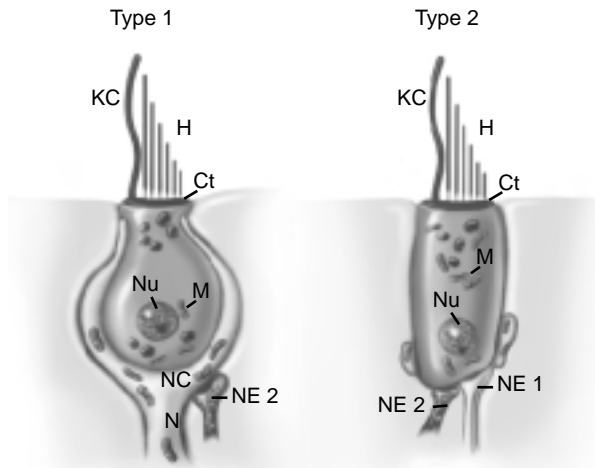
The vestibular nerve in part also projects directly to the phylogenetically oldest parts of the cerebellum—namely, the flocculus, nodulus, ventral uvula, and the ventral paraflocculus—on its way directly through the vestibular nucleus. Better known as the vestibulocerebellum, this area also receives input from other

neuronal pathways in the central nervous system (CNS) responsible for conjugate eye movements, especially smooth-pursuit eye movements, which, in addition to the VOR, are responsible for holding the image of a moving target within a certain velocity range on the fovea of the retina. The Purkinje's cells of the flocculus are the main recipients of this information, of which some appears to be directed back toward the ipsilateral vestibular nucleus for the purposes of modulating eye movements in relation to gaze (eye in space) velocity with the head still or during combined eye-head (vestibular signal-derived) tracking.<sup>9,10</sup> Important for cancelling the effects of the VOR on eye movement when it is not in the best interest of the individual (think of twirling ballet dancers or figure skaters and how they can spin without getting dizzy), the vestibulocerebellum is also important in the compensation process for a unilateral vestibular loss.<sup>7,9,10</sup>

### The Hair Cells

The fundamental unit for vestibular activity on a microscopic basis inside the inner ear consists of broadly classified type 1 and 2 hair cells (Figure 2-5).

Type 1 hair cells are flask-shaped and surrounded by the afferent nerve terminal at its base in a chalice-like fashion. One unique characteristic of the afferent nerve fibers that envelop type 1 hair cells is that they are among the largest in the nervous system (up to 20  $\mu\text{m}$  in diameter). The high amount of both tonic (spontaneous) and dynamic (kinetic) electrical activity at any time arising from type 1 hair cells has probably necessitated this feature for the neurons that transfer this information to the CNS. Type 2 hair cells are more cylindrical and at their base are typically surrounded by multiple nerve terminals in contradistinction.<sup>11</sup>

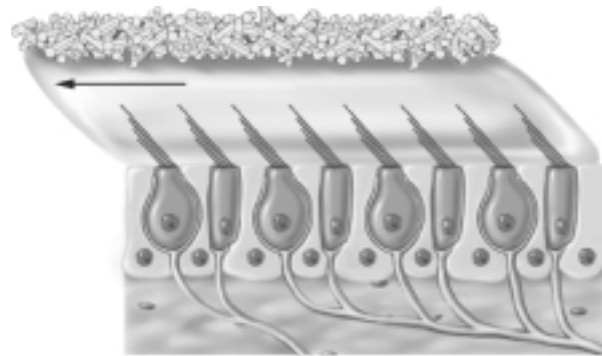


**Figure 2-5** Schematic representation of type 1 and type 2 hair cells. Ct = cuticular plate; H = hairs; KC = kinocilium; M = mitochondria; NC = nerve chalice; NE = nerve ending; Nu = nucleus.

