Dizziness and Vertigo

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- Read the enclosed course.
- Complete the questions at the end of the course.
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Faculty

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Faculty Disclosure

Contributing faculty, Mark Rose, BS, MA, LP, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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The division planners and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Audience

This course is designed for physicians and nurses involved in the diagnosis, treatment, and care of patients with dizziness and/or vertigo.

Accreditations & Approvals

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NetCE designates this continuing education activity for 10 ANCC contact hours.

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Course Objective

The purpose of this course is to provide clinicians with the information necessary to appropriately diagnose and treat causes of dizziness and vertigo and improve patients' quality of life.

Learning Objectives

Upon completion of this course, you should be able to:

1. Identify models used to describe vertigo and dizziness.
2. Outline anatomy and physiology of structures involved in vestibular disorders.
3. List peripheral etiologies of vertigo.
4. Describe the clinical presentations of central etiologies of vertigo.
5. Discuss the causes and underlying pathophysiology of other dizziness/vertigo etiologies (e.g., trauma).
6. Devise a best practice, cost-effective diagnostic workup for patients presenting with dizziness and/or vertigo.
7. Apply diagnostic reasoning and appropriate clinical evaluation and management strategies to the differential diagnosis of dizziness and vertigo.
8. Compare and contrast pharmacotherapy agents that may be used to manage vertigo and dizziness.
9. Analyze the role of vestibular rehabilitation in the clinical management of dizziness/vertigo.
10. Describe other approaches to the management of specific dizziness etiologies.
11. Outline preventive approaches and safety considerations for patients with dizziness/vertigo.

EVIDENCE-BASED PRACTICE RECOMMENDATION

Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

INTRODUCTION

Advances in knowledge of pathophysiology and newer imaging techniques have led to a paradigm shift in the classification system and diagnostic algorithm for managing dizziness and vertigo. With this newly identified connectivity between vestibular, balance, and anxiety disorders comes an enhanced ability to identify the stroke mimics of benign dizziness or vertigo. These and other breakthroughs are transforming the clinical care of patients with dizziness and vertigo complaints, connecting clinical syndromes previously considered unrelated, and expanding the range of effective treatment options for patients.

The modern paradigm for the clinical management of dizziness and vertigo was introduced by Drachman and Hart in a seminal 1972 publication [1]. Based on patient response to the question "What do you mean by 'dizzy?'," dizziness was classified into one of four types that best reflected the subjective descriptions of the symptoms [2; 3]:

- Vertigo: Dizziness experienced as a definite sensation of movement or rotation in space
- Presyncope: A sensation of impending faint or loss of consciousness
- Disequilibrium: A sense of unsteadiness or loss of balance without head sensations
- Lightheadedness: Cannot be classed as vertigo, syncope, or disequilibrium

The Drachman-Hart model also suggested that vertigo had a vestibular cause, presyncope a cardiovascular cause, disequilibrium a neurologic cause, and nonspecific dizziness (lightheadedness) a psychiatric or metabolic cause [4]. In accordance with this framework, the character of symptoms reported by the patient determined the type (pathophysiology) of disorder and guided subsequent clinical evaluation, differential diagnosis, testing, and treatment [3].

By current standards, the Drachman-Hart model was based on weak evidence and developed in the absence of modern diagnostic imaging. In reality, patients often have difficulty describing their symptoms and may give conflicting accounts at different times. In one study, an estimated 62% of patients presenting to the emergency department (ED) with past-week dizziness selected more than one type of dizziness on a multi-response questionnaire, and 52% chose a different type when retested six minutes later [5; 6]. As such, the character and quality of symptoms alone does not reliably predict the cause of dizziness or serve as a dependable guide to management.

Primary care providers see at least 50% of patients who seek medical attention for dizziness or vertigo. The differential diagnosis is large, and each common etiology accounts for 5% to 10% of cases [7]. The central task for providers is to distinguish benign from serious or life-threatening causes of dizziness and vertigo, such as posterior circulation stroke. Misdiagnoses are common and diagnostic testing can be costly, especially if too much reliance is placed on this outdated diagnostic paradigm [8].

These factors can make the medical care of patients with dizziness/vertigo seem daunting. However, a new diagnostic paradigm has replaced the standard symptom-based approach with an algorithm that streamlines the differential diagnosis, increases diagnostic accuracy for benign and dangerous causes alike, and reduces the use of expensive and unhelpful brain imaging [3; 9].

A "timing and triggers" approach to patient history guides the diagnostic workup. The onset (timing), precipitating factors/events (triggers), evolution, associated symptoms and signs, and the context of dizziness episodes can be used to classify cases as triggered or spontaneous forms of episodic, acute, or chronic vestibular syndromes. Placement within one of six vestibular syndromes informs the differential diagnosis, targeted physical exams, and testing. Targeted exams are a range of procedures that assess for peripheral or central causes of dizziness/vertigo without using less accurate, expensive brain imaging [8].

ANATOMY AND PHYSIOLOGY

The labyrinth in each inner ear houses the systems that serve the functions of hearing (auditory) and balance (vestibular). The auditory system involves the cochlea, which transmits sound signals to the brainstem via the cochlear branch of the 8th cranial nerve. The vestibular system is comprised of the vestibular end-organs in the labyrinth, the vestibular nuclei in the brainstem and cerebellum, and the vestibular branch of the 8th nerve, which relays labyrinthine input to the vestibular nuclei. The 8th cranial nerve is also called the vestibulo-cochlear nerve [10; 11; 12].

Within each labyrinth are five vestibular end-organs (three semicircular canals and two otolith organs) that help maintain spatial orientation, postural control, and egocentric perception. Changes in angular and linear head acceleration, movement, and orientation to gravity are detected and signaled via the 8th nerve to brainstem and cerebellar circuits, through thalamic and spinal vestibular projections, and finally to the cerebral cortex [13; 14; 15].

This vestibular input, along with visual input from the eyes and proprioceptive input from peripheral sensory nerves (via the spinal cord), is relayed to the cerebral cortex, which integrates the sensory inputs and adjusts outgoing motor responses to maintain balance, posture, and gaze stabilization of retinal images (via the vestibulo-ocular reflex) [11; 14; 16].

Vertigo, dizziness, spatial disorientation, and disequilibrium can result from: asymmetrical vestibular inputs; vestibular hypofunction causing sensory mismatch in brain integration of sensory inputs; pathologies that affect any peripheral (e.g., inner ear, 8th cranial nerve) or central (e.g., vestibular nuclei and brainstem or cerebellar connections) vestibular system component; or a host of systemic, drug-effect, psychiatric, and physical trauma-related factors [14; 16; 17]. Around 80% of dizziness or vertigo cases are peripheral and 20% are central in origin [11].

EPIDEMIOLOGY

Dizziness is a general, umbrella term that encompasses symptoms of impaired spatial perception. Vertigo is often consolidated into the umbrella term dizziness due to highly variable descriptions of the experience. Dizziness/vertigo is the second most common complaint in the ambulatory setting and constitutes 25% of neurology outpatient referrals, 13% of ED neurology consultations, and more than 3 million ED visits annually [9; 18]. The primary complaint of dizziness accounts for 5.6 million clinic visits annually in the United States. Vertigo is roughly two-thirds more common in women than men. Prevalence increases with age but varies depending on the etiology [19].

Benign paroxysmal positional vertigo (BPPV) is the most frequent vestibular disorder and the most common cause of peripheral vertigo, with a lifetime prevalence of 10% [20]. In the general population, the one-year prevalence rate is about 5% for vertigo, 1.6% for BPPV, and <1% for vestibular migraine [19]. An estimated 17% to 42% of vertigo cases are diagnosed as BPPV [21].

Peripheral causes of vertigo are usually, but not always, benign, while central vertigo often indicates a more serious pathology [11]. The negative impact of vertigo should not be underestimated; around 80% of patients report interruption in daily activities, including employment, from symptoms and the need for medical attention [19].

Dizziness, vertigo, and associated symptoms do not always fall easily into either a peripheral or central syndrome or disorder. Patients can have a dominant group of symptoms more closely tied to peripheral or central origin, while others will show a mix of both groups [22].

In the following discussion of pathophysiology, the diagnostic entities associated with dizziness or vertigo are mainly organized by peripheral or central origin and by shared etiologies or clinical features in a few instances. Throughout this course, "benign" is a pathologic and not a clinical descriptor; "benign" vestibular conditions can be intensely distressing for the patient.

PERIPHERAL CAUSES OF DIZZINESS AND VERTIGO

BENIGN PAROXYSMAL POSITIONAL VERTIGO

As indicated by the name, BPPV describes benign (not life-threatening or malignant) paroxysmal (comes in sudden, brief spells) positional (triggered by certain head positions or movements) vertigo [23]. It is characterized by rotational vertigo induced by head position changes, especially when extending or turning the neck, lying down, or rolling over in bed [20].

Epidemiology

As noted, BPPV is the most frequent vestibular disorder and the most common cause of peripheral vertigo, with a lifetime prevalence of 10% [20]. Women are more often affected than men, with a female-to-male ratio of 1.5–2.2 to 1 [21; 24; 25].

The most frequent age of onset is between the fifth and seventh decades of life. BPPV has an overall prevalence of 3.4% in persons older than 60 years of age and is present in 40% of geriatric patients seen for dizziness [26]. The incidence increases with age due to age-related degeneration of the otolithic membrane [9]. The adverse impact on health and quality of life is more severe in older individuals, and BPPV is an important health concern in the elderly because it contributes to falls and associated morbidity and mortality [15; 21].

With a 27% to 50% rate of spontaneous resolution, BPPV can be self-limiting or may persist to become a chronic recurrent disorder [15; 21]. An estimated 85% of patients experience interrupted daily activities/lost days at work, 68% reduce their workload, 4% change their job, and 6% quit their job from the disruptive impact of BPPV [27].

The direct and indirect costs of BPPV are significant. Delayed diagnosis and treatment is frequent. It costs an average $2,000 to arrive at the correct diagnosis, and costs related to BPPV diagnosis alone approach $2 billion annually [21].

Only 10% to 20% of patients with BPPV seen by a physician receive recommended repositioning therapy. Before specialist referral, more than 65% of patients receive potentially unnecessary diagnostic testing or treatment, including magnetic resonance imaging (MRI) (70%), computed tomography (CT) (45%), electrocardiogram (41%), and medication therapy (53%). Delayed diagnosis and treatment of BPPV has cost and quality-of-life implications for patients and their caregivers [21; 27].

Across disciplines, the practice variations in BPPV management are considerable, and medication treatment of BPPV varies substantially among primary care providers and across specialties [21].

Pathophysiology

The vestibular system includes three semicircular canals (or simply "canals") and two otolith organs (the saccule and utricle). The canals (posterior, lateral, and anterior) are positioned at right angles to each other to detect angular accelerations of the head. The canals are organized as functional pairs (left and right ear) in the same spatial plane; any rotation in that plane excites one pair member and inhibits the other [28; 29]. The canals are filled with endolymph fluid and lined with sensitive hair cells to act like a gyroscope. Motion from head rotation induces endolymph movement in the canal oriented in the spatial plane, which stimulates hair cells, activates the ampulla (the motion sensor) and cupula, and sends sensory output to the brain via the vestibular nerve [15; 28].

The saccule and utricle contain sensory epithelium and function to detect linear or translational acceleration forces (e.g., gravity, accelerating or braking a car) [15]. Hair cells in the saccule and utricle are embedded in a matrix of calcium carbonate crystals (otoliths). Deflection of otoliths by gravity stimulates or inhibits neuronal output from the attached hair cells [11].

Otoliths that dislodge and migrate into a canal are called otoconia. Endolymph fluid is usually non-reactive to gravity, but otoconia moves with gravity, causing inappropriate endolymph motion and hair cell stimulation and false signaling of head motion to the brain [23].

The brain receives and integrates peripheral sensory inputs. A false vestibular input conflicts with inputs from ocular, proprioceptive, and the unaffected vestibular systems. This causes a sensory mismatch in the brain integration, perceived as a spinning sensation (vertigo) normally lasting less than 60 seconds after cessation of head movement and inappropriate endolymph motion [23; 30].

BPPV is subtyped by afflicted canal and mechanism. Posterior canal BPPV (85% to 95%) is the most common. Lateral canal BPPV (5% to 15%) is less common, likely because it self-resolves sooner. Anterior canal BPPV (<1%) is uncommon due to the orientation. Rare variants include multi-canal and bilateral multi-canal BPPV [15; 21].

Otoconia contact abnormally stimulates the cupula, triggering vertigo and nystagmus. BPPV is subtyped as [20; 31]:

- Canalithiaisis: Head movements cause free-floating otoconia to stimulate the cupula
- Cupulolithiasis: Otoconia attach to the cupula, rendering it hypersensitive to linear acceleration and gravity

Canalithiasis is much more common because the otoconia particulate mass required to exceed the symptomatic threshold is much lower than in cupulolithiasis (0.087 ug vs. 0.69 ug) [20; 32].

Recurrence and Cardiovascular Risk Factors

Cardiovascular comorbidities are significantly associated with, and potentially important risk factors for, recurrent BPPV. In a nationwide study of 2,682 patients with BPPV (mean age: 59.3 years; 61% female), the prevalence of high blood pressure (55.8%), hypercholesterolemia (38.6%), diabetes (17.7%), and family history of cardiovascular disease (49.4%) were significantly higher than the national averages [33]. A high percentage of patients had hearing loss (42.9%), tinnitus (41.2%), or both (26.8%). The presence of hypertension, dyslipidemia, and pre-existing cardiovascular comorbidities were significantly related to recurrent BPPV episodes, and the presence of diabetes or thyroid/autoimmune disease was also relevant [33].

VIRAL OR BACTERIAL INFECTIOUS CAUSES

Vestibular Neuritis

Vestibular neuritis, the second most common cause of vertigo (after BPPV), is a viral or post-viral inflammatory disorder affecting the vestibular portion of the 8th cranial nerve. It most commonly affects persons 30 to 50 years of age, and men and women are equally affected. New cases are more common in the spring and early summer [10; 34]. Histopathologic nerve studies of these patients are consistent with a viral inflammatory etiology [15].

Vestibular neuritis is characterized by the sudden, acute onset of severe vertigo, nausea, vomiting, and gait instability without hearing loss, typically preceded by an upper respiratory tract infection [35]. The course and treatment of vestibular neuritis and viral labyrinthitis are similar; in both, the severity of acute vestibular symptoms can raise concerns of a central etiology, and the severity of vertigo, nausea, and vomiting reflects the severity of vestibular asymmetry [7; 15; 34].

Viral Labyrinthitis

Labyrinthitis is an inflammatory disorder affecting both the vestibular and cochlear components of the 8th cranial nerve, caused by local or systemic viral or bacterial infection resulting in acute loss of vestibular and hearing function [10]. Viral labyrinthitis, the most common form of labyrinthitis, often results from varicella zoster, influenza, or herpes simplex-1 infection [35]. Sudden sensorineural hearing loss in the affected ear is due to pan-labyrinthine inflammation affecting the cochlea. The estimated prevalence of sudden sensorineural hearing loss is 1 case in 10,000 persons; up to 40% of these patients have prominent vertigo or disequilibrium symptoms, and up to 15% of patients presenting with positional vertigo have viral labyrinthitis [35].

The acute onset of sudden sensorineural hearing loss with severe vertigo, nausea, and vomiting can leave patients bedridden until the symptoms subside. Upper respiratory tract infection precedes the onset of vestibulo-cochlear symptoms in up to 50%. Vertigo usually resolves after several days to weeks, due to spontaneous partial recovery of vestibular function and central compensation of residual unilateral vestibular deficits. Unsteadiness and positional vertigo can persist for months, and return of hearing usually coincides with return of vestibular function [34; 35].

Herpes zoster oticus (Ramsay-Hunt syndrome) is labyrinthitis due to reactivation of a latent varicella zoster virus infection. Inflammation of the vestibulo-cochlear nerve causes vertigo and symptoms of deep, burning, auricular pain followed by eruption of a vesicular rash in the external auditory canal and concha. Symptoms usually improve after several weeks, but permanent hearing loss is common [15; 19].

Bacterial Labyrinthitis

Viral labyrinthitis should be differentiated from the more dangerous disorder of bacterial labyrinthitis, which occurs through direct bacterial invasion (suppurative labyrinthitis) or passage of bacterial toxins and other inflammatory mediators into the inner ear (serous labyrinthitis) [35; 36]. The bacteria that cause labyrinthitis are the same bacteria responsible for meningitis and otitis; potential bacterial causes include *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Streptococcus* species, *Staphylococcus* species, *Escherichia coli*, and *Mycobacterium tuberculosis* [35].

Profound hearing loss, severe vertigo, ataxia, and nausea and vomiting are common symptoms of bacterial labyrinthitis. Suppurative labyrinthitis almost always results in permanent, profound unilateral hearing loss (or bilateral loss with meningitis). Serous labyrinthitis results in unilateral, high-frequency hearing loss in the affected ear. Regardless of etiology, bacterial labyrinthitis accounts for 35% of all adult-onset cases of hearing loss [35].

MÉNIÈRE DISEASE

Ménière disease is a clinical syndrome of cochlear and vestibular symptoms with a prevalence of 34 to 190 per 100,000 population, an age of onset ranging from the third to seventh decades of life, and a slight female predominance. The odds of Ménière disease are greater among older subjects, persons of European descent, and severely obese persons. Common comorbid conditions in Ménière disease include arthritis, psoriasis, gastroesophageal reflux disease, irritable bowel syndrome, and migraine [15; 37].

The clinical features of Ménière disease are characterized by sudden, fluctuating, unilateral low-frequency sensorineural hearing loss with tinnitus and aural fullness and by spontaneous attacks of vertigo with nausea and vomiting, usually lasting hours [15]. Cochlear symptoms can occur between vertigo episodes. Vertigo is often more frequent in the first years of Ménière disease, but the clinical course is variable, with cochlear and vestibular symptoms taking years to develop in some patients. Bilateral sudden sensorineural hearing loss, migraine, BPPV, or systemic autoimmune disease develops in a subgroup of patients [37].

Ménière disease is idiopathic but is also associated with endolymphatic hydrops, a process whereby accumulation of excess pressure within the inner ear endolymphatic system causes fluctuating hearing loss, episodic vertigo, tinnitus, and aural fullness (i.e., pressure and uncomfortable fullness in the ears) [38]. An interaction of genetics and environmental factors is thought to determine the onset of Ménière disease. While associated with the accumulation of endolymph in the cochlear duct and vestibular organs, endolymphatic hydrops per se does not fully account for the frequency of vertigo attacks, progression of hearing loss, and other clinical features of Ménière disease [37].

EVIDENCE-BASED PRACTICE RECOMMENDATION

The Bárány Society recommends that familial Ménière disease should be considered if at least one other relative (first- or second-degree) fulfills all the criteria of definite or probable Ménière disease.

(http://www.jvr-web.org/images/55807-Lopez-Escamez.pdf. Last accessed September 23, 2021.)

Level of Evidence: Expert Opinion/Consensus Statement

BILATERAL VESTIBULOPATHY

Bilateral vestibulopathy (also called bilateral vestibular loss) has both central and peripheral processes. The cardinal symptoms of bilateral vestibulopathy reflect the pathophysiology, including motion-dependent postural vertigo with unsteady gait and stance that worsens in darkness and on uneven ground (vestibulo-spinal impairment), and oscillopsia with blurred vision when walking or moving the head (vestibulo-ocular reflex impairment). Patients with bilateral vestibulopathy are typically symptom-free when sitting or lying [39; 40].

The prevalence of bilateral vestibulopathy in the U.S. adult population is 28 per 100,000. The age distribution ranges from youth to old age, depending on etiology, and the mean age at diagnosis is 50 to 60 years. About 60% of patients develop bilateral vestibulopathy slowly and progressively; depending on etiology, 40% of patients have a clinical course marked by episodes of dizziness leading incrementally to bilateral loss of vestibular function [40; 41].

Bilateral vestibulopathy involves atrophy of the hippocampus, with associated impairments in spatial memory and navigation. It is the most frequent cause of motion-dependent postural vertigo in older patients. The three most frequently identified causes of bilateral vestibulopathy are ototoxic aminoglycosides, bilateral Ménière disease, and meningitis, but most cases are idiopathic [39; 40].

A connection between bilateral vestibulopathy and degenerative cerebellar diseases has been established. A syndrome comprised of bilateral vestibulopathy, sensory axonal polyneuropathy, cerebellar ataxia, and oculomotor disturbances accounts for around 30% of cases previously considered idiopathic [39; 42]. Bilateral vestibulopathy can be severely debilitating but is partially reversible with vestibular rehabilitation. It is important for clinicians not to overlook this condition when assessing patients with complaints of dizziness/vertigo [43].

VESTIBULAR PAROXYSMIA

Vestibular paroxysmia is characterized by recurrent spontaneous vertigo attacks that are brief (several seconds up to one minute), and frequent (up to 30 per day) [44]. In one study, vestibular paroxysmia accounted for 3.7% of 17,718 consecutive outpatients in a multidisciplinary vertigo and balance disorders center. Men are affected twice as often as women, and the bimodal age of onset peaks in early childhood and again between 40 and 70 years of age [45].

Vestibular paroxysmia symptoms are triggered by neurovascular compression involving the anterior inferior cerebellar artery and the 8th cranial nerve. More than 95% of cases show vessel-nerve contact at the exit point of the 8th nerve from the brainstem, but the finding is nonspecific because it may be seen in healthy, asymptomatic adults as well [46].

CENTRAL CAUSES OF DIZZINESS AND VERTIGO

The vestibular nuclei and its connections to cerebellar, brainstem, spinal cord, and higher cortical structures comprise the central vestibular system. Dizziness, vertigo, ataxia, or disequilibrium can result from pathologies involving central vestibular structures, the most common of which are migraine-related vestibulopathy, brainstem strokes, head trauma, multiple sclerosis, and cerebellar degeneration [47].

Vertigo, vestibular dysfunction, and anxiety disorders are now recognized as co-factors, and the interrelationship is substantial. Dizziness and vertigo are associated with diverse systemic disorders, trauma, and toxic exposures. Etiologies in psychiatric and systemic disorders are complex and diffuse.

Central abnormalities cause about 20% of dizziness complaints, and patients may present with disequilibrium or ataxia rather than vertigo. Dizziness/vertigo may be the sole presenting symptom of an impending cerebrovascular event origination in the brainstem or cerebellum [7]. In these presentations, distinguishing benign from potentially or imminently dangerous cerebrovascular causes has been the focus of extensive research effort.

VESTIBULAR MIGRAINE

Vestibular migraine is the most common central cause of recurrent spontaneous attacks of vertigo. "Vestibular migraine" is the preferred name for this disorder, because patients may experience a range of vestibular symptoms not limited to vertigo (e.g., dizziness, nausea, vomiting) [18; 48].

Vestibular migraine accounts for 7% of patients seen in dizziness clinics and 9% of patients seen in headache clinics, but it remains underdiagnosed [48]. It is three times more common in women and occurs most often between 20 and 50 years of age. A family history of migraine is a risk factor, and vestibular migraine may involve a genetic susceptibility to enhanced excitability during sensory information processing, which induces interactions of vestibular and pain pathways [7; 48].

Pain and vestibular sensory inputs converge in brainstem structures that modulate pain sensitivity and anxiety responses to pain and vestibular signaling. Vestibular stimulation activates some higher cortical regions involved in pain perception. Vestibular and pain pathways also overlap at brainstem and thalamic levels. This may explain, in part, the frequent clinical overlap of migraine (including vestibular migraine), balance, and anxiety disorders [48; 49].

Vestibular migraine is a clinical diagnosis in which central and peripheral mechanisms arise from genetic and environment interactions. Mechanistic interactions cause excessive sensitivity to pain perception (e.g., headache, allodynia), hearing (e.g., phonophobia), vestibular stimulation (e.g., vertigo, motion sickness, visual vertigo), vision (e.g., photophobia), and sense of smell (e.g., osmophobia) [48; 49; 50].

Vestibular migraine is diagnosed primarily by patient history and exclusion of alternative causes; neurologic exams performed between episodes generally show normal findings [48]. The migraine may occur with episodic vertigo, chronic motion sensitivity, or other vestibular symptoms. Vertigo and motion sickness, with or without headache, is the common presentation, and some patients report mild, transient auditory symptoms of tinnitus, muffled hearing, or ear pressure [15; 18].

CEREBROVASCULAR ETIOLOGIES

Patients with potentially serious or life-threatening stroke may present with vestibular symptoms without other focal neurologic signs. This acute presentation is linked to stroke involving one of several branches that supply the brainstem, cerebellum, or inner ear. Early differentiation is an area of intense research focus. Early recognition of isolated vertigo as a stroke sign allows specific intervention and secondary prevention. Misdiagnosis of stroke-related vertigo as a peripheral cause may result in significant morbidity or mortality, and overdiagnosis of stroke as peripheral vertigo leads to expensive and unnecessary workups, medication, and hospital admissions [51; 52].

Vertebrobasilar Artery Territory (Posterior Circulation) Infarcts or Strokes

Around 25% of all ischemic events occur in the vertebrobasilar artery territory, with dizziness/vertigo the sole presentation in up to 33% of patients [53]. Inferior cerebellar and small brainstem infarctions are an increasingly recognized cause of isolated vertigo, and transient isolated vertigo is a common manifestation of vertebrobasilar artery ischemia.

Vertebrobasilar artery transient ischemic attacks (TIAs) typically last eight minutes on average [51; 53]. Several syndromes are associated with TIAs, ischemia, or infarcts in vertebrobasilar artery territories (e.g., the brainstem, cerebellum) [47].

Numerous arteries extend from the posterior inferior cerebellar artery to supply the medial, lateral, and dorsal aspects of the medulla. Vertigo is more frequent in posterior inferior cerebellar artery strokes, and these are the most common cerebellar infarcts [54]. Dizziness/vertigo is one of the most common symptoms of cerebellar ischemic stroke. A large prospective study showed 11% of patients with cerebellar infarction had isolated vertigo, of whom 96% had an infarct in the medial branch of the posterior inferior cerebellar artery [55].

Medial Medullary Infarcts

Medial medullary infarctions usually cause a vertiginous labyrinthian syndrome that mimics peripheral vestibulopathy. Severe vertigo and nystagmus are prominent, and some patients describe feeling as if being pulled to the ipsilateral side by a magnet [52].

Lateral Medullary Infarcts

The vestibular nuclei are more vulnerable to ischemia than other structures in the posterior fossa, and ischemia of the lateral medulla (including the vestibular nuclei) may be a common mechanism of isolated vascular vertigo [51]. Wallenberg syndrome describes a lateral medullary infarction that presents with a range of focal neurologic signs [53].

Vestibulo-cerebellar symptoms/signs are almost always present, because lateral medullary infarcts involve the vestibular nuclei and their connections. The symptoms/signs include dizziness or disequilibrium; acute vertigo, nausea, or vomiting; ipsilateral facial pain, numbness, and ataxia (falling to the side of the infarct); and decreased contralateral pain and thermal sensitivity. The nystagmus has horizontal and rotational components [47; 52; 53].

Dorsal Medullary Infarcts

Less prevalent than medial or lateral medullary infarction, dorsal medullary infarcts typically cause dizziness/vertigo, imbalance, and ocular motor abnormalities. This is because the dorsal medulla also contains the vestibular nuclei and other structures that relay and process vestibular and ocular motor signals [56].

Anterior Inferior Cerebellar Artery Distribution

The anterior inferior cerebellar artery supplies the lateral pons and branches off to form the internal auditory artery, which irrigates the cochlea and vestibular labyrinth. The labyrinth is especially vulnerable to ischemia, because the internal auditory artery is an end-artery with minimal collaterals. Isolated acute audio-vestibular loss may herald an impending anterior inferior cerebellar artery territory infarction. Auditory artery occlusion causes loss of auditory and vestibular function [47; 51].

Pontine syndrome is a partial pontine ischemia produced by anterior inferior cerebellar artery occlusion, characterized by vertigo, tinnitus, and hearing loss [47; 53].

STRUCTURAL ABNORMALITIES AND LESIONS

Malformations or lesions that affect the vestibular system can cause dizziness or vertigo, as can any process that leads to acute vestibular asymmetry. The brain may adapt to this asymmetry over time to prevent or diminish vertigo, but imbalance may persist when vestibulo-cerebellar pathways are impacted. For example, sudden-onset vertigo is more likely with stroke, but less likely with a slow-growing acoustic neuroma (a vestibular tumor) because central adaptation to the asymmetry is gradual and imperceptible [15].

Superior Canal Dehiscence Syndrome

Superior canal dehiscence syndrome is caused by an abnormal opening (dehiscence) in the thin bony roof of the superior semicircular canal. This is thought to be related to congenital thinning of the temporal bone and occurs in 0.1% of the population. Development of the bony opening renders the membranous labyrinth unusually susceptible to changes in sound and pressure. In addition to dizziness and sensitivity to loud noises, patients with superior canal dehiscence syndrome experience autophony, whereby one's voice, breathing, or bodily sounds are excessively audible [57]. The dizziness/vertigo induced by sound and pressure stimuli can be associated with auditory symptoms of conductive or mixed hearing loss [58].

Chiari Malformation

A Chiari malformation is defined as descent of the cerebellar tonsils ≥5 mm past the foramen magnum [18; 47]. This occurs when the lower part of the cerebellum does not fully migrate rostrally during fetal development. Compression of the cerebellum from this condition may lead to occipital headaches, vertigo, nystagmus, and ataxia in early childhood or later in life [15]. Patients also commonly describe occipital and neck pain provoked by physical activity or maneuvers that increase intracranial pressure [18].

Symptomatic Chiari malformations should be referred for neurosurgical evaluation and considered for posterior fossa decompression. Asymptomatic Chiari malformations can be discovered incidentally during MRI for dizziness from a different etiology. Asymptomatic patients should be spared the risks of surgery [18].

Acoustic Neuroma (Vestibular Schwannoma or Schwann Cell Tumors)

Acoustic neuromas are tumors of the vestibular portion of the 8th cranial nerve, diagnosed in roughly 3,000 cases annually. Acoustic neuromas can expand and compress surrounding structures along the brainstem, potentially leading to sensorineural hearing loss and vertiginous symptoms [19; 59].

DEMYELINATING AND NEURODEGENERATIVE DISORDERS

Multiple Sclerosis

Multiple sclerosis (MS), an idiopathic demyelinating disorder of the central nervous system (CNS), is considered an autoimmune disease most likely caused by an autoantigen to a myelin protein [47]. Data from a study published in 2019 indicate that the estimated prevalence of MS is 363 cases per 100,000 individuals in the United States, and it affects three times as many women than men [60].

CNS demyelinization usually occurs in the white matter, where plaque formation disrupts signal conduction and leads to symptoms [47]. Demyelinating plaques that develop in central vestibular pathways may cause recurrent episodes of vestibular symptoms, especially during illness and with heat exposure (Uhthoff phenomenon). The plaques may be visible on MRI [18; 19].

Vertigo is the presenting symptom at onset in 5% of MS cases, and more than 50% of patients present with vertigo at some point in the disease course. MS can mimic an 8th cranial nerve lesion when plaque develops in the entry of the nerve root in the brainstem to produce vertigo and horizontal nystagmus [47].

MS may present with dizziness, vertigo, or imbalance, especially with brainstem or cerebellum lesions that affect the vestibular system; these lesions may also result in nystagmus, ataxia, slurred speech, and diplopia. Despite the increased risk of CNS vertigo in patients with MS, non-MS (peripheral and central) causes (e.g., BPPV, vestibular migraine) can co-occur [15].

Parkinson Disease and Parkinson-Plus Syndromes

Dizziness may be a manifestation of many neurodegenerative disorders. At presentation, patients with Parkinson disease may describe the shuffling or festinating gait as being "dizzy" or "off balance." Medications such as levodopa or dopamine agonists (e.g., pramipexole, ropinirole) may cause orthostatic hypotension, and hence presyncopal dizziness [18].

The Parkinson-plus syndromes (e.g., multiple system atrophy, dementia with Lewy bodies) often cause many symptoms that are construed as "dizziness." Multiple system atrophy causes dysautonomia (causing orthostatic presyncope or syncope), vertigo, nystagmus (causing oscillopsia), and/or cerebellar findings (leading to gait ataxia). Progressive supranuclear palsy often presents with falls and complaints of imbalance; loss of downgaze often causes imbalance when descending stairs [18].

Cerebellar Vertigo Syndromes

Neurodegenerative and hereditary diseases of the cerebellum often lead to postural vertigo, gait disorders with ataxia, and cerebellar oculomotor disorders such as saccadic dysmetria, gaze saccades, gaze nystagmus, and downbeat nystagmus [61].

Episodic ataxia type 2 is a rare but important disorder to identify because the random attacks of vertigo, ataxic gait, and slurred speech lasting minutes to days often respond dramatically to acetazolamide. The onset of recurrent episodes may occur in childhood or early adulthood, but the condition is often undiagnosed into late adulthood. This disorder is due to a voltage-sensitive calcium channel mutation [15].

PERSISTENT POSTURAL PERCEPTUAL DIZZINESS

Persistent postural perceptual dizziness (PPPD) develops when a precipitating condition (typically an acute vestibular event, vestibular migraine, panic attacks, or anxiety with prominent dizziness) occurs in individuals with a maladaptive behavioral response to the acute symptoms [62]. In this way, PPPD is a new diagnostic entity that bridges previous knowledge gaps by connecting persistent nonvertiginous dizziness, perceptual hypersensitivity, and chronic anxiety [15; 62].

PPPD may be a highly prevalent cause of chronic non-vertiginous dizziness. The population and primary care prevalence is not yet known, but the female-to-male ratio is 5:1. PPPD symptoms are often worsened by sleep deprivation and stress but not by head motion to the degree seen with most vestibular disorders [15; 62].