Each hair cell contains on its top a bundle of 50 to 100 stereocilia and one long kinocilium that project into the gelatinous matrix of the cupula or macula. It is thought that the location of the kinocilium relative to the stereocilia gives each hair cell an intrinsic polarity that can be influenced by angular or linear accelerations. It is important to realize that an individual is born with a maximum number of type 1 and 2 hair cells that cannot be replaced or regenerated if lost as a result of the effects of pathology (eg, ototoxicity or surgical trauma) or aging (the postulated presbyvestibular dropout from cellular apoptosis). Presumably the same process holds for the type I and II neurons that comprise the vestibular nerve.

**APPLIED PHYSIOLOGY**

At the microscopic level, movements of the head or changes in linear accelerations deflect the cupula or shift the gelatinous matrix of the otolithic organs with its load of otolithic crystals that will either stimulate (depolarize) or inhibit (hyperpolarize) electrical activity from type 1 and 2 hair cells. Displacement of the stereocilia either toward or away from the kinocilium influences calcium influx mechanisms at the apex of the cell that causes either the release or reduction of neurotransmitters from the cell to the surrounding afferent neurons (Figures 2-6 and 2-7).<sup>12</sup> The electrical activity generated is then transferred along the vestibular nerve to the vestibular nuclei in the brainstem. Information above the tonic (spontaneous) firing rate of the type 1 hair cells transmitted along type I neurons is largely thought to have a stimulatory effect in contrast to a more inhibitory effect attributable to type 2 hair cells and type II neurons.

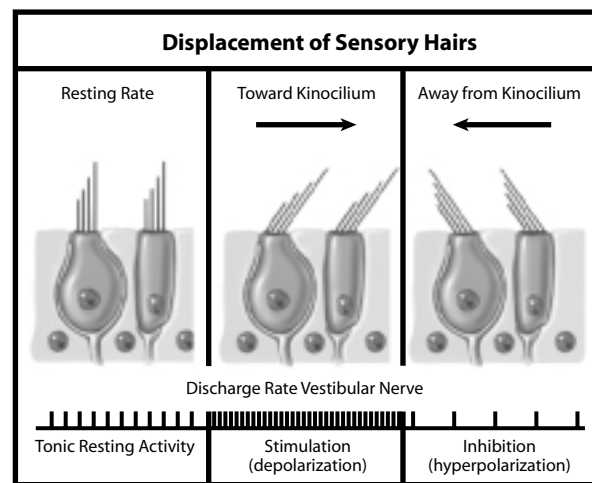


With Otolithic Displacement

**Figure 2-6** Physiology of macular stimulation and inhibition from otolithic shift and its shearing effect on stereocilia and kinocilium of the hair cells.

The SCCs largely appear to be responsible for the equal but opposite corresponding eye-to-head movements better known as the VOR. The otolithic organs are primarily responsible for ocular counter-rolling with tilts of the head and for vestibulospinal reflexes that help in the maintenance of body posture and muscle tone.

In order to ultimately produce conjugate versional VOR-mediated movements of the eyes, each vestibular nucleus receives electrical information from both sides that is exchanged via the vestibular commissure in the brainstem. The organization is generally believed to be specific across the commissure. Neurons in the right vestibular nucleus, for example, that receive type I input from the right horizontal SCC project across the commissure to the neurons found in the left vestibular nucleus that are driven by the left horizontal SCC receiving contralateral type II input and vice versa.<sup>7</sup>



**Figure 2-7** The physiology of motion and position sense. Concept of hair cell signal (electrical activity generation) at rest (resting discharge rate) and with respect to effects of movement resulting in depolarization (stimulation) and hyperpolarization (inhibition).

## KEY CONCEPTS

According to Leigh and Zee's seminal text, the key concepts of vestibular physiology can be best appreciated in the context that "the push-pull pairings of the canals, the resting vestibular tone and exchange of neural input through the vestibular commissure maximize vestibular sensitivity in health and provide a substrate for compensation and adaptation."<sup>7</sup>

### VOR Gain

In order to maintain a stable retinal image during head movement, the eyes should move in an equal but opposite direction to head movement. Anything less than unity (corresponding eye movement/head movement) may result in the perception of visual blurring with head movement—*oscillopsia* being the classic symptomatic complaint of an individual with a bilateral peripheral vestibular loss as might result from gentamicin vestibulotoxicity.