The central etiology relates to behavioral factors, neurotransmitter function, and other probable CNS mechanisms [15]. Brain imaging of patients with PPPD shows reduced connectivity in multisensory vestibular processing and spatial cognition, with increased connectivity between visual and emotional processing. Dizziness burden, anxiety, and depression correlate with connectivity in clinically relevant brain regions [63]. PPPD may linger following minor head injury and become entwined with other symptoms of post-concussive syndrome [15].

MAL DE DÉBARQUEMENT SYNDROME

A transient experience of "sea legs" after returning to land from riding on a boat is not uncommon, but in mal de débarquement syndrome it persists for weeks, months, or years. Mal de débarquement syndrome is an uncommon vestibular disorder in which a sense of rocking first appears soon after disembarking and is most common in women. Travel by aircraft or automobile can also trigger the persistent unsteadiness. Symptoms typically abate during passive motion (e.g., a boat or car ride) but resume when motion ceases. The cause is unknown, but it may be a disorder of the vestibular velocity storage mechanism with a limited adaptive ability [15; 62].

SYSTEMIC ETIOLOGIES

Dizziness and vertigo are associated with systemic diseases or conditions as symptoms, comorbidities, risk factors, or shared pathophysiologic pathways. These most commonly involve hemodynamic (orthostatic hypotension), metabolic (diabetes), cigarette smoking, and cardiovascular origins.

ORTHOSTATIC HYPOTENSION

Orthostatic hypotension is typically defined by a sustained decline in blood pressure of at least 20 mm Hg systolic or 10 mm Hg diastolic within three minutes of standing, with symptoms of lightheadedness or presyncope on arising. Vertigo is a common and under-appreciated symptom [8].

Orthostatic hypotension is common in older people and a frequent complication of (excessive) hypertensive medication. Such patients experience postural dizziness without documented syncope based on transient reductions in cerebral blood flow. Orthostatic hypotension may occur 5 to 30 minutes after remaining asymptomatic in the upright position, or when orthostatic vital signs have been normal. It may be missed as a cause of periodic syncope or presyncopal dizziness [15].

DIABETES

Vestibular dysfunction is a complication of type 2 diabetes, with reported rates 70% higher compared with age-matched controls. Both central and peripheral vestibular dysfunction are observed in type 1 and type 2 diabetes. Hypertension mediates 42% of the association between type 2 diabetes and BPPV, suggesting that hypertension provides the mediating pathway for diabetes' impact on the vestibular system [64].

CIGARETTE SMOKING

In one study, the association between peripheral vestibular disorders and smoking was examined in patients (mean age: 65.3 years) treated for hypertension, dyslipidemia, or diabetes in primary care and followed over one year for new peripheral vestibular disorder events [65]. Compared with never-smokers, the risk of new-onset peripheral vestibular disorder was 2.22 times greater for ever-smokers and 2.70 for all ever-smokers with ≥30 pack-years. Compared with male never-smokers, the risk of new onset peripheral vestibular disorder was 4.41 greater for male ever-smokers with ≥30 pack-years. There were too few female heavy smokers to compare against female never-smokers [65].

VESTIBULAR IMPAIRMENT, ANXIETY, AND PERCEPTION

Clinically relevant vestibular system interactions with traumatic stress, depressive disorders, and other psychiatric disorders have been described. However, vestibular-anxiety interactions are the most extensively studied and compelling and will be the focus of this section.

Anxiety disorders account for 8% to 10% of cases with vestibular symptoms as primary complaints [66]. In patients presenting with dizziness concerns, the rates of panic disorder are 5 to 15 times greater than the general population. Patients with panic disorder frequently experience significant dizziness and often demonstrate vestibular dysfunction [67].

The high co-occurrence of vertigo and anxiety has been described since antiquity [50]. By the late 1800s, dizziness and vertigo, anxiety, autonomic arousal, appraisal of spatial orientation, and threat assessment were appreciated as core contributors to agoraphobia; otologic disease was found to precipitate agoraphobia in patients with anxiety. As otology, neurology, and psychiatry matured into separate specialties in the early 20th century, agoraphobia became a psychiatric disorder and lost its spatial and motion context [62; 68].

While traditional medical teaching describes a narrow range of vestibular system functions (e.g., gaze stability, balance) and dysfunctions (e.g., dizziness, unsteadiness, vertigo), vestibular involvement in brain processes beyond balance, spatial orientation, and gait is established. The inter-relationship of anxiety and balance disorders is being rediscovered more than a century later [69; 70; 71].

Increasingly demonstrated is the extent of multidirectional connectivity and interaction between threat/anxiety, vestibular, visual, and somatosensory systems, and how this helps explain the shared pathophysiology, clinical features, and prevalent comorbidity [72]. As such, it is important to assess for, and treat when present, anxiety disorders, cognitive impairment, and perceptual disturbances in

patients with dizziness/vertigo complaints [49; 69; 70]. The suggestion is made that dichotomous thinking (structural disease vs. "emotional issues") should be discarded in order to effectively assess vestibular, psychiatric, and perceptual dysfunction. Each of these domains should be addressed simultaneously for favorable treatment outcomes [73].

SHARED CLINICAL FEATURES

Patients with vestibular or balance disorders often have anxiety symptoms. Likewise, patients with anxiety disorders often show vestibulo-ocular and/or peripheral vestibular dysfunction [74]. Vestibular and balance abnormalities are especially common in panic disorder with agoraphobia [71].

Chronic anxiety and anxiety disorders may be causes or complications of vestibular symptoms or disorders. These psychiatric disorders affect 30% to 50% of patients who seek specialist care for vestibular symptoms, and they adversely affect the treatment outcomes of patients with vestibular disease, especially when unrecognized [62; 72]. Vestibular function is linked to emotional states through complex bidirectional interactions; vertigo worsens emotional symptoms, and emotional states can amplify perceptions of vertigo or disequilibrium [70].

ANXIETY, BALANCE, AND VESTIBULAR INTERACTIONS

Anxiety can impair ocular motor reflexes and gaze control, which may contribute to visual and visual-vestibular syndromes. Anxious states can amplify a normative gaze bias toward potentially threatening stimuli in the visual field, which, in patients with social anxiety disorder, may drive hypervigilance-avoidance gaze patterns. The impairing effect of anxiety on gaze control reduces gaze stability on visual targets, which may underlie dizziness and visual symptoms in PPPD [74; 75].

Exposure to heights reflexively increases body sway in normal subjects by reducing visual feedback to body sway (in the absence of motion). Body sway is more pronounced in subjects with height phobia, and anxiety-related gaze diversion may increase gait instability in patients with fear of falling [75; 76].

Space-motion discomfort describes symptoms of uneasiness over spatial orientation and hyperawareness of motion stimuli. In affected individuals, space-motion discomfort is triggered by movement in visually rich environments and exposure to moving or patterned objects while stationary. It is especially prevalent in patients with panic disorder and agoraphobia; persons with panic symptoms often become destabilized under conflicting sensory conditions. Visual vertigo and other situation-specific interactions between balance and anxiety may be part of a broader space-motion discomfort profile [62; 74; 77].

DISRUPTED MULTISENSORY INTEGRATION

The vestibular system maintains equilibrium through vestibular spinal reflexes, stabilizes visualization through the vestibular-ocular reflex, and contributes to spatial orientation [78]. Accurate perception of gravity and maintenance of spatial orientation, balance, and gait rely on brain integration of visual, vestibular, proprioceptive, and somatosensory signals and cognitive processes [79].

The brain normally resolves mismatched sensory information by updating and realigning the internal spatial representation of the body with the surrounding space. Impairment of one sensory signal is compensated by reweighting of intact sensory inputs [62; 78]. Unsuccessful reweighting impairs multisensory integration, leading to incongruity between visual and vestibular information and visual-vestibular sensory mismatch. This can elicit an erroneous cortical representation of the body within the surrounding space, producing spatial disorientation, anxiety, dizziness, balance problems, and increased risk of falls [62; 78; 79; 80].

Visual Dependence

Visual dependence is an over-reliance on visual information to maintain spatial orientation, which compensates for vestibular dysfunction that impairs multisensory integration. Space-motion discomfort, a prominent feature resulting from the visual-vestibular conflict, may cause symptoms of imbalance, discomfort, anxiety, or phobic avoidance in situations where moving, complex, or conflicting visual environments trigger intense dizziness/vertigo symptoms [71; 80].

Depersonalization and Derealization

Depersonalization and derealization are perceptual abnormalities, described primarily from the psychiatric perspective for more than a century. Depersonalization (feeling detached, numb from one's emotions, experiences), derealization (objects, people, and surroundings experienced as unreal, distant, artificial, lifeless), and intact reality testing are symptoms of depersonalization/derealization disorder in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) [81; 82]. The DSM-5 also lists derealization and depersonalization as potential panic attack symptoms in the diagnostic criteria for panic disorder [82].

Trauma history and anxiety disorders are prevalent co-factors and antecedents of depersonalization/derealization. Phencyclidine or cannabis use can trigger acute symptoms [83]. Derealization symptoms are particularly distressing, if not profoundly intolerable; an anxious or panic response can amplify depersonalization/derealization symptoms, creating a vicious cycle [81].

Patients diagnosed with depersonalization/derealization disorder have high rates of past-year inpatient hospitalization (25.6%) and ongoing outpatient psychotherapy (40.4%). Depersonalization/derealization disorder has been described as highly chronic, severely underdiagnosed, and often refractory to pharmacotherapy and psychotherapy [84].

The psychiatric perspective is important, but inadequate by failing to consider recent evidence implicating vestibular dysfunction, impaired multisensory integration, and sensory mismatch in depersonalization/derealization [85; 86]. Vestibular inputs provide a frame of reference within which spatial information from other senses is interpreted. Depersonalization/derealization associated with vestibular dysfunction is a consequence of a sensory mismatch between disordered vestibular input and other sensory signals of orientation, creating a misleading frame of reference and impaired bodily representation in the cortex. This leads to a perception of disembodiment and other "unreal" perceptions [85; 86; 87].

Stimulation of semicircular canals or otoliths can provoke depersonalization/derealization symptoms in healthy volunteers without a history of depersonalization/derealization [87]. However, depersonalization/derealization symptoms in vestibular patients with anxiety are more frequent, more severe, and qualitatively distinct from symptoms in patients without anxiety. Anxiety is essential to the appearance and intensity of depersonalization/derealization symptoms in vestibular patients [88].

Out-of-Body Experiences

Out-of-body experiences are states in which the individual experiences the center of awareness as located outside his or her physical body, with the sensation of seeing the environment from this elevated vantage point. Persistent vestibular dysfunction disrupts the integration of visual, somatosensory, and vestibular signals. Perceptual incoherence, a byproduct of the resultant visual-vestibular mismatch, can produce an out-of-body experience, with anxiety a significant co-factor in out-of-body experience etiology. In non-dizzy persons, out-of-body experience is associated with depersonalization or derealization symptoms [89].

COGNITIVE FUNCTION

Vestibular input activates a broad neural network in the cortex for visuospatial processing and memory. Vestibular function is strongly linked to visuospatial ability—how the mind organizes and understands two- and three-dimensional space. Impaired vestibular input can fundamentally change one's mental representation of, and awareness of one's position in, three-dimensional space [70].

Vestibular dysfunction is also implicated in impaired attention, cognitive processing ability, memory, and executive function [70]. This is especially relevant in the elderly, for whom cognitive impairment from vestibular dysfunction is broader and more diffuse. It should be considered in any older patient with dizziness or vertigo [90].

POST-TRAUMA OR TOXIC EXPOSURE

POST-CONCUSSIVE AND CERVICOGENIC VERTIGO

Patients with post-concussive syndrome or cervicogenic dizziness following a whiplash can experience chronic dizziness with headache, insomnia, cognitive symptoms, or mood lability [62].

Post-Concussion Syndrome

In the United States, there are approximately 3.8 million sports-related concussions annually in adolescents and adults. Concussion, the mildest form of traumatic brain injury (TBI), is a transient functional disorder caused by direct trauma, rapid acceleration-deceleration of the head, or blast forces. Post-concussion syndrome persists beyond three months in up to 20% of affected individuals [91].

Headache and dizziness are common symptoms. Other symptoms include light and sound sensitivity, nausea, tinnitus, cognitive dysfunction (mental fog), problems with visual focus, sleep changes, depression, anxiety, and irritability. Dizziness may be due to the direct CNS effects of the trauma (e.g., axonal injury, other microstructural damage), vestibular migraine, or neuropsychiatric disorders (e.g., anxiety, depression, post-traumatic stress disorder). Post-concussion BPPV is not uncommon. A detailed history and examination are crucial when assessing dizziness in these patients, because treatment should address the underlying etiology [92; 93].

Mild TBI

Balance disorders, migraine, and anxiety are also components of mild TBI that appear following exposure to blunt-force or blast trauma, along with symptoms of headache, nausea, vomiting, dizziness/balance problems, fatigue, sleep disturbances, and difficulty with memory or concentration [91; 93]. Dizziness and headache are reported in more than 70% of cases presenting acutely or chronically post-exposure; vertigo emerges sub-acutely. Other significant sequelae are hearing loss, emergent and delayed post-traumatic balance disorders, and chronic migrainous disorders without radiologic evidence of damage, often accompanied by tinnitus and sensitivity to light or sound [49].

Patients with chronic (at least six months) post-traumatic head injury vestibular symptoms (e.g., imbalance, dizziness) show high rates of multiple peripheral and central vestibular disorders. Despite expert neuro-otologic management, 20% of patients have persistent vestibular symptoms at two years. Treatment-resistant vestibular symptoms in these patients may result from brain trauma-induced impairment of brain plasticity-mediated repair mechanisms [94].

Cervicogenic Vertigo

Cervicogenic dizziness is characterized by imbalance, unsteadiness, disorientation, neck pain, limited cervical range of motion, and headache. It is closely related to changes in cervical spine position or cervical joint movement. Common etiologies are post-whiplash injury and inflammatory, degenerative, or mechanical cervical spine dysfunction. The cause of imbalance, unsteadiness, and disorientation symptoms is suggested to involve pain, faulty cervical proprioceptive inputs, and disrupted signaling from upper cervical proprioceptor to vestibular nuclei [95].

Cervicogenic dizziness is diagnosed after mimics are ruled out, including central and peripheral vestibular disorders, vestibular migraine, labyrinthine concussion, cervical arterial dysfunction, and whiplash-associated disorder [95].

EXPOSURE TO TOXINS

Lead or mercury exposure can be ototoxic and may cause vertigo through temporary or permanent damage to the inner ear or auditory nerve [96].

ADVERSE DRUG EFFECTS

Dizziness or vertigo can occur as a direct side effect of medication that resolves after discontinuation without cochleo-vestibular damage, or it may develop (and persist) secondary to cochleo-vestibular damage (ototoxicity).

SIDE EFFECTS

The list of drugs that may cause vertigo or dizziness is extensive and diverse. Medications consistently associated with dizziness include the antihypertensive drugs amlodipine and hydrochlorothiazide; the antibiotics ciprofloxacin, amoxicillin, and clavulanic acid; pantoprazole (a proton pump inhibitor); aripiprazole (an atypical antipsychotic); and atazanavir (a protease inhibitor). Selective serotonin reuptake inhibitors (SSRIs) such as paroxetine and sertraline can induce vertigo or dizziness as side effects or with abrupt cessation; mirtazapine may cause dizziness side effects [96].

Antiepileptic drugs in particular are linked to adverse effects on auditory or vestibular systems that may be reversible or irreversible. Even at therapeutic dose ranges, long-term treatment with oxcarbazepine, carbamazepine, lamotrigine, phenytoin, valproate, gabapentin, or vigabatrin may result in auditory, central, and/or peripheral vestibular dysfunction [97].

OTOTOXIC DRUGS

Ototoxic drugs can damage cochleo-vestibular structures, which may result in hearing loss, tinnitus, dizziness, or disequilibrium [98]. Cochlear damage can present acutely as tinnitus. Early hearing loss, which patients may not recognize, manifests in the highest frequencies (>4,000 Hz). With progression, the lower frequencies are affected, and patients may become profoundly deaf if the drug is continued. Stopping the drug early, before extensive damage, may prevent further loss. Partial recovery of auditory thresholds is possible, but the loss is usually permanent [98; 99].

Vestibular toxicity typically includes imbalance and visual symptoms. As with bilateral vestibulopathy, imbalance is worse in the dark or situations in which footing is uncertain; oscillopsia occurs when the head is moving. Patients do not present with nystagmus or vertigo complaints, because vestibulotoxicity is usually bilateral [98].

Ototoxicity is linked to more than 100 drug classes [98]. The best-known and most ototoxic are aminoglycosides, amiodarone, macrolides, vancomycin, loop diuretics, antineoplastic agents, salicylates, and antiseptics.

Aminoglycosides

Aminoglycosides are the most vestibulotoxic of all ototoxic drugs. The introduction of streptomycin in 1944 for treatment of tuberculosis brought ototoxicity to clinical attention, as a substantial number of treated patients developed irreversible cochleo-vestibular dysfunction [98; 99].