### Nystagmus

Defined as a rhythmic to-and-fro, back-and-forth movement of the eyes, nystagmus represents the cardinal sign of unilateral peripheral vestibular or central vestibular dysfunction.

In an acute unilateral loss of peripheral vestibular activity that might occur from topical aminoglycoside drops or certain disinfectant surgical preparation solutions used in the presence of a tympanic membrane defect, injury to the end-organ causes a difference in neural activity between the left and right vestibular nuclei. Should the push-pull pairings of the canals be affected as a result of pathology, the eyes are typically driven with a slow movement toward the affected side only to be corrected by a fast corrective saccade generated within the CNS away from the side of the lesion in a repetitive fashion. Although somewhat misguided, the direction of the nystagmus by convention refers to the fast phase, typically away from the side of the lesion under circumstances of an acute unilateral peripheral vestibular loss.

### Habituation and Adaptation

In humans the CNS may *habituate* (show a reduced response) the VOR depending on the environmental circumstances. This may happen in individuals who are blind or in those exposed to constant velocity rotations or continuous low-frequency oscillations (such as on a ship). The mechanisms for *adaptation* or the *adaptive plasticity* of the VOR are usually visually driven and have been experimentally studied by subjects wearing reversing prisms.<sup>13</sup> This phenomenon is frequently experienced by those wearing new prescriptive glasses with the explanation that "they take some time to get used to." Eventually one adapts to the new lenses as the

gain of the VOR changes accordingly. The same holds true to some extent for those with a unilateral peripheral vestibular loss, where the gain can be somewhat influenced, though not perfectly.

### Compensation

Clinical improvement following acute unilateral peripheral vestibular deafferentation requires the presence of intact central vestibular connections primarily at the level of the vestibulocerebellum.<sup>4,7</sup> The loss of tonic or spontaneous vestibular activity from the end-organ is ultimately replaced by the development of spontaneous electrical activity arising within the vestibular nuclei of the affected side.<sup>14</sup> At rest the asymmetries that would be expected from the push-pull effects from the canals are kept in check, and as a result there is the gradual resolution of the once-present spontaneous nystagmus. Quick head movements producing changes in the dynamic electrical activity, however, can never be completely compensated through this mechanism on the affected side, and a bilateral loss of inner ear function never does despite the insertion of midrotation corrective saccades. For a more detailed explanation of the phenomenon of compensation and why it often fails in the setting of a bilateral vestibular loss see Chapter 19, "Monitoring Vestibular Toxicity."

## CLINICAL MANIFESTATIONS OF VESTIBULAR DYSFUNCTION

Loss of vestibular function is associated with several signs and symptoms.

### Unilateral Peripheral Vestibular Loss

With a loss of unilateral vestibular function the patient acutely experiences the sensation of true vertigo from interruptions of VOR pathways and tends to lie perfectly still, as any movement aggravates vegetative symptoms such as nausea and vomiting that arise from the emetic centers. Nystagmus beating away from the side of lesion is the cardinal physical sign that obeys *Alexander's law* (the quick phase of the nystagmus induced by the imbalance in activity at the level of the vestibular nuclei is greatest in amplitude and frequency when the eyes are turned away from the side of the lesion).<sup>15</sup> Interruption in vestibulospinal tract pathways causes the patient to fall or list toward the affected side. Findings of ipsilateral hemispheric cerebellar dysfunction presenting with behaviors such as past-pointing, an inability to perform rapid alternating movements (dysdiadochokinesis), and gait ataxia reflect acute vestibulocerebellar tract involvement. Features distinguishing peripheral from central mediated nystagmus can be found in Table 2-1.