The aminoglycosides remain widely used and differ in cochleo-vestibular toxicity. Kanamycin, amikacin, neomycin, and dihydrostreptomycin are preferentially cochleotoxic. Gentamicin affects both cochlear and vestibular systems but is primarily vestibulotoxic, as are streptomycin, tobramycin, and netilmicin [98; 99].

The onset or progression of hearing loss can occur long after cessation of treatment, because aminoglycosides are cleared more slowly from inner ear fluids than from serum. Patients should be monitored for vestibulotoxic effects up to six months after discontinuation [98; 99].

Amiodarone

Amiodarone is a widely used antiarrhythmic drug. Reports of amiodarone-induced vertigo and gait instability followed its introduction in the 1980s, and the drug was first implicated in bilateral vestibulopathy causality in 2017. The prevalence of bilateral vestibulopathy is as high as 81 per 100,000. Most cases are idiopathic, and amiodarone may account for a substantial proportion of bilateral vestibulopathy with unexplained causation [100].

Macrolides

Erythromycin has been sporadically linked to reversible ototoxicity in patients with ototoxic risk factors. Azithromycin and clarithromycin have also been suggested as possibly ototoxic [98].

Vancomycin

Vancomycin is a glycopeptide antibiotic introduced in the 1950s and commonly used for efficacy in methicillin-resistant staphylococcal infections. Ototoxicity is reported in patients with other risk factors, but vancomycin monotherapy at therapeutic doses has not shown ototoxicity [98].

Loop Diuretics

Loop diuretics are used for treating congestive heart failure, renal failure, cirrhosis, and hypertension. The most effective and widely used (i.e., ethacrynic acid, furosemide, and bumetanide) can cause ototoxicity [98].

Antineoplastic Agents

Antineoplastic agents most associated with ototoxicity are the platinum-based compounds cisplatin and (to a lesser extent) carboplatin. Ototoxicity and nephrotoxicity are dose-proportional with both compounds [98].

Salicylates

Salicylate (aspirin) can produce tinnitus and a generally reversible flat sensorineural hearing loss at low doses, especially in elderly patients [98].

Antiseptics

Some antiseptics used for surgical preparation are ototoxic. Povidone-iodine is safe for middle ear surgeries. However, chlorhexidine is toxic if it reaches the inner ear and should not be used, and VoSol and Gentian violet also show ototoxicity [101].

DIAGNOSIS: THE "TIMING AND TRIGGERS" WORKUP

As mentioned, the prevailing clinical model in dizziness and vertigo is being replaced by the "timing and triggers" approach to streamline the differential diagnosis, increase diagnostic accuracy, and reduce unnecessary imaging tests and misdiagnosis.

Publications have brought into focus the misdiagnosis of patients with stroke who present with isolated dizziness. The "timing and triggers" approach is shown to reduce this highly concerning problem largely resulting from [8]:

- Over-reliance on the symptom quality approach
- Lack of familiarity with key physical exam findings
- Overweighting traditional stroke risk factors for patient screening (e.g., age, vascular risk factors) and not considering stroke in younger patients
- Over-reliance on CT

The "timing and triggers" approach departs from the Drachman-Hart model by de-emphasizing patient descriptions of symptom quality, dropping presyncope and lightheadedness as dizziness and vertigo classes, and limiting use of the vague term "lightheadedness" [2; 7]. The term "dizziness" is used as a generic descriptor for disturbed balance or spatial orientation, vertigo, lightheaded, spinning, rocking, and others.

Accurate diagnosis is an essential precondition for effective treatment of dizziness and vertigo, best ensured by defining the rapidity of onset, the context, associated symptoms, intermittent or persistent nature of dizziness, and triggers of intermittent symptoms during patient history-taking. This is called the "timing and triggers" diagnostic workup. The workup is structured using the algorithm Triage-TiTrATE-Test [8; 36; 102]:

- Triage: Identify dangerous causes by noting the presence of prominent associated symptoms, abnormal vital signs, altered mental status, or ancillary test results.
- Timing: In the history of presenting illness, classify the pattern of dizziness attacks as episodic, acute, or chronic in duration.
- Triggers: In the history and review of systems, seek an underlying pathophysiologic mechanism by searching for obvious triggers or exposures.
- Targeted exam: Differentiate benign from dangerous causes within a timing-trigger category by using specific exam findings, emphasizing a targeted eye movement exam.
- Test: Choose the best laboratory or imaging test when clinically relevant uncertainty remains about a dangerous cause that has not been ruled out.

The timing and triggers history of the TiTrATE algorithm divides patients into six vestibular syndrome categories [8; 36]:

- Acute vestibular syndrome (AVS)
  - Postexposure (traumatic/toxic) (t-AVS)
  - Spontaneous (s-AVS)
- Episodic vestibular syndrome (EVS)
  - Triggered (t-EVS)
  - Spontaneous (s-EVS)
- Chronic vestibular syndrome (CVS)
  - Context-specific (t-CVS)
  - Spontaneous (s-CVS)

In this context, "vestibular" refers to vestibular symptoms and not etiology. Vestibular symptoms include vertigo, dizziness, nausea, vomiting, and nystagmus [48].

The large differential diagnosis of potential dizziness etiologies is daunting to many clinicians. Triage-TiTrATE-Test greatly streamlines this process such that every forward step eliminates potential etiologies, substantially narrows the range, and by the final step, an accurate diagnosis is already evident or confirmed by referral for specialized testing [8]. This differential diagnosis process has been referred to as a funnel approach [36].

TRIAGE

Some patients with a primary symptom of dizziness have obvious associated symptoms (e.g., gastrointestinal bleeding) or context (e.g., new antihypertensive medications, anticonvulsant toxicity), abnormal vital signs, altered mental status, and/or ancillary test results that usually point to a likely diagnosis. These potential medication, toxicity, metabolic, cardiac, or psychiatric etiologies of dizziness are examined and patients are treated or referred for further evaluation as needed [10; 36].

Other dizziness, medical, and major neurologic etiologies lack prominent associated features, but can be ruled out by assessing [19]:

- Neurologic history
- Recent viral or bacterial infection
- Patient medication list
- Social history for alcohol and substance use
- Psychiatric history

Important associated symptoms to note include headache, hearing loss, tinnitus, nausea and vomiting, impaired vision, focal weakness, and difficulty walking. The severity of impairment should be assessed by asking about impact on work, driving, and recreational and social functioning [11].

Review of systems should seek symptoms of causative disorders, including upper respiratory infection symptoms (inner ear disorders); chest pain and palpitations (cardiovascular disease); dyspnea (pulmonary disease); dark stools (anemia from GI blood loss); and weight change and heat or cold intolerance (thyroid disease) [11]. Past medical history should note recent head trauma (usually obvious by history), migraine, diabetes, heart or lung disease, and regular or daily drug and alcohol use. Identify all current medications, including recent changes in drugs, dosages, or both [11].

After major medical and other etiologies are ruled out, patients with dizziness or vertigo, with or without associated headache, otologic, autonomic, or balance symptoms, should receive a timing and triggers evaluation [36].

TIMING

Timing refers to the onset, duration, and evolution of the dizziness attacks. Narrow the differential diagnosis by classifying the pattern of dizziness attacks as episodic, acute, or chronic in duration by defining the following [36; 103]:

- Onset of dizziness attacks: Sudden or gradual and ill-defined
- Duration of dizziness attacks (minimal and maximal): Seconds to minutes, several minutes to hours, or several hours to days
- Evolution of dizziness attacks:
  - Episodic dizziness lasting seconds to minutes, several minutes to hours, or several hours to days
  - Acute with symptoms lasting days to weeks
  - Persisting symptoms more than three months (chronic)

TRIGGERS

Almost all patients with vertigo feel worse with head movements. The critical distinction is whether head movements trigger (symptoms appear only when provoked by movements) or exacerbate (movements worsen pre-movement vertigo) symptoms [8; 19].

Head movement usually exacerbates dizziness/vertigo of any vestibular cause (benign or dangerous, central or peripheral), but the worsened dizziness is often conflated with a triggered peripheral cause, potentially missing a serious or life-threatening central etiology [6; 8; 36].

Explicitly assess for the following symptom-triggering circumstances and note whether symptoms are triggered, exacerbated, or improved [15; 103]:

- Rolling over in bed, looking up, changing head position relative to gravity
- Turning the head to the side
- Any head movement
- When standing up or walking
- When supine or recumbent
- Vibration or loud sounds
- Seeing objects in motion

Assessment of triggers establishes the distinctions between positional (change of head orientation with respect to gravity), head motion-induced (head motion regardless of direction), and orthostatic position changes. Obligate triggers are specific triggers that consistently cause dizziness [8].

TARGETED EXAMS

Eye Movement Assessments

At this point in the workup, the patient is placed into one of six vestibular syndromes after some possible etiologies were ruled out during the patient history. The differential diagnosis does not extend beyond possible etiologies within the vestibular syndrome, which substantially narrows the range.

The next task is to differentiate dangerous central mimics from benign causes in acute and episodic vestibular syndromes and to diagnose BPPV by identifying the affected canal. This involves the use of targeted examinations, also called "bedside examinations," which emphasize the assessment of eye movements to detect and localize the underlying pathology of dizziness. The accuracy of eye movement assessment is superior to CT or MRI

imaging in differentiating serious CNS from benign causation. Healthcare costs are also reduced by eliminating (in many but not all cases) expensive but unhelpful brain imaging.

Nystagmus is a repetitive, involuntary movement of the eyes, and nystagmus assessment is a core component of the diagnostic workup. Whether spontaneous or triggered, the characteristics of nystagmus help to localize the pathology and suggest a diagnosis. The nystagmus is tested first, because some disorders are diagnosed solely by the nystagmus characteristics [10; 19; 47; 104].

The vestibulo-ocular reflex keeps vision focused on a target during head movement. When looking to one side, the labyrinth on that side signals the head-turn, and the eyes automatically move in the opposite direction to maintain fixed gaze. The vestibulo-ocular reflex maintains gaze for continued reading while turning the head alternately to each side [104; 105]. Vestibulo-ocular reflex assessment is used in the diagnosis of vestibular disorders, because vestibular dysfunction causes inappropriate activation of the vestibulo-ocular reflex that manifests in nystagmus [16].

With vestibular disturbance, when the head is rapidly turned toward the affected side, the eyes move with the head and visual fixed gaze is broken, followed by a refixation ("catch-up") saccade back to the original visual target [105]. This is nystagmus.

In peripheral or central vestibular disorders, understanding the simple "rules" of nystagmus allows rapid, confident diagnoses. With peripheral causes of nystagmus, the fast-phase direction is away from the affected side (of canal/vestibular nerve), and this direction remains constant, regardless of gaze direction. The pattern is primarily horizontal with a torsional component—never purely torsional or vertical. In central nystagmus, the fast-phase varies with the direction with gaze (i.e., right-beating on rightward gaze, then left-beating on leftward gaze). The pattern is any direction, but primarily torsional or vertical.

HINTS is an acronym for three ocular motor tests—the head impulse test (HIT), gaze testing for nystagmus, and alternate cover test for skew deviation—that are combined to differentiate central from peripheral causes of dizziness. Nystagmus is a key observed response. Normal visual fixation can suppress mild nystagmus, but Frenzel lenses worn by the patient block visual fixation and magnify examiner view of eye movements [8; 10; 19]. When conducting the HIT, have the patient fixate his/her gaze on a midline target (e.g., the examiner's nose), then rapidly rotate his/her head 20 degrees to the right or left, bring head back to midline, then rotate to the other side. The presence of a corrective saccade is "positive" for abnormal vestibulo-ocular reflex, which generally indicates a peripheral vestibular process. Gaze that remains locked on the midline target is normal. A normal HIT in patients with AVS is highly suspicious for stroke, but HIT is only useful in patients with AVS and nystagmus. In patients with dizziness (with urosepsis or dehydration) without nystagmus, a normal HIT is a misleading false-positive for stroke.

Gaze testing for nystagmus consists of having the patient look straight ahead ("neutral" or "primary" gaze) and observing for eye movements. Patients whose eyes drift leftward and snap back horizontally to the right have right-beating horizontal nystagmus. Next, look for "gaze-evoked" nystagmus by having the patient look to the right and then to the left, each for several seconds; observe for nystagmus and direction of its fast-beating component. Two patterns suggest stroke or other central cause:

- Dominantly vertical or torsional nystagmus in any gaze position
- Dominantly horizontal nystagmus that changes direction in different gaze positions, termed bilateral or gaze-evoked nystagmus

However, the most common pattern in patients with AVS and stroke is direction-fixed horizontal nystagmus, an acute vestibular neuritis mimic that requires further testing.

Skew deviation is a vertical misalignment of the eyes due to imbalance in gravity-sensing vestibular pathways. Alternate eye cover testing checks for ability to maintain vertical alignment of the eyes. Have the patient gaze directly on a midline target (e.g., the examiner's nose), then cover one eye, and the other, alternating back and forth every one to two seconds.

Skew is shown by slight upward vertical correction on one side, and downward on the other side, appearing the moment the eye is uncovered. Horizontal movements are irrelevant; no vertical misalignment equals no skew. This test is very specific for central etiologies.

The timing-and-trigger syndrome should be identified before targeting the exam, because the same clinical feature can predict a benign condition in one syndrome and a dangerous condition in another syndrome [6; 36].

ACUTE VESTIBULAR SYNDROME

AVS is defined by acute-onset, persistent dizziness lasting days to weeks, sometimes with lingering sequelae. The temporal evolution at onset and progression during the first week is more important diagnostically than total illness duration. Many patients have an early peak in symptom severity, rapid symptom improvement over the first week, and gradual recovery over weeks to months. Unusual cases resolve in less than 48 to 72 hours [36].

Triggered AVS

For diagnostic purposes, AVS is classified into acquired (postexposure/triggered) and spontaneous forms. Triggers in t-AVS refer to behavior or exposures that precipitate dizziness. Patients with AVS typically experience worsening of dizziness (exacerbation) with head movement. This feature can be confusing or misleading, as for example when triggered dizziness in a patient with vestibular neuritis or stroke is misdiagnosed as BPPV [8].

Triggered AVS results from trauma or toxic exposure and is typically diagnosed largely based on exposure history, which is usually obvious. The most common causes are blunt head injury or ingestion of prescribed or illicit drugs affecting the brainstem, cerebellum, or peripheral vestibular apparatus. Carbon monoxide exposure and acute toxicity is a rare but important consideration [36].

Most patients experience a single, acute attack resolving gradually over days to weeks following the exposure. Depending on the nature of trauma or toxin, other symptoms (e.g., headache, altered mental status) may predominate. Rotatory vertigo, spontaneous nystagmus (when looking straight ahead), and head-motion intolerance may be absent or unimpressive if the pathologic effects are bilateral and relatively symmetric (as with most toxins) [36].

Head Injury

Blunt head trauma, blast injuries, whiplash, or barotrauma may lead to direct vestibular nerve injury, labyrinthine concussion, or mechanical disruption of inner ear membranes to result in an AVS presentation. Basal skull fracture and traumatic vertebral artery dissection should always be considered. TBI may cause post-concussion syndrome, typically with a combination of dizziness, headache, fatigue, and minor cognitive impairment, with dizziness the most common symptom in the first two post-injury weeks [36].

Drug Side Effects/Toxicity

Anticonvulsant side effects or toxicity are a frequent cause of dizziness and vertigo seen in the ED. As mentioned, aminoglycoside toxicity is an established cause of acute bilateral vestibular failure. Gentamicin can cause profound, permanent loss of vestibular function with relatively spared hearing; toxicity may occur after just a single antibiotic dose. Patients usually show gait unsteadiness and oscillopsia (bouncing vision) while walking [36].

Spontaneous AVS

Spontaneous AVS is defined as acute onset of persistent dizziness and vertigo associated with nausea or vomiting, gait instability, nystagmus, or head motion intolerance. A focused physical exam is often diagnostic, because patients are usually symptomatic at presentation [8]. Prototype causes include vestibular neuritis and labyrinthitis [10]. Possible dangerous causes include posterior circulation stroke of the cerebellum or brainstem (the most frequent), bacterial labyrinthitis, and labyrinthine stroke (much less frequent) [8; 36].

Peripheral causes of s-AVS are more common, but central causes are not infrequent and can be fatal if missed, especially with vertebro-basilar ischemia [18]. This would not be as concerning if patients with posterior circulation TIA or stroke presented with classical focal neurologic signs along with the vestibular symptoms of AVS, as the diagnosis would be straightforward [56; 106]. However, this is often not the case.

The 1975 National Institutes of Health (NIH) recommendation that isolated dizziness or vertigo not be considered a TIA persists as a standard teaching [107]. This has contributed to missed diagnoses of TIA and stroke, because many patients with posterior circulation TIA or stroke present with isolated dizziness or vertigo without focal neurologic signs [36; 106; 108]. Patients with s-AVS presenting to the ED with dizziness are at high risk (25%) for stroke. Of nearly 800,000 annual strokes in the United States, 18% are strokes in the posterior fossa (within the brainstem or cerebellum) and up to 70% present with dizziness [8; 18].

An estimated 45,000 to 75,000 patients with stroke are misdiagnosed annually. Roughly 28% to 59% of cerebellar strokes are misdiagnosed in the ED, and isolated dizziness is a risk factor for this misdiagnosis. Posterior circulation strokes are missed more than twice as often as anterior circulation strokes, and cerebellar strokes are four times more likely to be misdiagnosed than stroke misdiagnosis overall. These misdiagnosed patients suffer higher mortality and disability at follow-up [10; 109; 110; 111].

CT is widely used but ineffective to rule out ischemic stroke in s-AVS; MRI with diffusion-weighted imaging (MRI-DWI) is markedly superior. However, within the first 48 hours of symptom onset, MRI-DWI is falsely negative in 12% to 18% of patients with AVS and 53% of patients with small brainstem strokes. Posterior circulation strokes are five times more likely to be falsely negative than anterior circulation strokes. Indiscriminate CT angiography also has very low utility (1.3%) [8; 51; 112].

In the first 48 hours, physical examination outperforms MRI. If the initial physical examination suggests stroke, a negative MRI result should not be interpreted as excluding stroke. Delayed MRI (three to seven days post-onset) may be required to confirm the presence of a new infarct [8]. Posterior circulation stroke should be differentiated from benign peripheral vestibular disorder (***Table 1***) [8; 10; 18]. Nearly all patients with AVS due to a peripheral cause exhibit nystagmus, which may be inhibited if benzodiazepines/other vestibular suppressants are taken before the exam. When possible, assess for nystagmus before medications to manage symptoms are administered [8; 10].

EPISODIC VESTIBULAR SYNDROME

Whether intermittent dizziness is triggered or spontaneous, the duration of dizziness episodes (seconds, minutes, hours) is more important than total illness duration. EVS excludes relapsing and remitting symptoms lasting weeks at a time [36].

Triggered EVS

Triggered EVS is characterized by brief episodes of dizziness lasting seconds to minutes (depending on etiology), precipitated by an obligate trigger. Common triggers are changes in head position or body posture, as when rising from a seated or lying position, tipping the head back to wash one's hair, or rolling over in bed. Uncommon triggers include loud sounds and the Valsalva maneuver. Patients with nausea or vomiting may overestimate the episode duration, but this can usually be clarified by careful history-taking [8].

TESTING TO DIFFERENTIATE POSTERIOR CIRCULATION STROKE FROM BENIGN PERIPHERAL VESTIBULAR DISORDER

HINTS is performed in sequence. Test nystagmus first; HINTS is validated only in patients with nystagmus, and gaze testing is non-intrusive (i.e., head movement unnecessary).

- Gaze testing: Is there a central pattern of nystagmus?
- Alternate cover test: Is skew deviation present?
- HIT: Is the head impulse test result negative?

Patients with s-AVS and worrisome nystagmus, skew deviation, or bilateral normal HIT have a presumed stroke and should be admitted to a hospital. If all three tests seem reassuring, perform a targeted neurologic exam to determine if there are any CNS signs. This involves testing for:

- 4D symptoms:
  - Diplopia (double vision)
  - Dysphagia (difficulty swallowing)
  - Dysarthria (difficulty with speech)
  - Dysmetria (lack of coordination)
- The cranial nerves for hearing
- Anisocoria (unequal pupil size)
- Facial loss of pain or temperature sensation
- Cerebellar function for limb ataxia.

The next step is gait testing to determine if the patient can walk unassisted.

If the answer to any of these questions is yes, the cause is presumed central and treated as stroke. If the answer to all questions is no, the cause is presumed peripheral. All answers must be no in order to exclude stroke because none is sufficiently sensitive individually.

Source: [8; 10; 18] *Table 1*

As mentioned, clinicians should distinguish triggers from exacerbating features [36]. Prototype t-EVS causes are BPPV and orthostatic hypotension; less commonly, it is caused by superior canal dehiscence syndrome [8]. Possible dangerous causes include central paroxysmal positional vertigo and serious causes of orthostatic hypotension, such as internal bleeding. Patients with panic or anxiety disorders may also complain of episodic vertigo, lightheadedness, or dizziness during panic attacks that are triggered or spontaneous. Studies show a high prevalence of vestibular dysfunction for these patients [113].

Episodic positional symptoms are common to all causes of t-EVS, differentiated by targeted history and exams. BPPV is identified by maneuvers that reproduce dizziness combined with an observed pattern of nystagmus. Orthostatic hypotension is diagnosed by observing a significant fall in blood pressure upon sitting and standing. Dangerous t-EVS mimics are identified by careful attention to the corresponding signs and symptoms that differentiate these benign conditions from potentially more serious disorders [36]. Positional triggers, such as rolling over in bed or reclining, are common in BPPV but should not occur in orthostatic hypotension [8]. Unlike head position changes in BPPV, the vertigo and oscillopsia attacks in superior canal dehiscence syndrome are triggered by pressure-related changes of the external auditory canals (e.g., loud sounds, Valsalva maneuver) [21].

The nystagmus characteristics of BPPV and central paroxysmal positional vertigo are distinct. Atypical nystagmus (downbeat or horizontal) is suggestive of central paroxysmal positional vertigo, and pure vertical (up- or downbeating) nystagmus should be considered of central origin until proven otherwise [8; 22]. Central mimics of BPPV less often involve strokes and more often involve posterior fossa neoplasm, hemorrhage, or demyelination recognized by association with other abnormalities [105; 114].

Central paroxysmal positional vertigo also includes common, benign causes, such as alcohol or sedative intoxication. Such patients are more apt to complain of continuous, persistent dizziness exacerbated (not triggered) by position change, often readily diagnosed based on context and other signs of intoxication [8; 36].

In general, BPPV is not associated with vertiginous episodes provoked simply by head and body movements in general, but by sudden positional changes relative to gravity. Moreover, unprovoked (spontaneous) episodes while immobile or the constant sensation of unsteadiness also suggest a diagnosis other than BPPV [21].

BPPV

Within any (semicircular) canal, BPPV is caused by abnormal stimulation of the cupula by otoconia that are free-floating (canalithiasis) or have attached to the cupula (cupulolithiasis) [115]. With head motion in the plane of the affected canal, cupula stimulation produces error signaling that triggers eye movement patterns (nystagmus) specific to the afflicted canal [21]. BPPV should be differentiated from other causes of imbalance, dizziness, and vertigo. Patients should also be assessed for factors that modify management, including impaired mobility or balance, CNS disorders, lack of home support, and increased risk for falling. In patients meeting BPPV diagnostic criteria, it is not necessary to obtain radiography or order vestibular testing in the absence of signs/symptoms inconsistent with BPPV [21].

Provoked nystagmus is used clinically to diagnose BPPV by positioning the head to spatially align the plane of the affected canal with gravity. Gravity challenge moves otolithic debris in the canal, inducing excitation and resultant nystagmus. This identifies the afflicted canal, determines the canal-specific therapy, and distinguishes BPPV from central causes of vertigo [15; 23; 39; 115].

Head movement tests are canal-specific. Because posterior canal BPPV is the most common type, the Dix-Hallpike maneuver is used first. For this maneuver, the patient is moved quickly from sitting upright with head turned 45° in the direction of the involved ear, to supine position with head still turned 45° and neck extended 20° off the end of the exam table with the affected ear down [20; 21].

Before initiating physical maneuvers that involve head rotation, the neck should be evaluated to determine if the procedure should be modified or avoided. The Dix-Hallpike maneuver should be performed with caution or avoided in patients with a current or past neck or back injury, surgery, or painful condition [23; 115].

A diagnosis of BPPV affecting the posterior canal (pc-BPPV) is confirmed by vertigo with torsional (rotatory), upbeating (toward the forehead) nystagmus, with onset 5 to 20 seconds after completion of the Dix-Hallpike maneuver (latency) and duration less than 60 seconds. Provoked nystagmus that lasts longer than 60 seconds with no or brief latency identifies cupulolithiasis [20; 21]. If the initial maneuver is negative, it should be repeated with the opposite ear down.

Before performing the Dix-Hallpike maneuver, the patient should be advised that sudden, intense vertigo or nausea is possible but should subside within 60 seconds. The sequential steps and expected results of the maneuver should be explained, orienting the patient to the supine position and location of the head and providing reassurance that the head and body will be supported and guided safely and securely through the maneuver [20; 21].

There are two types of BPPV affecting the lateral canal (lc-BPPV)—geotropic or apogeotropic—with two types of direction-changing positional nystagmus [21; 39]. When BPPV is suspected and the Dix-Hallpike maneuver is negative, the supine roll test should be used to assess for lc-BPPV. The supine roll test provokes a linear, horizontal nystagmus in patients with lc-BPPV. In cases of lc-BPPV caused by canalithiasis, the nystagmus beats to the ear under the head (i.e., higher intensity on the affected side). If the condition results from cupulolithiasis, the nystagmus beats to the upward ear (i.e., higher intensity on the non-affected side).

EVIDENCE-BASED PRACTICE RECOMMENDATION

According to the American Academy of Otolaryngology, if the patient has a history compatible with BPPV and the Dix-Hallpike test exhibits horizontal or no nystagmus, the clinician should perform, or refer to a clinician who can perform, a supine roll test to assess for lateral semicircular canal BPPV.

(http://journals.sagepub.com/doi/pdf/10.1177/0194599816689667. Last accessed September 23, 2021.)

Strength of Recommendation: Recommendation (Benefits exceed the harms, but the quality of evidence is not as high)

The Dix-Hallpike maneuver also provokes vertigo and nystagmus in BPPV affecting the anterior canal (ac-BPPV), which shows downbeating nystagmus, sometimes with a torsional component, toward the affected ear. Downbeating positional nystagmus may reflect brainstem or cerebellar lesion, which should be ruled out [20; 39]. BPPV can also mimic orthostatic hypotension by producing dizziness on arising and often goes undiagnosed in the elderly.

Serious Causes of Orthostatic Hypotension

As noted, vertigo is a common but under-appreciated symptom in orthostatic hypotension. Older patients taking antihypertensives can show incidental orthostatic hypotension. Orthostatic dizziness and hypotension are not always related; orthostatic dizziness without systemic orthostatic hypotension may indicate hemodynamic TIA or intracranial hypotension [8].

Serious causes of orthostatic hypotension include fluid loss from bleeding, vomiting, diarrhea, and excessive urination/sweating. Occult internal bleeding is the primary dangerous concern [2]. Concomitant chest, back, abdominal, or pelvic pain suggests an intrathoracic or intra-abdominal emergency [36]. Myocardial infarction, occult sepsis, adrenal insufficiency, or diabetic ketoacidosis may present with severe orthostatic hypotension without other overt signs [8].

Spontaneous EVS

s-EVS is marked by recurrent, spontaneous episodes of dizziness that range in duration from seconds to days, with most lasting minutes to hours. Spells sometimes occur up to several times per day, but they are usually less frequent and can be separated by months or even years, depending on etiology [8].

Unlike t-EVS, dizziness episodes in s-EVS cannot be provoked and diagnostic evaluation relies almost entirely on patient history [36]. Vestibular migraine is the most common cause of s-EVS, with a population prevalence of roughly 1% [36]. The classical Ménière disease symptom triad of episodic vertigo, unilateral tinnitus and aural fullness, and reversible sensorineural hearing loss is initially present in only 25% of patients. Patients with suspected Ménière disease should generally be referred to an otolaryngologist, but care should be taken to avoid missing TIA mimics with audio-vestibular symptoms [36].

Reflex (vasovagal) syncope is also a common cause. In reflex syncope, episodes of near-syncope without loss of consciousness substantially outnumber true syncope. Patients usually have prodromal symptoms for 3 to 30 minutes, most commonly dizziness (70% to 75% of cases) that can manifest in vertigo. Diagnosis is based on clinical history, exclusion of dangerous mimics (especially cardiac arrhythmia), and confirmation (if needed) by formal head-up tilt table testing [8; 36].

s-EVS has been reported in panic attacks; episodes begin rapidly, usually peak within 10 minutes, and are accompanied by additional autonomic, cognitive, and perceptual symptoms. Panic attacks can be precipitated by situational stress, such as airplane travel, but often occur spontaneously [116]. Panic attack mimics include ictal panic attacks from temporal lobe epilepsy that usually last seconds with altered mental status, hypoglycemia, cardiac arrhythmias, and basilar TIA, which can produce dizziness and neurologic and autonomic features [8].

Another cause of s-EVS is vestibular paroxysmia, a condition that should be considered when the patient reports 10 or more spontaneous vertigo attacks per day lasting less than one minute (sometimes mere seconds). These attacks respond to a carbamazepine or oxcarbazepine trial [44].

The most common dangerous causes of s-EVS are vertebrobasilar TIA and cardiac arrhythmias. Less commonly, episodes have been observed with other cerebrovascular (e.g., subarachnoid hemorrhage), cardiorespiratory (e.g., unstable angina, pulmonary embolus), and endocrine (e.g., hypoglycemia) disorders. Carbon monoxide exposure is a rare serious cause [36].

Vestibular symptoms associated with s-EVS cannot be reproduced by bedside examination, and patients may be asymptomatic by the time they present to outpatient care. The history is used to distinguish vestibular migraine from TIA or other causes. Diagnosis of benign s-EVS causes can be clear-cut in typical cases, but as mentioned, classical features of vestibular migraine, vasovagal syncope, Ménière disease, or panic attacks are often absent [36].

Isolated attacks of spontaneous dizziness are the most common symptom of an imminent posterior circulation TIA and are frequent in the days to weeks preceding posterior circulation stroke [8; 36]. TIA presenting with isolated dizziness is easily missed; 90% of patients who seek medical attention for transient dizziness that preceded vertebrobasilar stroke are initially misdiagnosed [108]. Dizziness is the most common presenting symptom of basilar artery occlusion and vertebral artery dissection. Prompt diagnosis is critical; 5% of patients with TIA suffer a stroke within 48 hours, but the risk is much greater with posterior circulation TIA. Prompt treatment lowers stroke risk after TIA by 80% [8; 117; 118].

The clinical presentation of vestibular migraine is highly variable. The duration of attacks ranges from seconds to days. Nystagmus (peripheral or central), headache, and nausea, vomiting, photophobia, phonophobia or visual auras can be present or absent during an attack. Hearing loss or tinnitus can occur, mimicking Ménière disease [8].

Vestibular migraine is diagnosed by clinical findings of recurrent migraine headache episodes: five or more episodes characterized by moderate-to-severe vestibular symptoms; ≥50% of episodes have pulsating, impairing headache; photo- or phonophobia; and/or visual aura [48].

The prevalence of migraine syndrome is high in patients with Ménière disease, and when such patients present with attacks of s-EVS, the diagnostic attribution may seem difficult. The presence of low frequency hearing loss favors the diagnosis of Ménière disease [18; 48].

Cardiac arrhythmia should be suspected when syncope or exertion is the precipitating factor for the onset of dizziness. Clinical features may increase or decrease the odds of a dangerous cardiac cause, but cardiac specialist testing is often required for diagnostic confirmation [8; 36].

CHRONIC VESTIBULAR SYNDROME

Triggered CVS

Central compensatory mechanisms can ameliorate vestibular symptoms over time, but to an unpredictable extent, and lasting vestibular compensation does not develop or incompletely develops. Thus, some vestibular syndromes become chronic, with persistent dizziness or unsteadiness lasting months to years, with oscillopsia, nystagmus, and/or gait disturbance. CVS develops from poorly compensated unilateral or bilateral vestibulopathy or cerebellar degeneration [119]. Other etiologies include PPPD, autoimmune or neoplastic disease, central vestibular syndromes with downbeat or upbeat nystagmus, and dizziness due to isolated causes [120]. In t-CVS, dizziness or vertigo is provoked by head movement (as in uncompensated vestibular loss), medication side effects, and/or anxiety, depression, or other psychiatric conditions [119].

Bilateral vestibulopathy is a CVS characterized by unsteadiness when walking or standing that worsens in darkness, on uneven ground, or during head motion. Patients may describe head or body movement-induced blurred vision or oscillopsia. Symptoms usually remit when sitting or lying down.

Bilateral vestibulo-ocular reflex function is significantly impaired or absent in bilateral vestibulopathy and is assessed using the HIT, video-HIT, or other tests [40].

As discussed, PPPD is a newly defined CVS that unifies key features of chronic subjective dizziness, phobic postural vertigo, and related disorders. Patients with PPPD often develop gait disorder, anxiety, avoidance behaviors, and severe disability [121].

A PPPD diagnosis requires dizziness, unsteadiness, or non-spinning vertigo present on most days for at least three months, exacerbated by posture, movement, and/or moving/complex visual stimuli. Symptoms are precipitated by any condition that causes vertigo, unsteadiness, dizziness, or problems with balance and cause significant distress or impairment [62].