With compensation (implying the existence of a normal functioning CNS and contralateral peripheral vestibular system) there may be minimal symptoma-

**Table 2-1** Characteristics of Nystagmus/Oculomotor Abnormalities in Peripheral Vestibular vs Central Pathology

<i>Feature</i>	<i>Acute Unilateral Peripheral Loss</i>	<i>Bilateral Peripheral Loss</i>	<i>Central</i>
Direction of nystagmus	Mixed horizontal torsional (arching)	None expected	Mixed or pure torsional or vertical
Fixation/suppression	Yes	Yes	No
Slow phase of nystagmus	Constant	No nystagmus expected	Constant or increasing/decreasing exponentially
Smooth pursuit	Normal	Normal	Usually saccadic
Saccades	Normal	Normal	Often dysmetric
Caloric tests	Unilateral loss	Bilateral loss	Intact/direction of nystagmus often perverted (reverse direction)
CNS symptoms	Absent	Absent	Often present
Symptoms	Severe motion aggravated vertigo/vegetative symptoms	Oscillopsia/imbalance/gait ataxia, vertigo not a complaint	Vertigo not as severe as in acute unilateral loss

CNS = central nervous system.

tology that is only brought out by very rapid head movements. The spontaneous nystagmus disappears, vegetative symptoms resolve, gait improves, and in the case of a chronic condition the patient may experience only a slight imbalance when turning quickly.

**Bilateral Peripheral Vestibular Loss**

Vertigo is not a feature of a bilateral vestibular loss even when it occurs in an acute fashion. Injury to the end-organs as might occur in systemic aminoglycoside vestibulotoxicity causes a bilateral loss of function that tends to be electrically symmetric at the level of the vestibular nuclei in the brainstem. Instead the patient tends to complain of oscillopsia and imbalance. The gait is typically broad-based and ataxic, especially with eyes closed. Falls are not infrequent and in many instances

the patient requires assistive devices for ambulation or is relegated to a wheelchair. Compensation is generally unlikely to occur despite the best efforts of vestibular rehabilitation therapy and a greater reliance on information from visual and proprioceptive receptors.

**SPECIAL CLINICAL TESTS OF VESTIBULAR FUNCTION**

The following clinical tests are used at the bedside in the assessment of vestibular function and are specific for the VOR. A summary can be found in Table 2-2.

**High-Frequency Head Thrust or Halmagyi Maneuver**

Perhaps the most specific test for horizontal VOR function, the high-frequency head thrust, shares the

**Table 2-2** Special Clinical Tests of Vestibular Function

<i>Clinical Vestibular Test</i>	<i>Purpose</i>
High-frequency head thrust (Halmagyi maneuver)	High-frequency test of VOR function usually performed in the horizontal plane. Presence of refixation saccades to stabilize eyes on a target following fast head movement suggests a defect in the horizontal VOR
Head shake test for 15–20 seconds	High-frequency vestibular test. Presence of post-headshake nystagmus correlates well with increasing right/left excitability difference on caloric testing. Fast phase of nystagmus usually directed away from side of lesion.
Oscillopsia test	Visual loss of more than 5 lines with rapid horizontal head shaking while looking at a standard Snellen’s chart suggests a bilateral vestibular loss.
VOR suppression test	Inability to visually suppress nystagmus during head rotations suggests a defect at the level of the vestibulocerebellum. Pursuit eye movements are invariably saccadic

VOR = vestibulo-ocular reflex.

same physiologic basis as the “doll’s eye” maneuver in neurology. During a quick head movement to the normal side with the patient focusing on a target, there should be almost perfect compensatory conjugate versional movement of the eyes in an equal but opposite direction to head movement. When a defect occurs in the VOR, quick movements of the head are usually associated with incomplete compensatory conjugate eye movements often requiring refixation saccades to stabilize gaze.<sup>16,17</sup> Not surprisingly patients with a unilateral vestibular loss often volunteer subjective blurring of vision when they move their head to the affected side.