In addition to timing and triggers, the diagnostic approach should also capture the dynamic features of patient history to uncover the nuances of psychologic distress, maladaptive coping, and differential diagnosis. Patients who fulfill diagnostic criteria for PPPD after a TBI or whiplash should receive the diagnosis. The presence of other injury sequelae determines additional diagnoses [62].

EVIDENCE-BASED PRACTICE RECOMMENDATION

According to the Bárány Society, the differential diagnosis of PPPD includes chronic sequelae of acute precipitants, recurrent attacks of episodic precipitants, ongoing manifestations of chronic precipitants, other chronic vestibular syndromes, medical or psychiatric disorders that produce persistent unsteadiness or dizziness, and adverse effects of regularly consumed prescription or non-prescription medications.

(https://content.iospress.com/articles/journal-of-vestibular-research/ves622. Last accessed September 23, 2021.)

Level of Evidence: Expert Opinion/Consensus Statement

Spontaneous Chronic Vestibular Syndrome

s-CVS conditions include chronic dizziness or vertigo associated with nystagmus, blurred vision, or impaired visual acuity from oscillopsia, originating from cerebellar or brainstem degeneration or atrophy [122]. Other central etiologies of s-CVS include cervical vertigo and Chiari malformations [119]. Several cerebellar syndromes due to neurodegenerative and hereditary diseases can lead to ataxia and postural instability associated with cerebellar oculomotor disorders (e.g., downbeat nystagmus, gaze-evoked nystagmus) [122].

Episodic ataxia type 2, the most frequent inherited cerebellar ataxia syndrome, is characterized by recurrent attacks of dizziness and ataxia lasting several hours, often elicited by physical activity, alcohol consumption, or stress. More than 90% of patients with episodic ataxia type 2 have oculomotor disorders such as downbeat nystagmus [119].

The vertigo symptoms are usually associated with degenerative cervical spine disease and may resemble BPPV due to proprioceptive abnormalities related to cervical spine dysfunction. However, cervical vertigo may be triggered by rotating the head relative to the body while upright, as opposed to the vertigo triggered by changes in head position relative to gravity in BPPV [21; 123].

CLINICAL MANAGEMENT

Returning to the funnel analogy, a range of possible dizziness and vertigo etiologies (e.g., orthostatic hypotension, vasovagal syncope, head injury, medication side effects/toxicity, posterior circulation TIA/stroke, central paroxysmal positional vertigo, and cardiac arrhythmias) would be excluded or diagnosed. Certain patients would be treated, and others referred to specialists or admitted to an ED. This would include all etiologies categorized as t-AVS.

After vestibular disorders have been differentiated and diagnosed, treatment selection can be divided into approaches that focus on symptom control, those specific to the underlying vestibular etiology, and those aimed at promoting recovery [124]. Thera-

peutic approaches broadly used across vestibular etiologies are discussed first, followed by treatments specific to acute, episodic, and chronic vestibular syndromes.

COMMON PHARMACOTHERAPIES

Most pharmacotherapies for dizziness or vertigo related to peripheral or central vestibular, cerebellar, or oculomotor disorders fall into one of seven groups, or the 7 As [61]:

- Antiemetics
- Anti-inflammatory
- Anti-Ménière
- Anti-migraine
- Antidepressants
- Anticonvulsants
- Aminopyridines

Patients with severe nausea or vomiting greatly prefer non-oral administration [124]. As such, vestibular suppressants are usually administered in non-oral routes initially for rapid symptom control, followed by oral medications.

Vestibular Suppressant Medications

As discussed, dizziness, vertigo, disequilibrium, and associated symptoms can arise from diverse central or peripheral disturbances of vestibular function. By suppressing vestibular sensory input, vestibular suppressant medications can reduce conflicting sensory input, control undesirable perceptions, and diminish patient distress [13].

Many distressing vestibular-related symptoms are mediated by the vomiting center in the medulla. The vomiting center is activated through neurotransmitter release involving vestibular and CNS (histamine, acetylcholine), visceral (gut) (dopamine, serotonin), and chemoreceptor trigger zone (dopamine, serotonin) pathways [125]. These pathways are therapeutic targets of most vestibular suppressants, which are effectively used for symptomatic control in nearly all AVS or EVS subtypes, regardless of underlying etiology. These medications are variously effective for controlling dizziness, vertigo, motion sickness, associated symptoms (e.g., nausea, vomiting, diarrhea), and patient distress or anxiety during episodes, which can be severe [21; 126].

Drug classes and agents commonly used as vestibular suppressants include antihistamines, benzodiazepines, scopolamine, dopamine antagonists, and ondansetron (***Table 2***). Antihistamines (e.g., meclizine, diphenhydramine, dimenhydrinate) block the release of histamine and acetylcholine and are especially beneficial in vestibular-mediated nausea, vomiting, and motion sickness. Side effects include sedation, confusion, dry mouth, and urinary retention. Meclizine is preferred because it has minimal anticholinergic effects, causes less sedation, and is effective in the treatment of vertigo due to labyrinth dysfunction. It is also the drug of choice in pregnancy [124]. Diphenhydramine is recommended for the treatment of Ménière disease [127].

Benzodiazepines (e.g., diazepam, clonazepam, lorazepam) potentiate the inhibitory effects of the gamma-amino butyric acid system to produce anxiolytic, sedative, muscle-relaxant, and anticonvulsant effects. Benzodiazepines can be highly effective in vertigo unresponsive to antihistamines and for calming intensely distressed patients, but they are sedating and mainly used when antihistamines are inadequate [124]. They also may be used for patients requiring prophylaxis for canalith-repositioning procedures [21].

Scopolamine is a belladonna alkaloid that blocks CNS neurotransmission of acetylcholine and is one of the most effective agents for preventing motion sickness. Scopolamine is also effective for vestibular-mediated nausea/vomiting and is better tolerated as a transdermal patch than when taken orally. Common side effects are sedation, constipation, dry mouth, and urinary retention [115; 125].

Dopamine antagonists (e.g., metoclopramide, domperidone, promethazine, prochlorperazine) block dopamine stimulation in the intestines and chemoreceptor trigger zone, limiting emetic input to the medullary vomiting center. Promethazine and prochlorperazine also inhibit central muscarinic and histamine receptors, which contributes to their antiemetic and sedative properties [125].

VESTIBULAR SUPPRESSANT MEDICATIONS	
Medication	**Dosage and Route**
Antihistamine Agents	
Diphenhydramine	50 mg PO twice daily 10–50 mg IM or IV
Meclizine	25–50 mg PO three to four times per day
Promethazine	12.5–50 mg PO every four to six hours 50 mg RS four times per day 10–50 mg IM or IV
Benzodiazepines	
Lorazepam	0.5–2 mg PO two to three times per day
Diazepam	2–5 mg PO three to four times per day
Clonazepam	0.25–1 mg PO two to three times per day
Antiemetic Agents	
Metoclopramide	10–20 mg PO every four to six hours 10–20 mg IM or IV
Prochlorperazine	10–20 mg PO every four to six hours 25 mg RS every six hours 5–10 mg IM or IV
Domperidone	10–20 mg PO every six to eight hours
Ondansetron	8 mg PO every 6 to 12 hours 4 mg SL, IM, or IV
Anti-Motion Sickness	
Scopolamine	1 TD patch (1.5 mg) every three days
IM = intramuscular; IV = intravenous; PO = oral; RS = rectal suppository; SL = sublingual; TD = transdermal.	
Source: [15; 21; 120; 124; 128]	*Table 2*

Ondansetron inhibits serotonin-5HT3 receptors in the small bowel, vagal nerve, and chemoreceptor trigger zone, suppressing serotonergic activation of the vomiting center to alleviate nausea and vomiting. Adverse effects are uncommon but can include headache, constipation, diarrhea, and fatigue [125].

Extrapyramidal symptoms, including irreversible tardive dyskinesia (an involuntary movement disorder), are a potential risk with all central dopamine antagonists. Extended use (duration of 12 or more weeks) increases the risk of tardive dyskinesia [129]. However, dopamine antagonists are considered safe for use as acute therapy and are usually reserved for patients with severe vomiting [124].

In peripheral vestibular disorders, all vestibular suppressants can interfere with central compensation, and their use is recommended to not exceed three days [15; 21; 128]. The goal is for patients to rapidly receive specialist care, but patients may not get an immediate appointment and remain highly symptomatic. In this context, vestibular suppressants should continue for symptom control until optimized treatment is initiated by a specialist [120].

Vestibular suppressants can cause drowsiness and interfere with driving. In particular, the use of benzodiazepines is a significant risk factor for falls; this risk increases with polypharmacy, common in the elderly [15; 21]. Antihistamines carry added risks of impaired cognitive functioning, gastrointestinal motility, and vision in elderly patients [21]. Some patients can develop psychologic dependence to benzodiazepines and have difficulty discontinuing the medication [120].

Betahistine

First approved for use in Europe in the 1970s, betahistine has been prescribed to more than 100 million patients with vestibular disorders and is the first-line treatment of Ménière disease in Germany. Betahistine is not approved by the U.S. Food and Drug Administration, but it may be obtained through compounding pharmacies in the United States with a prescription [15; 130]. It reduces vestibular symptoms but seems to differ from vestibular suppressants by promoting vestibular compensation. Histamine regulates sensory coding in the peripheral vestibular system. Betahistine (dihydrochloride or dimesylate), a structural analogue of histamine, is a potent histamine H3 receptor antagonist and a weak histamine H1 receptor agonist [15]. Betahistine reduces the frequency and severity of vertigo, nausea, and vomiting in diverse unilateral vestibular etiologies. Central and peripheral histamine receptor activity is a presumed mechanism [130; 131; 132].

Betahistine dose-dependently increases vestibulocochlear blood flow, increases central and vestibular system histamine turnover, decreases peripheral vestibular system input, and reduces histamine-induced excitation in vestibular cells through local H3 receptor blockade. These mechanisms are thought to improve vestibular compensation, reduce functional asymmetry of vestibular organs, and improve labyrinth microcirculation by rebalancing the production and resorption of endolymphatic fluid [130; 131; 132]. In this course, all discussions of betahistine refer to betahistine dihydrochloride, unless otherwise stated.

Antidepressant Drugs

Monoamines are the neurochemicals serotonin, norepinephrine, and dopamine. Dysregulated monoamine neurotransmission is implicated in anxiety disorders and depression. A bi-directional relationship between impaired monoamine neurotransmission and vestibular signaling dysfunction is suggested, with asymmetric vestibular system release of serotonin, norepinephrine, or dopamine linked to vestibular migraine and other dizziness/vertigo etiologies [50; 61; 120].

Antidepressant drugs include SSRIs (e.g., fluoxetine, escitalopram), serotonin norepinephrine reuptake inhibitors (SNRIs) (e.g., venlafaxine, duloxetine), and tricyclic antidepressants (e.g., nortriptyline, imipramine, amitriptyline). They modulate serotonin, norepinephrine, and dopamine neural pathways (with varying specificities) and are first-line treatments for anxiety disorders and depression. These agents are increasingly recommended for use in some vestibular-related disorders [50; 120; 133].

Aminopyridines

Aminopyridines are potassium-channel blockers, established as pharmacotherapy for cerebellar diseases that include downbeat nystagmus, upbeat nystagmus, central positional nystagmus, episodic ataxia type 2, and gait disorders in cerebellar ataxia [61].

Aminopyridines used in these disorders are 3,4-diaminopyridine (3,4-DAP) and 4-aminopyridine (4-AP). 4-AP crosses the blood-brain barrier more easily and is superior to 3,4-DAP in some cases. Both drugs are well-tolerated and without major side effects apart from nausea, transient paresthesia, or headache [122].

QT Interval Prolongation

Some vestibular disorder pharmacotherapies may interact with other medications to risk QT interval prolongation [120]. A prolonged QT interval is a symptom of disordered myocardial repolarization that increases the risk of potentially life-threatening ventricular tachycardia (i.e., torsades de pointes) [134]. A complete list of medications that prolong the QT interval is available at https://www.crediblemeds.org.

VESTIBULAR REHABILITATION

Vestibular rehabilitation, another therapeutic modality broadly used across dizziness and vertigo etiologies, is a specific physical therapy for patients with peripheral or central vestibular disorders. Vestibular rehabilitation reduces symptoms and improves functioning by promoting CNS compensation through exercise-based strategies [135; 136].

Following an acute peripheral vestibular event, clinical recovery occurs in advance of improved peripheral vestibular function. This suggests that most of the early recovery and a substantial portion of total recovery derives from central compensation (long-term changes in neuronal responses to head movements) that is multisensory and is the primary target of vestibular rehabilitation. Early rehabilitation (during a critical period of adaptation and compensation) may be more effective than late intervention. As such, vestibular rehabilitation should begin shortly after symptom onset [135; 137].

Patients typically receive supervised therapy one to two times per week and are taught daily home exercises. The average duration of therapy is 6 to 12 weeks for patients with peripheral vestibular disorder and longer for patients with central vestibular disorder or mobility-impairing comorbidities [43; 136].

EVIDENCE-BASED PRACTICE RECOMMENDATION

The American Physical Therapy Association concludes that clinicians may prescribe a home exercise program of gaze stability exercises consisting of a minimum of 3 times per day for a total of at least 12 minutes per day for patients with acute/subacute vestibular hypofunction and at least 20 minutes per day for patients with chronic vestibular hypofunction.

(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4795094. Last accessed September 23, 2021.)

Strength of Recommendation: D (Expert opinion from the clinical experience of the guideline development team)

General Components

Vestibular rehabilitation uses several approaches to reduce symptoms and impairment and to promote function in patients with dizziness, postural instability, and gaze instability. Visual-vestibular interaction (adaptation) exercises strengthen the vestibulo-ocular reflex and gaze stability to promote central compensation for reduced vestibular input, improving gaze instability, balance, and dizziness [43; 135; 136].

Strategic substitution exercises promote the use of sensory stimuli and spatial cues from vision and proprioception to substitute for loss of vestibular inputs. Cervico-ocular reflex input is strengthened to reduce spatial uncertainty, and alternative spatial cues can improve balance and walking [43; 135; 136].

Balance and gait training under challenging sensory and dynamic conditions facilitates visual and somatosensory cues to offset vestibular hypofunction. Equipment to augment training includes gaming technology, optokinetic drums, and virtual reality [43].

Habituation exercises reduce visual motion sensitivity (e.g., visual vertigo, space and motion discomfort) through systematic exposure to noxious stimuli evoking mild, temporary symptoms. Approaches include optokinetic stimuli and virtual reality for immersion in repetitive moving and visually challenging environments [43; 135; 136].

Vestibular rehabilitation can help counteract the negative effects of deconditioning, common in vestibular patients, to avoid symptom provocation [43]. Psychologic deconditioning can progress to PPPD (phobic postural vertigo) to become the greatest obstacle to recovery. After a vestibular event, elderly patients can develop fear of falling, avoidance behavior, and indefinite mobility limitation without vestibular rehabilitation [75].

Based on strong evidence and a preponderance of benefit over harm, patients with acute, subacute, or chronic unilateral or bilateral vestibular hypofunction should be offered vestibular rehabilitation [43]. Without head movements, saccadic or smooth-pursuit exercises should not be used alone as gaze stability exercises.

Acute Peripheral Vertigo

For cases of acute peripheral vertigo, vestibular rehabilitation begins with the patient focusing on an object with a blank background, then moving the head slowly (to avoid severe nausea) to the right and left, and then up/down. This is done two to three times per day for several minutes, and the patient is encouraged to increase the speed as tolerated [135].

Chronic Peripheral Vestibular Hypofunction

The vestibular rehabilitation approach for chronic peripheral vestibular hypofunction is more aggressive, with increasingly more difficult tasks while keeping symptoms manageable. Tasks include eye and head movements while standing, walking forward, walking backward, and standing or walking on compliant or uneven surfaces [135].

Bilateral Vestibular Loss

Central adaptation is much less likely with bilateral vestibular loss than in unilateral loss, but vestibular rehabilitation can promote strategic substitution through strengthening saccadic eye movements and optimizing the efficacy of neck stretch receptors. Vestibulo-ocular exercises are initiated when residual vestibular function is a possibility. Improved balance and gait speed help offset the bilateral loss [138]. Education on fall prevention is critical, because these patients have an especially high fall risk, compounded by darkness and uneven surfaces [135].

Central Vertigo

Recovery of vestibular function in patients with central vertigo is limited because pathologic involvement of central vestibular structures restricts compensation, and improvement takes longer than with peripheral vestibular dysfunction [136]. For these patients, vestibular rehabilitation emphasizes gait and balance activities, along with eye and head movements. Adaptive methods to perform activities of daily function are often taught. If nausea is limiting, antiemetic medications used in conjunction with vestibular rehabilitation may improve participation and final outcomes [135].

ANXIETY AND DIZZINESS

The demonstrable interconnectivity between threat/anxiety, vestibular, visual, and somatosensory systems, and the interactions between anxiety disorders and vestibular morbidity point to the importance of a multimodality treatment approach for patients with anxiety and dizziness [72].

Studies have followed patients with dizziness over time and made several important findings [62; 72]. A highly anxious response to the acute dizziness/vertigo of new-onset vestibular neuritis or BPPV predicts continued dizziness 3, 6, and 12 months later. This initial psychologic response has a far greater impact on long-term outcomes than measurable vestibular dysfunction at baseline or follow-up. Patients with emerging symptoms of PPPD who receive cognitive-behavioral therapy within eight weeks of onset have marked reductions in dizziness and avoidance of provocative situations six months later. A highly anxious response to a precipitating event may be the pivotal initiating pathophysiologic process in PPPD (the leading cause of long-term vestibular disability), and early symptom-specific interventions might counter this effect.

Patients with poor recovery from acute vestibular neuritis have higher rates of visual dependence, autonomic arousal, anxiety, and fear of vestibular symptoms [139; 140]. Poor recovery is also unrelated to vestibular function, but significantly related to acute visual dependence and failure of sensory integration mechanisms to down-regulate visual contribution to central compensation processes. These data highlight the importance of [139; 140]:

- Early identification of abnormal visual dependence and concurrent anxiety
- Early treatment to improve long-term outcomes by reducing visual dependence with sensory re-weighting strategies
- Combining pharmacotherapy and cognitive therapies to reduce anxiety and autonomic arousal

In vestibular patients, successful treatment outcomes require the simultaneous assessment of vestibular, psychiatric (anxiety), and functional (phobic vertigo) disorders. Only when identified can they be addressed by systematically applied treatment that incorporates patient education, vestibular rehabilitation, cognitive-behavioral therapies, and medications to control morbidity and increase the potential for sustained remission [73].

SPONTANEOUS ACUTE VESTIBULAR SYNDROMES

Acute Unilateral Vestibulopathy/ Vestibular Neuritis

This acute, spontaneous, peripheral vestibular disorder is characterized by the rapid onset of severe vertigo with nausea, vomiting, and gait instability. The symptoms can be severe and disabling in the short term; patients may need to be hospitalized for intravenous fluids and medications [128; 141]. Panic disorder has been found to develop in 10% of patients followed for two years after the initial acute vestibular neuritis episode [142].

Vertigo, nausea, and vomiting can be treated with a combination of vestibular suppressants, not exceeding seven days to avoid disrupting CNS adaptation and compensation [15; 128]. The vestibular nerve is selectively vulnerable to inflammation-related swelling and entrapment by its pathway in a narrow, bony canal [34]. Oral corticosteroids may help reduce the severity of vestibular neuritis if initiated in the first few days. The recommended agents are [15; 120]:

- Methylprednisolone initiated at 100 mg/day and then reduced by 20 mg every fourth day, OR
- Prednisone 60 mg/day for one week

When acute symptoms subside, patients should begin vestibular rehabilitation to promote CNS adaptation and sensory re-weighting [15; 128].

Labyrinthitis

A presumed viral acute labyrinthitis is reasonable to treat with corticosteroid therapy, such as a 10-day course of prednisone with 60 mg/daily on days 1 through 5, reduced to 10 mg/daily on days 6 through 9, and 5 mg on day 10. Some evidence suggests corticosteroid therapy may hasten recovery but does not change the long-term prognosis [141]. Patients with bacterial labyrinthitis should be referred to an ENT specialist.

Herpes Zoster Oticus

Patients with herpes zoster oticus should be treated with corticosteroids and a high-dose oral antiviral (acyclovir, famciclovir, or valacyclovir) when reactivation of latent varicella zoster virus is suspected. Carefully look for painful vesicles on the external ear and within the back of the external ear canal. Even in the absence of visible vesicles, treatment with an antiviral agent is probably prudent with significant localized ear pain and normal tympanic membrane [15].

TRIGGERED EPISODIC VESTIBULAR SYNDROMES

Benign Paroxysmal Positional Vertigo

Canalith repositioning procedures (CRPs) are the first-line therapy option and the most effective treatment for BPPV for patients with prolonged symptoms and/or frequent recurrences. Vestibular suppressants are generally avoided, though a brief course of an antihistamine (e.g., meclizine) may be indicated for initial symptom control. This may be all that is needed for patients with mild, self-limited symptoms and infrequent recurrences. Rarely, BPPV can be refractory to CRPs and require surgical occlusion of the affected semicircular canal [15].

Outcome assessment within one month of initial observation or treatment is necessary to document symptom resolution or persistence. Patients with persistent symptoms should be evaluated for treatment failure. Referral to a specialist is recommended to identify unresolved BPPV and/or an underlying peripheral or central vestibular disorder.

In general, CRPs move the patient through a sequence of head position changes that use gravity to move otolith debris (including the pathologic trigger) out of the affected canal and back into the vestibule [21]. CRPs used in canalithiasis or cupulolithiasis appear similar [21]. These procedures should only be performed after the affected canal is identified by diagnostic positioning techniques. Patients should be informed that dizziness, vertigo, or a sense of falling can develop during a CRP. Patients who had severe nausea or vomiting with the Dix-Hallpike should receive antiemetics 30 to 60 minutes before the procedure [21; 120].

Posterior Canal BPPV

CRP is strongly recommended as initial therapy for pc-BPPV [21]. It has a demonstrated high success rate in improving vertigo and in restoring gait and balance in persons with pc-BPPV [143]. The Epley maneuver is the preferred CRP for pc-BPPV and has more than 20 years of evidential support. Meta-analyses have found that, compared with sham or control groups, the Epley led to significantly greater rates of complete vertigo resolution and conversion from a positive to a negative Dix-Hallpike. After 12 months, the Epley was superior to sham maneuver in conversion to negative Dix-Hallpike and perceived disability [21; 144].

EVIDENCE-BASED PRACTICE RECOMMENDATION

The American Academy of Otolaryngology recommends clinicians should treat, or refer to a clinician who can treat, patients with posterior canal BPPV with a canalith repositioning procedure (http://journals.sagepub.com/doi/pdf/10.1177/0194599816689667. Last accessed September 23, 2021.)

Strength of Recommendation: Strong recommendation (Benefits of the recommended approach clearly exceed the harms and that the quality of the supporting evidence is high)

The Semont maneuver uses inertial and gravitational forces to move patients briskly down into a side-lying position and then through a rapid 180° arc. In this manner, the Semont repositions free-floating debris from the posterior canal into the vestibule or breaks off canalith from adherence to the cupula [120].

The Semont and Epley maneuvers are comparably effective in pc-BPPV [21]. With speed of rotation critical for a successful Semont, and adequate neck extension and flexibility required for a successful Epley, patient features such as obesity and neck mobility can guide CRP selection [20]. The Semont is a suggested alternative to the Epley for patients with back problems [120].

Lateral Canal BPPV

Compared with apogeotropic lc-BPPV, the geotropic form is the best-researched and most clinically responsive form. The most frequently used repositioning approaches in lc-BPPV are [20; 21; 39]:

- Gradual rotations around the longitudinal axis of the body toward the nonaffected ear
- Lying for 12 hours overnight on the nonaffected ear (for geotropic) or on the affected ear (for apogeotropic)
- The Gufoni maneuver, which moves the patient from sitting to lying sideways with the head turned downward, holding, and repeating

The Gufoni maneuver can effectively treat canalithiasis or cupulolithiasis lc-BPPV and has the advantage of eliminating the need to determine the involved form [39; 145]. An alternative is to first convert cupulolithiasis of the lateral canal to canalithiasis by shaking the head after bending it 90° forward into the vertical plane [39].

Anterior Canal BPPV

The Gufoni maneuver or a reverse Epley maneuver has demonstrated symptom resolution in more than 75% of patients with ac-BPPV [146]. A new maneuver, called the short CRP and based on simulation with a biomechanical model, was compared with classic CRP in one analysis [147]. Using a previously published 3-dimensional biomechanical model of the human labyrinths for the study of BPPV, the researchers analyzed conventional CRP in the treatment of anterior canalithiasis. The expected position of free otoliths near the anterior ampulla of the anterior semicircular duct was followed while recreating the sequential positions of the CRP. Although standard CRP was effective, certain enhancements (e.g., elimination of position 4 of the standard CRP) were found to increase successful repositioning [147].

Vestibular Suppressant Treatment

Routine use of vestibular suppressants is not recommended in BPPV, as they may interfere with central compensation and obscure Dix-Hallpike findings. None are as effective as CRPs and cannot be used as CRP substitutes [15; 21].

In some patients, acute/short-term pharmacotherapy can be indicated. Anxiety and BPPV often co-occur; anxiety levels of patients with panic disorder and agoraphobia diagnosed with BPPV remained significantly elevated 14 days after CRP [148]. Thus, benzodiazepines have a role in patients with significant anxiety or who are too anxious to proceed with CRP [15; 21].

Dimenhydrinate, scopolamine, or diazepam may be required in severely symptomatic patients before CRP, patients who become severely symptomatic after CRP, or those who refuse CRP. Patients exceptionally prone to motion sickness should receive meclizine [15; 21; 115]. CRP plus betahistine more effectively reduced vertigo symptoms than CRP alone [149]. If prescribed, clinicians should educate patients that vestibular suppressants can increase risks of cognitive impairment, falls, drug interactions, and machinery or driving accidents [21].

BPPV and CNS Disorders

Aside from migraine, BPPV in patients with pre-existing central neurologic disorders is rarely addressed in the literature. In one study of 93 patients with BPPV, 31.2% had a central neurologic disorder, with cerebrovascular disease and migraine the most common. The efficacy of repositioning therapy was excellent for BPPV with or without a pre-existing central neurologic disorder [150].

Post-CRP Residual Dizziness

Residual dizziness following successful repositioning is common in patients with BPPV, described as continuous or intermittent imbalance, lightheadedness, or unsteadiness without positional vertigo. The duration of vertigo before CRP is linked to residual dizziness and incomplete central adaptation. Residual dizziness is significantly associated with anxiety disorders, and subjects with high anxiety show more durable and disabling dizziness even after the resolution of acute vertigo in absence of otolithic or vestibular dysfunction [131; 151].

Anxiety is highly prevalent in elderly patients with BPPV, and the adverse impact of residual dizziness on psychologic, social, and daily functioning can be severe. Early recognition and treatment of BPPV and comorbid anxiety is recommended to decrease the incidence of residual dizziness [131].

Refractory BPPV

If BPPV remains refractory despite a correct diagnosis and competently performed repositioning maneuvers, surgery may be indicated. The two surgical options are partial neurectomy of the vestibular nerve (singular nerve) or occlusion of the affected (mainly posterior) semicircular canal. Of the two, posterior canal occlusion is favored based on symptom reduction and complications [152].

Superior Canal Dehiscence Syndrome

In superior canal dehiscence syndrome, sound- or pressure-induced dizziness with auditory symptoms of autophony, hyperacusis, or tinnitus results from a bony dehiscence of the superior semicircular canal. Surgical repair of the canal is the recommended treatment [120].

SPONTANEOUS EPISODIC VESTIBULAR SYNDROMES

For patients with vestibular migraine or Ménière disease, vertigo attacks are unpredictable and difficult to control or avoid. The unpredictable, distressing experience may elevate patient anxiety over the next attack sufficiently to induce a secondary panic-like disorder, substantially adding to the psychologic burden [50].

Migraine and anxiety disorders share common genetic and environmental risk factors, and an interaction between migraine and anxiety is established. Auditory center, limbic system, and vestibular system interconnections may account for high rates of anxiety in patients with persistent tinnitus, fluctuating hearing loss, and vertigo symptoms in vestibular migraine or Ménière disease [50; 153].

Ménière Disease and Endolymphatic Hydrops

The episodic vertigo, hearing loss, and tinnitus in Ménière disease is associated with endolymphatic hydrops in the labyrinthine system of the affected ear [128]. Ménière disease should be viewed and managed as a chronic condition, and treatment

is tiered by disease stage and severity [154]. Acute symptomatic relief does not address the underlying pathophysiology, and the clinical goal is to minimize recurrent vertigo attacks and hearing symptoms to prevent new or additional damage to vestibular structures [155].

First Tier

Patients with Ménière disease are vulnerable to dietary and environmental factors that can impact hearing and balance. Triggers for Ménière disease may include high salt intake, caffeine, alcohol, nicotine, stress, monosodium glutamate, and allergies. Patients who identify and avoid triggers may greatly reduce their Ménière disease symptoms [155]. Therefore, lifestyle modification is the cornerstone of first-tier treatment.

Caffeine and nicotine are vasoconstrictors that may reduce microvascular flow in the labyrinthine system. Alcohol also causes fluid and electrolyte shifts that can stress a fragile ear. Smoking cessation and limiting daily intake to one caffeinated or alcoholic beverage are typically recommended [155].

When dietary and environmental changes fail to control the episodes, combinations of diuretic and as-needed vestibular suppressant/antiemetic agents are effective to control vertigo episodes in many patients, but do not protect hearing loss. Off-label use of sublingual lorazepam (0.5–1 mg up to four times per day) is anecdotally effective in achieving relief from acute vertigo attacks [155].

Betahistine is a conservative treatment option widely used in Europe for Ménière disease. It is believed to decrease symptoms by improving microcirculation in the inner ear and re-balancing endolymph production with resorption [156]. In one study, patients with mixed vestibular etiologies including Ménière disease received betahistine 48 mg/day. The decrease in average vertigo attacks per month from baseline to 60 days on betahistine persisted unchanged at 60 days off betahistine, which may suggest durable vestibular compensation [132]. As mentioned, demonstrating a treatment effect separate from spontaneous remission is difficult in Ménière disease and other s-EVS disorders.

Based on clinical experience with long-term treatment in patients with Ménière disease, long-term, high-dose betahistine is the recommended therapy, initiated at 48 mg three times per day [39; 61]. If symptom alleviation is insufficient after three months, the dose can be increased up to 480 mg/day [120; 157]. As noted, betahistine can be obtained at compounding pharmacies in the United States with a prescription [15].

Second Tier

Intratympanic injection (ITI) of corticosteroids is suggested for patients with Ménière disease-related disabling vertigo attacks despite conservative treatments, as the complication rates are low and side effects minimal. ITI of 0.4–1.0 mL high-dose dexamethasone solution (12 mg/mL) can improve vertigo symptoms and patient functioning, which may remain durable over 6 to 24 months [120]. However, patients may require repeated injections to maintain efficacy that can wane over time, and intratympanic gentamicin may be more effective [155].

Third Tier

Intratympanic gentamicin, a vestibulotoxic antibiotic, is a favored approach for Ménière disease refractory to less invasive options. Gentamicin induces unilateral vestibular loss to facilitate central compensation, reduce Ménière disease symptoms, and improve overall function [98; 158]. Meta-analyses of published clinical trials found 92.7% of patients achieved complete or substantial vertigo control and 74.7% achieved complete vertigo control with intratympanic gentamicin [99; 159].

ITI of gentamicin is ototoxic in some patients and has mainly been reserved for patients with Ménière disease and pre-existing hearing loss. To offset this limitation, a newer technique injects a minimal dose of gentamicin (0.5–0.75 mL of a 40 mg/mL solution) into the middle ear. A single injection provided good vertigo control over four years in 76% of patients; 15% to 20% required a second injection [155].

ITI gentamicin (2.0 mL of 40.0 mg/mL solution; up to two injections) was superior to ITI dexamethasone (4 mg/mL, three injections over seven days) in achieving complete vertigo control (81.0% vs. 43%) and complete or substantial vertigo control (93.5% vs. 61%). Significant hearing loss (>10 dB) developed in 13% of patients taking gentamicin [155; 160].

A 2020 systematic review and meta-analysis compared five treatment arms that included placebo, ITI gentamicin, oral high-dose betahistine, ITI steroid, and ITI steroid plus high-dose betahistine for treatment of Ménière disease [161]. The reviewers found that, among the treatment arms compared, ITI steroid plus high-dose betahistine performed best for both hearing preservation and vertigo control. Although ITI gentamicin also performed well, it may be detrimental to hearing preservation with high cumulative dosage and short interval between injections. The authors noted that ITI steroid plus high-dose betahistine has not been compared in head-to-head trials against other interventions, with the exception of ITI steroid alone in one trial, and stated that future trials are needed to establish comparative effectiveness with direct evidence [161].

Intractable Bilateral Ménière Disease

Ménière disease may become bilateral in 15% to 20% of patients, usually within the first several years of onset. Bilateral involvement limits some vestibular ablation options, because treating both ears can result in bilateral vestibular loss [15]. Treating one side may not relieve vertigo, and interventional treatment can cause permanent hearing loss in a patient already at risk of hearing loss in both ears [128].

Options for intractable Ménière disease include endolymphatic mastoid shunt procedures, vestibular neurectomy, or labyrinthectomy, the latter used only in patients already deaf in the affected ear. Ablative surgical procedures are mainly reserved for ITI gentamicin failure. Because the development of Ménière disease is multifactorial, no single approach to therapy is expected to become the standard for all patients [152].