Although a positive head thrust maneuver is always indicative of pathology somewhere along the course of VOR, false-negative findings can arise. This can occur when an individual throws in corrective midrotation saccades that are imperceptible to the human eye. Identification with advanced eye-movement recording systems such as magnetic scleral coil search studies would typically be required.<sup>18</sup>

### Head Shake Test

Rapid horizontal head shaking for 15 to 20 seconds occasionally results in horizontal post-headshake nystagmus usually (but not always) directed away from the side of a unilateral vestibular loss.<sup>19</sup> Frenzel’s glasses are generally worn to prevent ocular fixation and suppression of nystagmus by vision. Headshake nystagmus is generally thought to occur when asymmetries in resting vestibular tone are exaggerated at the level of the postulated central velocity storage mechanism in the brainstem.<sup>20</sup>

### Dynamic Visual Acuity (Oscillopsia Testing)

Complaints of oscillopsia are best assessed by asking the patient to read the lowest line possible on a standard Snellen’s chart. While repetitively shaking the head in the horizontal plane (at a frequency  $> 2$  Hz) the patient is asked to read the lowest line possible for comparison purposes. A loss of more than five lines during active head-shaking is considered definitely clinically significant for a bilateral vestibular loss.<sup>21</sup> The test can also be performed using an optotype such as the letter “E” (the so-called dynamic illegible “E,” or DIE, test) presented in random orientations and different sizes on a chart or monitor. Comparison between the static and dynamic optotypes correctly identified has been used to determine if a bilateral vestibular loss exists.<sup>22,23</sup>

### VOR Suppression Testing (Fixation of Vestibular-Induced Nystagmus)

This test assesses the ability of the CNS to suppress a vestibular signal. It can be assessed by asking patients to follow with the head in the same direction an object that rotates (eg, patients look at their outstretched

hands held together while seated in a chair that rotates). If the vestibulocerebellum is intact then the eyes should remain stable in the orbit from visual fixation and suppression of the VOR. In central vestibular pathology, oculomotor testing typically reveals pursuit eye movements that are saccadic associated with the presence of a breakthrough nystagmus during head rotations as fixation is incomplete.<sup>24</sup> VOR suppression testing is somewhat analogous to the parallel phenomenon of failure of fixation suppression during caloric testing when visual fixation does not suppress caloric-induced nystagmus.

### SUMMARY

- The vestibular system is responsible for the perception of both the sense of position and motion. Angular accelerations are perceived by the SCCs, linear accelerations by the otolithic macula of the utricle and saccule.
- Vestibular pathways include the VOR, vestibulospinal tracts, and vestibulocerebellar tracts. Overall the VOR remains the most important and most clinically studied vestibular pathways, being responsible for the maintenance of a stable retinal image with active head movement. Defects in these pathways arising from pathology demonstrate several well-recognized physical signs, the cardinal sign of a unilateral peripheral vestibular loss being nystagmus.
- The concepts of VOR gain, nystagmus, habituation or adaptive plasticity, and compensation all have their substrates in the push–pull pairings of the canals, resting vestibular tone, and exchange of neural input through the vestibular commissure from peripheral and central vestibular pathways that maximize vestibular sensitivity in health and demonstrate pathologic features when diseased. (For detailed information regarding oculomotor and vestibular physiology, see Leigh and Zee<sup>7</sup> and Baloh and Honrubia.<sup>4</sup>)
- True vertigo is usually present in an acute unilateral peripheral vestibular loss. A bilateral peripheral vestibular loss typically results in oscillopsia (visual blurring with head movement) and imbalance that worsens in the absence of visual clues. True vertigo is rarely ever a feature of bilateral peripheral vestibular loss.
- Clinical bedside tests apply the concepts of vestibular physiology and are important in recognizing disease pathology involving the vestibular system. The high-frequency head thrust (Halmagyi maneuver) is probably the most specific clinical test of vestibular function. Other tests include the headshake test, oscillopsia testing, and VOR suppression and fixation.

**ACKNOWLEDGMENTS**

The author thanks Mr David Mazierski (medical illustrator), Ms Elise Walmsley (medical illustrator, TriFocal Communications), and Solvay Pharma Canada (illustrations and permissions).

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