Vestibular Migraine

Treatment efficacy for vestibular migraine is not well-studied, partially because the disorder was only defined in 2013 [162]. Established treatments for migraine and/or vertigo are primarily recommended as abortive or prophylactic therapies for migraine symptoms in vestibular migraine. These medications may improve both headache and vertigo symptoms but can be hit or miss, and patients may need several different trials to find an individualized therapy [162; 163].

Symptomatic Treatment of Acute Episodes

Acute attacks of vestibular migraine are treated with vestibular suppressants that include benzodiazepines (e.g., clonazepam, lorazepam), antiemetics (e.g., promethazine), antihistamines (e.g., meclizine, dimenhydrinate), and anticholinergic agents (e.g., scopolamine) [163]. Patients with excessive nausea or vomiting may prefer non-oral (e.g., IV, nasal spray, suppositories, subcutaneous injections) routes [164].

Abortive Treatment

Acute migraine treatment with triptans may offer benefit for patients with vestibular migraine. Sumatriptan was particularly efficacious in improving vertigo; rizatriptan helped prevent motion sickness symptoms. Zolmitriptan probably has little benefit in vestibular migraine [163].

Prophylactic Treatment

Treatment with migraine prophylactic medication may be needed when symptoms are frequent or severe and interfere with quality of life [15]. The indications for prophylactic therapy in vestibular migraine mirror those in migraine, which consider the frequency, duration, and disabling nature of attacks [120]. If caffeine and other triggers play a role in inciting episodes, they should be avoided when possible, as avoidance may enhance the efficacy of prophylactic therapy in vestibular migraine [48; 163].

Medications evaluated for prophylactic efficacy in vestibular migraine include antiepileptic drugs (e.g., topiramate, valproate/valproic acid, lamotrigine), beta-adrenergic blockers (e.g., propranolol, meto-

PROPHYLACTIC PHARMACOTHERAPY FOR VESTIBULAR MIGRAINE	
Characteristic	**Recommended Agent(s)**
By Available Evidence	
High-quality evidence of efficacy	Topiramate 25–100 mg/day Valproate 300–900 mg/day Metoprolol sustained-release 50–200 mg/day
Moderate-quality evidence of efficacy	Propranolol 40–240 mg/day Flunarizine 5–10 mg/day
Low-to-moderate-quality evidence of efficacy	Amitriptyline 50–100 mg/day Verapamil extended-release 120–360 mg/day Cinnarizine 37.5–75 mg/day
Lowest-quality evidence of efficacy	Acetazolamide 250–750 mg/day
By Attack Frequency	
Three or more attacks per month or long-lasting/disabling attacks	First-line: Propranolol 80–240 mg/day, metoprolol 50–200 mg/day, or bisoprolol 5–10 mg/day Second-line: Flunarizine 5–10 mg/day Third-line: Topiramate 25–100 mg/day or valproic acid 500–600 mg/day
Fifteen migraine attacks or more than eight migraine headaches per month for longer than three months	First-line: Topiramate 25–100 mg/day Second-line: A trial of onabotulinum toxin type A (155 MU) is reasonable but unlikely to improve vestibular symptoms
By Clinical Profile	
Prominent nausea and/or headaches and less prominent or minimal anxiety	Verapamil 120–240 mg/day (well-tolerated medication with good efficacy) Alternative: Topiramate 50–200 mg/day (often effective)
Prominent vertigo or dizziness, less frequent migraine headache	Lamotrigine 25–100 mg/day to reduce the frequency of vertigo episodes; less effective in reducing headache frequency
Severe vestibular migraine	Combination of two or three migraine prophylactic medications from different drug classes Consider zonisamide or acetazolamide
Source: [15; 120; 164; 165; 166; 167]	*Table 3*

prolol sustained-release, bisoprolol), calcium channel blockers (e.g., flunarizine, verapamil extended-release, cinnarizine), and antidepressants (e.g., venlafaxine, nortriptyline, imipramine, amitriptyline). Prophylactic recommendations have been based on available evidence, attack frequency, and clinical profile (***Table 3***).

Vestibular Migraine and Anxiety

Patients with vestibular migraine are more anxious than patients with non-vestibular migraine [168]. Anxiety is so prevalent in vestibular migraine, migraine, and vestibular disorders that a new disorder—migraine-anxiety-related dizziness—was proposed to define the association [48].

The recommended pharmacotherapy for vestibular patients with prominent anxiety, panic attacks, or depression and less prominent nausea is [15]:

- Venlafaxine 75 mg/day, OR
- A tricyclic antidepressant (e.g., nortriptyline, imipramine, amitriptyline) 50–75 mg/day

The established efficacy of venlafaxine in anxiety disorder treatment suggests a potential advantage over other vestibular migraine prophylaxis. One study evaluated patients with vestibular migraine randomized to venlafaxine (37.5 mg/day), flunarizine (10 mg/day), or valproic acid (1,000 mg/day) for three months [169]. Significant decreases in precipitating physical factors and functional consequences of

vestibular migraine were noted with all three medications. Improvements in emotional consequences of vestibular migraine (with venlafaxine only), vertigo attack severity (with venlafaxine and flunarizine but not valproic acid), and vertigo attack frequency (with venlafaxine and valproic acid but not flunarizine) were also noted. This suggests venlafaxine more effectively reduced emotional distress and anticipatory anxiety related to vestibular migraine attacks, as well as attack frequency and severity [169].

Other Treatment Options

Betahistine plus flunarizine leads to greater improvements in vertigo frequency and severity than betahistine alone. Decreases in headache frequency and severity are comparable [170].

Vestibular rehabilitation is effective, with improved symptoms and disability in patients with vestibular migraine as add-on treatment to medical therapy or as stand-alone treatment [48; 163].

Vestibular Paroxysmia

With vestibular paroxysmia, the characteristic brevity (seconds up to a few minutes, very seldom many hours) and frequency of recurring vertigo attacks makes the differential diagnosis generally straightforward [45]. The frequent vertigo attacks respond to carbamazepine (200–800 mg/day) or oxcarbazepine (300–900 mg/day), even in the lower dose range. Both drugs are recommended to start with a low dose, slowly progressing to higher doses as necessary [120].

Second-Line Therapies for Carbamazepine/ Oxcarbazepine Intolerance

Alternative drug options include phenytoin, gabapentin, valproate, lamotrigine, topiramate, and baclofen or other non-antiepileptic drugs used in trigeminal neuralgia [45]. Treatment should start with low doses. Options include [120]:

- Phenytoin 100 mg once daily, increased up to three times per day
- Gabapentin 300 mg once daily, increased to three times daily over four to seven days and further increased with insufficient symptom relief (up to a maximum 1,800 mg)
- Valproate dosing proportional to body weight (start with 10 mg per kg body weight, increasing the dose every three days up to 20 mg/kg)

Antiepileptic medications can themselves elicit dizziness and should be prescribed cautiously, ideally by specialists who can differentiate possible side effects from dizziness or vertigo sensations per se [120].

Refractory Vestibular Paroxysmia

Surgical microvascular decompression of the 8th cranial nerve is used for medically intractable cases or in rare cases with non-vascular compression of the 8th nerve by a tumor or cyst [45].

CHRONIC VESTIBULAR SYNDROMES

Context-Specific (Triggered) CVS

Most t-CVS syndromes have been defined too recently for consistently effective therapies to surface. There is some evidence for the treatment of bilateral vestibulopathy, PPPD, depersonalization and derealization disorder, and mal de débarquement syndrome.

Bilateral Vestibulopathy

The primary cause of bilateral vestibulopathy is aminoglycoside ototoxicity, typically gentamicin or streptomycin. In these cases, the ototoxic medication should be stopped or switched to a non-ototoxic drug. Other underlying causes of bilateral vestibulopathy include autoimmune processes, local or systemic infectious/inflammatory processes, bacterial or viral meningitis, bilateral Ménière disease, head trauma, neoplasms, or malformations. The cause should be identified and resolved or symptomatically managed [120].

Vestibular rehabilitation improves dynamic visual acuity, diminishes oscillopsia, and lessens asymmetry of vestibulo-ocular function by promoting adaptation and substitution using vision and proprioceptive cues to stabilize gait and mobility [171]. Vestibular rehabilitation is strongly recommended for patients with bilateral vestibulopathy [15; 120].

Persistent Postural Perceptual Dizziness

Cognitive-behavioral therapy, possibly combined with an SNRI such as venlafaxine or duloxetine, is strongly recommended for patients with PPPD. Patients should be encouraged to not stop taking the antidepressant too early; four to five weeks is required to assess effectiveness [15; 120]. Vestibular rehabilitation can help address phobic avoidance behavior.

Depersonalization and Derealization Disorder

Patients with depersonalization and derealization disorder have benefited from SSRIs, benzodiazepines, lamotrigine, opioid antagonists, and CNS stimulants, probably from targeting other mental disorders commonly associated with or precipitated by the disorder [81].

Mal de Débarquement Syndrome

There is no established treatment for mal de débarquement syndrome, but an uncontrolled trial suggests that inducement of re-adaptation of the vestibulo-ocular reflex may result in improvement. In this approach, patients are exposed periodically to a rocking that mimics the pace and direction of their perceived sway while in a full-field optokinetic stimulus [15; 172]. Other treatments under investigation include visual habituation, transcranial magnetic stimulation, and readaptation of the vestibulo-ocular reflex [173; 174].

Spontaneous CVS

Central Vestibular and Cerebellar Syndromes

The American Academy of Neurology has made the following treatment recommendations for cerebellar syndromes associated with nystagmus, vertigo, and ataxia [175]:

- Episodic ataxia type 2: 4-AP 15 mg/day
- Spinocerebellar ataxia or ataxia of mixed etiology: Riluzole
- Spinocerebellar ataxia type 3: Valproic acid 1,200 mg/day
- Spinocerebellar degeneration: Thyrotropin-releasing hormone over 14 days
- Degenerative ataxias: Inpatient rehabilitation (four weeks) to improve ataxia and function, transcranial magnetic stimulation to improve cerebellar motor signs

In episodic ataxia type 2, other treatment recommendations include [15; 120]:

- Acetazolamide 375–1,500 mg/day
- Dalfampridine sustained-release 10 mg PO once or twice per day

Cervicogenic Vertigo

With cervical vertigo, treatment options include manual therapy, muscle relaxant or anti-inflammatory medication, and tailored vestibular rehabilitation. With significant nerve compression that cannot be treated conservatively, interventional approaches remain a therapeutic option [120].

Post-Traumatic Vertigo

In patients with post-traumatic vertigo, the primary diagnosis should be treated. With BPPV present, CRP plus vestibular rehabilitation is the recommended approach. For patients with brainstem or labyrinthine concussion, use vestibular rehabilitation. Vestibular suppressants may be added in cases of labyrinthine concussion [21].

DIZZINESS AND FALLS PREVENTION IN OLDER PATIENTS

Dizziness and imbalance in older adults deserve specific attention. Among older adults (i.e., age older than 65 years), falls are the leading cause of disability, institutionalization, and premature mortality from injury and the fifth leading cause of death. Fear of falling, also called post-fall anxiety syndrome, is a well-recognized syndrome in older adults [176; 177; 178]. In 2015, the estimated cost of fall-related injuries in older adults in the United States was $50 billion [179].

As such, vestibular dysfunction is critical to identify in older adults. Dizziness is highly prevalent (up to 38%) in older patients, and symptomatic dizziness or vertigo substantially increases the risk for falls [180; 181].

During 2001–2004, an estimated 35.4% of adult Americans had vestibular dysfunction requiring medical attention. The prevalence of balance impairment and vestibular dysfunction increases with age—the rate is 75% among persons older than 70 years and 85% among persons 80 years of age or older. Persons with vestibular disorders have an eight-fold increase in risk of falling and resultant morbidity/mortality. Uncompensated vestibular hypofunction results in postural instability, visual blurring with head movement, and subjective complaints of dizziness and/or imbalance [43].

RISK FACTORS FOR FALLS IN THE ELDERLY

Falls typically result when age-related and environmental (e.g., unfamiliar surroundings, unsafe walking surface) risk factors intersect. Gait and balance impairment are the most consistent risk factors, followed by medications (e.g., benzodiazepines, antidepressants) and polypharmacy [182]. Older patients may have multiple risk factors, including vestibular dysfunction, cerebrovascular disease, cervical spine disorders, physical deconditioning, and postural hypotension. Visual impairment is common and promotes multisensory deficit [181; 183].

Postural control and balance rely on sensory input from proprioceptive and vestibular systems. Age-related changes in these systems impair postural control and increase the risk of falls; they include loss of proprioceptive sensitivity in the lower extremities and loss of labyrinthine hair cells, vestibular ganglion cells, and nerve fibers in the vestibular system [182]. Compounding the loss of proprioceptive and vestibular function are age-related changes in the CNS, including neuronal loss and neurotransmitter depletion, causing further impairments in postural control [182].

ASSESSMENT OF FALLS RISK

A targeted history and physical exam can identify patients at risk for falling. All older patients, especially patients with a dizziness/vertigo diagnosis, should be asked at least once yearly about falls [182]. Questions for initial screening of falls risk include [21]:

- Have you had a fall in the past year? How many times? Were you injured?
- Do you feel unsteady when standing or walking?
- Do you worry about falling?

With positive response, the clinician can perform a more detailed assessment or refer the patient to a specialist [21]. Treatment should be directed at the most readily modifiable fall risk factor(s) [181].

Clinicians should counsel patients and their families on the risk of falls with any balance, dizziness, or vestibular disorder, especially the frail elderly, who are more susceptible to serious injury from falling. Counseling should occur during the initial diagnosis and can include assessment of home safety, activity restrictions, and the need for home supervision until symptoms resolve. Healthcare providers should also ask about dizziness while driving, which may require intervention to prevent patient and public injury or fatality [21; 181; 184].

CONSIDERATIONS FOR NON-ENGLISH-PROFICIENT PATIENTS

As a result of the evolving racial and immigration demographics in the United States, interaction with patients for whom English is not a native language is inevitable. Because patient education is such an important aspect of the care of patients with dizziness/vertigo, it is each practitioner's responsibility to ensure that information and instructions are explained in such a way that allows for patient or caregiver understanding. When there is an obvious disconnect in the communication process between the practitioner and patient due to the patient's lack of proficiency in the English language, an interpreter is required.

In this multicultural landscape, interpreters are a valuable resource to help bridge the communication and cultural gap between patients and practitioners. Interpreters are more than passive agents who translate and transmit information back and forth from party to party. When they are enlisted and treated as part of the interdisciplinary clinical team, they serve as cultural brokers, who ultimately enhance the clinical encounter. In any case in which information regarding diagnostic procedures, treatment options and medication/treatment measures are being provided, the use of an interpreter should be considered.

CONCLUSION

Knowledge advances are transforming the clinical care of patients with dizziness and vertigo. A paradigm-changing classification system and diagnostic algorithm for dizziness and vertigo affords greater diagnostic ease and accuracy for clinicians. An expanded understanding of the vestibular system highlights the relationship of anxiety to vestibular dysfunction. The differentiation of potentially dangerous cerebrovascular mimics of benign vertigo and dizziness enhances early detection and rapid intervention. The important contribution of vestibular dysfunction to risk for falls in the elderly has been clarified, as falls are a leading cause of disability and death from injury in this population. Despite the demonstrated efficacy of repositioning therapy for the management of BPPV and the ease with which this can be used in the primary care setting, patients with BPPV frequently experience delayed diagnosis, unnecessary testing, and non-recommended treatment. Thus, continuing education has an important role in helping to ensure that clinicians and their patients benefit from current concepts, tools of evaluation, and strategies for managing dizziness and vertigo.

RESOURCES

Vestibular Disorders Association (VeDA)
https://vestibular.org

Fall Prevention Center of Excellence
http://stopfalls.org

David E. Newman-Toker, MD, PhD
Johns Hopkins Medicine

HINTS Video
https://collections.lib.utah.edu/details?id=177180

Dix-Hallpike Maneuver Video
https://collections.lib.utah.edu/details?id=177177

Supine Head Roll Video
https://collections.lib.utah.edu/details?id=177185

Implicit Bias in Health Care

The role of implicit biases on healthcare outcomes has become a concern, as there is some evidence that implicit biases contribute to health disparities, professionals' attitudes toward and interactions with patients, quality of care, diagnoses, and treatment decisions. This may produce differences in help-seeking, diagnoses, and ultimately treatments and interventions. Implicit biases may also unwittingly produce professional behaviors, attitudes, and interactions that reduce patients' trust and comfort with their provider, leading to earlier termination of visits and/or reduced adherence and follow-up. Disadvantaged groups are marginalized in the healthcare system and vulnerable on multiple levels; health professionals' implicit biases can further exacerbate these existing disadvantages.

Interventions or strategies designed to reduce implicit bias may be categorized as change-based or control-based. Change-based interventions focus on reducing or changing cognitive associations underlying implicit biases. These interventions might include challenging stereotypes. Conversely, control-based interventions involve reducing the effects of the implicit bias on the individual's behaviors. These strategies include increasing awareness of biased thoughts and responses. The two types of interventions are not mutually exclusive and may be used synergistically.

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